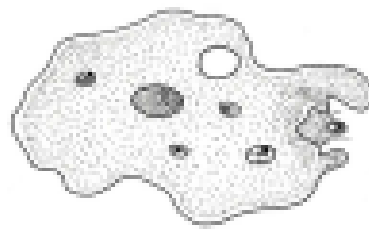
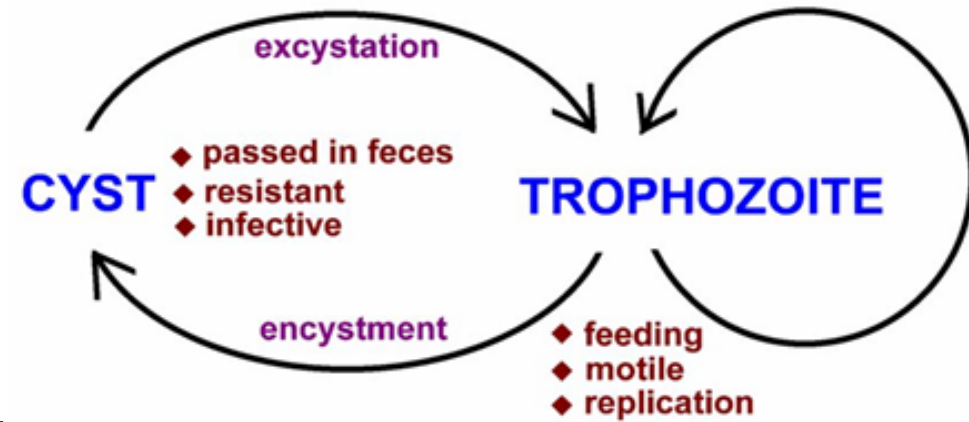


Amebiasis



Entamoeba histolytica Life Cycle



Amebiasis is infection with *Entamoeba histolytica*.

This organism can cause:

Asymptomatic intestinal infection..

Mild to moderate colitis.

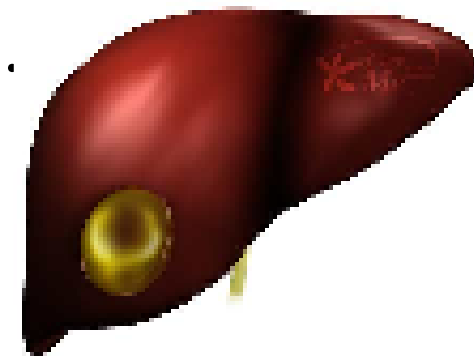
Severe intestinal infection (dysentery).

Ameboma (a tumor-like mass in the intestines in amebiasis which results in a large local lesion of the bowel).

Liver abscess and other extraintestinal infection.



Ameboma



Treatment of Specific Forms of Amebiasis

Asymptomatic Intestinal Infection

Asymptomatic carriers are treated with a **luminal amebicide**.

Standard luminal amebicides are:

Diloxanide furoate, Iodoquinol, and Paromomycin.

Therapy with a luminal amebicide is also required in the treatment of all other forms of amebiasis.

Amebic Colitis

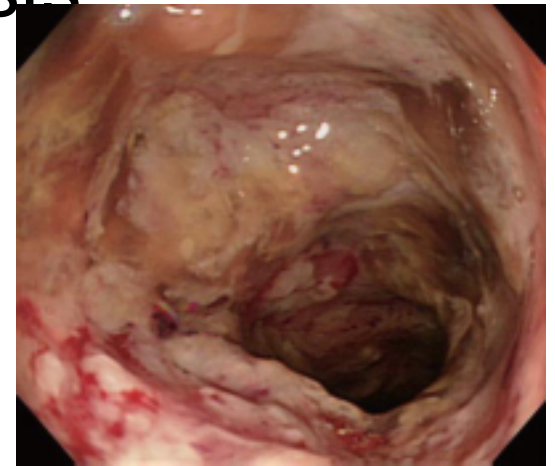
Metronidazole + a luminal amebicide

is the treatment of choice.

Tetracyclines and **erythromycin** are alternative drugs for moderate colitis but

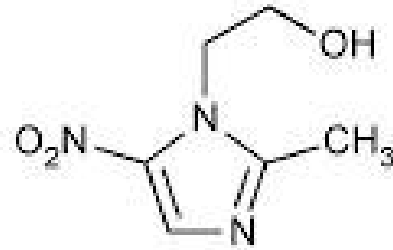
are not effective against extraintestinal disease.

