Anti-amoebic drugs

- Amoebiasis is an infection caused by Entamoeba histoytica.
- Anti amoebic are the drugs useful in infection caused by the protozoa *Entamoeba histolytica*.
- *E. histolytica* infections occur in both the intestine and in tissue of the intestine and/or liver.
- Other organs like lung, spleen, kidney and brain are rarely involved in extraintestinal amoebiasis

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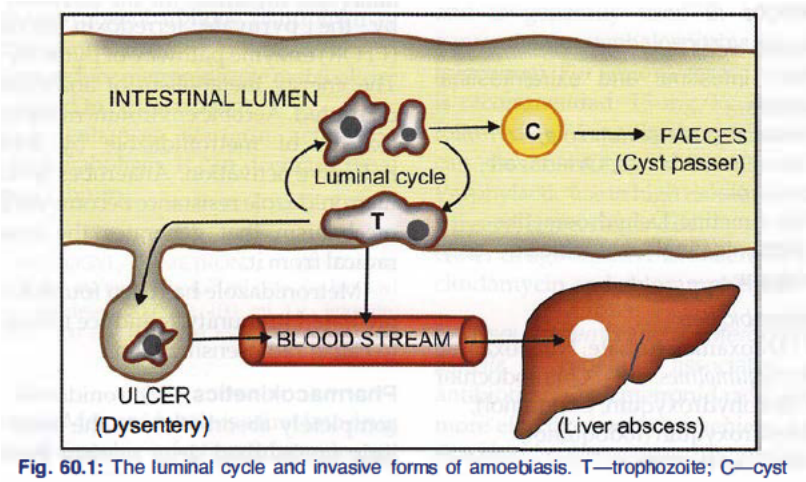

Fig. 60.1: The luminal cycle and invasive forms of amoebiasis. T—trophozoite; C—cyst

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Classification

A. tissue amoebicides

1. For both intestinal and extraintestinal amoebiasis: eg. Metronidazole, tinidazole, secnidazole, ornidazole, satranidazole, emetine

2. For extraintestinal amoebiasis: eg. Chloroquine

B. Luminal amoebicide

1. amide: diloxanide furoate
2. 8-hydroxyquinolines: Quinidochlor, diiodohydroxyquin
3. Antibiotics: tetracyclines

Metronidazole

- highly active amoebicide
- Broad spectrum cidal activity against protozoa.
- The chief drug used in this infection

MOA:

- is selectively toxic to anaerobic microorganism.
- After entering the cell by diffusion its nitro group is reduced by certain redox proteins which **exerts cytotoxicity by damaging DNA** and other critical biomolecules.

A/E: relatively frequent and unpleasant

- Anorexia, nausea, metallic taste (most common)
- Headache, dryness of mouth , dizziness (less)

C/I: first trimester of pregnancy, chronic alcoholism, blood dyscrasias.

Note: Patients should be advised to avoid alcohol for **24 hours after metronidazole**

- Produce the **disulfiram-like** reaction when ingested with alcohol.
- The disulfiram reaction is a very uncomfortable reaction characterized by **severe flushing**, and may be accompanied by **tachycardia and hypotension**.

metronidazole

Uses

1. amoebiasis: 400 mg-800 mg TDS for 5-7 days
2. giardiasis: 200 mg TDS for 7 days
3. trichmoniasis: 200-400 mg TDS
4. anaerobic bacterial infections: 400-800 mg TDS
5. H. pylori/ peptic ulcer: 400 mg TDS used along with amoxycillin/ clarithromycin and a proton pump inhibitor in triple drug for 1-2 weeks.
6. Pseudomembranous enterocolitis

Tinidazole

Similar to metronidazole; but side effects are less severe.

Dose:

Anaerobic infections: 2 g initially, followed by 1g daily in divided doses (500mg BD) daily for 5-7 days.

Amoebiasis: 2 g OD for 2-3 days

Giardiasis: 2 g single dose.

H pylori: 500 mg BD for 2 weeks in triple combination.

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Secnidazole

- Long acting and similar spectrum of activity and potency as metronidazole.
- It enters into micro-organism by diffusion and is reduced intracellularly. This forms cytotoxic products which disrupts the DNA function and structure.
- Single dose of 2 g preparation.
- Side effects and uses are similar as metronidazole.

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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 furoate exerts no antibacterial action.
- Combined use with metronidazole/ tinidazole is quite popular

A/E: flatulence, occasional nausea, itching and rarely urticaria.

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Drugs for Leishmaniasis

- Leishmaniasis is a disease caused by protozoan parasites of the genus Leishmania and spread by the bite of female sandfly phlebotomus.
- The disease can present in three main ways:
  1. cutaneous: Common form
  2. Mucocutaneous: destructive form
  3. visceral leishmaniasis (Kala-azar)- severe form

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Drug used in the treatment of leishmaniasis

Antimonial	Sodium stibogluconate (SSG)
Diamidine	Pentamidine
Antifungal drugs	Amphotericin B (AMB)
	Ketoconazole (KTZ)
Others	Miltefosine,
	Paromomycin
	Allopurinol

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Sodium stibogluconate

- Drug of choice for kala-azar
- **MOA**: unclear; probably –SH dependent enzymes are inhibited.

  act by blocking glycolytic and fatty acid oxidation pathways.
- **A/E**: Nausea, vomiting, cough pain, stiffness of injected muscle.

  Pancreatitis, liver and kidney damage, ECG changes (severe)

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Pentamidine

- are active against L. Donovani, Trypanosomes, Pneumocystis jiroveci, some bacteria and fungi (Blastomyces).

MOA: is not properly understood; probably interacts with kinetoplast DNA and inhibits topoisomerase II, or interferes with aerobic glycolysis and/ or utilization of polyamines.

A/E: toxicity is high. sharp fall in BP, dyspnoea, palpitation, fainting, vomiting, rigor and fever
Others: rashes, mental confusion, kidney and liver damage, ECG changes
Cause cytolysis of pancretic beta cells → release insulin→ hypoglycaemia.

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Paromomycin

Paromomycin is an antibiotic used to treat a number of infection including amebiasis, giardiasis, leishmaniasis, and tapeworm infection.
First line treatment for amebiasis or giardiasis during pregnancy
MOA: protein synthesis inhibitor

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Antihelmintics

- Anti helmintics are drugs which either kill (vermicide) or expel (vermifuge) infesting helminths.
- Drugs: Albendazole, Mebendazole, Pyrantel, Ivermectin, Diethyl carbamazine

Table 61.1: Choice of drugs for helminthiasis

	Worm	*First choice drugs*	*Alternative drugs*
1.	**ROUNDWORM** *Ascaris lumbricoides*	Mebendazole, Albendazole, Pyrantel	Piperazine, Levamisole Ivermectin
2.	**HOOKWORM**		
	Ancylostoma duodenale	Pyrantel, Mebendazole, Albendazole	Levamisole
	Necator americanus	Mebendazole, Albendazole	Pyrantel
3.	**THREADWORM** *Enterobius (Oxyuris) vermicularis*	Pyrantel, Mebendazole, Albendazole	Piperazine
4.	*Strongyloides stercoralis*	Ivermectin	Albendazole
5.	**WHIPWORM** *Trichuris trichiura*	Mebendazole	Albendazole
6.	*Trichinella spiralis*	Albendazole	Mebendazole
7.	**FILARIA** *Wuchereria bancrofti, Brugia malayi*	Diethyl carbamazine, Ivermectin	Albendazole
8.	**GUINEAWORM** *Dracunculus medinensis*	Metronidazole	
9.	**TAPEWORMS**		
	Taenia saginata	Praziquantel, Niclosamide	Albendazole
	Taenia solium	Praziquantel	Niclosamide, Albendazole
	Hymenolepis nana	Praziquantel	Niclosamide
	Neurocysticercosis	Albendazole	Praziquantel
10.	**HYDATID DISEASE** *Echinococcus granulosus, E. multilocularis*	Albendazole Albendazole	Mebendazole

Mebendazole

broad spectrum used in round worm, whip worm, hook worm, and thread worm infestations.

MoA:

- Its lethal action is slow, takes 2-3 days.
- It acts probably by blocking glucose uptake in the parasite and depletion of its glucose stores. This process leads to its immobilization and death.
- Hatching of nematode eggs and larvae are also inhibited.

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mebendazole

Mebendazole is used to treat:

- Common roundworms
- Hookworm infections
- Pinworms
- Whipworms
- More than one worm infection at a time.

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Albendazole:

Broad spectrum, excellent tolerability, and has the advantage of single dose administration in many cases.

One dose treatment has produced cure rates in ascariasis, hookworm and enterobiosis which are comparable to 3 day treatment of mebendazole.

MoA: similar to mebendazole.

A/E: well tolerated; dizziness, abdominal pain, diarrhea, prolonged use has caused headache, fever, alopecia, jaundice and neutropenia.

Contraindicated in pregnant women

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Pyrantel pamoate

Introduced in 1969 for threadworm infestation in children, use was soon extended to roundworm and hookworm as well.

Efficacy against *Ascaris*, *Enterobius* and *Ancylostoma* is high.

Inactive against *Trichuris* and other worms.

MoA:

- Depolarizing neuromuscular blocking agent of the worm
- Causes inactivation of nicotinic cholinergic receptors in the worms resulting in spastic paralysis. Worms are then expelled.

Adverse effect: occasional GI symptoms, headache and dizziness

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Niclosamide

Highly effective against cestodes infestations, *Taenia saginata*, *T. solium*, *Diphyllobothrium latum* and *Hymenolepsis nana*, as well as threadworm.

MOA

Inhibit oxidative phosphorylation in mitochondria and interfere with anaerobic generation of ATP by the tapeworm.

A/E

Well tolerated, minor GI symptoms. Safe in pregnancy and in patients with poor health.

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Piperazine

- Introduced in 1950, it is a highly active drug against Ascaris and Enterobius; achieves 90-100% cure rates.
- **MOA**: causes hyperpolarization of Ascaris muscle by a GABA agonistic action opening Cl- channels that causes relaxation and depresses responsiveness to contractile action of ACh. Flaccid paralysis occurs and worms are expelled out.
- **Adverse effect**: well tolerated; Nausea, vomiting, abdominal discomfort and urticaria are occasional.
- **safe in pregnant.**

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praziquantel

- Highly broad spectrum anthelmintic drug
- Schistosomiasis, cysticercosis and taenias
- **MOA**: apparently disrupts Ca2+ homeostasis in the parasite by binding to protein kinase C → prolongs muscular contraction and eventual paralysis.
- **Adverse effect:** It tastes bitter: can produce nausea and abdominal pain. Other side effects are headache, dizziness and sedation.

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Anti-Filariasis

- **Filariasis** (or **philariasis**) is a parasitic disease caused by an infection with round worms of the Filarioidea type.
- These are spread by blood feeding black flies and mosquitoes.
- Drugs for anti-filariasis are
  1. Diethyl carbamazine citrate (DEC)
  2. Ivermectin

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Diethyl carbamazine citrate (DEC)

- The first drug for filariasis.

MOA

- DEC has a highly selective effect on microfilariae.
- It causes alteration of Mf membranes, so that they are readily phagocytized by tissue fixed monocytes. Muscular activity of the Mf and adult worms is also affected causing hyperpolarization

Indications and doses

1. *Filariasis*: 2 mg/kg TDS
2. *Tropical eosinophilia*: 2-4 mg/kg TDS for 2-3 weeks

Side effects

Nausea, loss of appetite, headache, weakness, diziness

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Ivermectin

MOA

- Cause tonic paralysis
- acts through a special type of glutamate gated Cl- channel

Side effects

Pruritus, giddiness, nausea, abdominal pain, constipation, lethargy and transient ECG changes.

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