Dehydroemetine or emetine can also be used, but are best avoided because of toxicity.



Amebic Colitis

Metronidazole

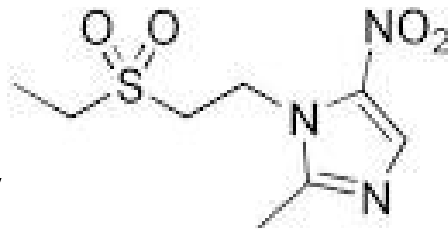


Drug of choice in the treatment of extraluminal amebiasis. It kills trophozoites but not cysts of *E histolytica* and effectively eradicates intestinal & extraintestinal tissue infections.



Trophozoite of *Entamoeba histolytica* in intestine.

Tinidazole



Similar activity

& better toxicity profile than metronidazole.



cysts of *E histolytica*

Pharmacokinetics & Mechanism of Action

Oral metronidazole and tinidazole are readily absorbed.

The half-life: Metronidazole 7.5 hours

Tinidazole 12–14 hours.

The nitro group of metronidazole is reduced in anaerobic bacteria and sensitive protozoans.

It inhibits nucleic acid synthesis by disrupting the DNA of microbial cells.

This function only occurs when **metronidazole** is partially reduced, and because this reduction usually happens only in anaerobic cells, it has relatively little effect upon human cells or aerobic bacteria.

The mechanism of tinidazole is the same.

Clinical Uses

Amebiasis

Metronidazole or tinidazole

The drug of choice in the treatment of all tissue infections with *E histolytica* . (hepatic abscess; intestinal wall/ extraintestinal infections)

- Not effective against luminal parasites and so **must be used with a luminal amebicide to ensure eradication of the infection.** kills trophozoites but not cysts

Giardiasis

Metronidazole is the treatment of choice

Efficacy after a single treatment is about 90%

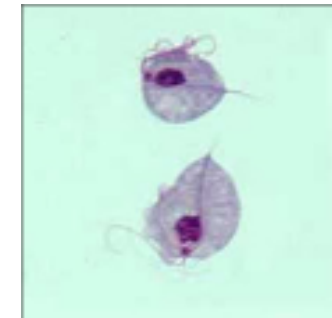
Tinidazole is equally effective.



Trichomoniasis

Metronidazole is the treatment of choice.

A single dose of 2 g is effective.



Trichomonas vaginalis

Adverse Effects & Cautions

Common:

Nausea, headache, dry mouth, metallic taste.

Infrequent adverse effects:

vomiting, diarrhea, insomnia, weakness, dizziness, thrush, rash, dysuria, dark urine, vertigo, paresthesias, and neutropenia.

Rare:

Pancreatitis and severe central nervous system toxicity (ataxia, encephalopathy, seizures)

Metronidazole has a **disulfiram -like effect**.

Tinidazole is better tolerated.

Metronidazole is best avoided in pregnant or nursing women, although congenital abnormalities have not clearly been associated with use in humans.

Iodoquinol

Luminal amebicide, but not against intestinal wall or extraintestinal **trophozoites**.

90% is excreted in the feces.

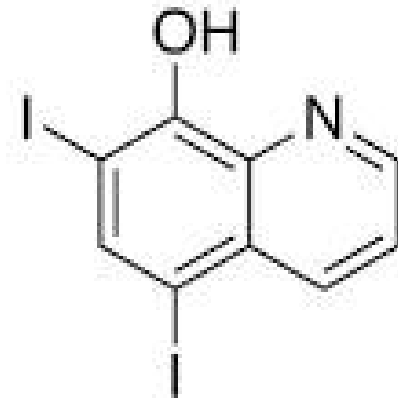
Infrequent adverse effects:

Diarrhea , anorexia, nausea, vomiting, abdominal pain, headache, rash, and pruritus.

Taken with meals to limit gastrointestinal toxicity.

Used with **caution** in patients with optic neuropathy, renal or thyroid disease, or nonamebic hepatic disease.

Should be discontinued if it produces persistent diarrhea or signs of iodine toxicity (dermatitis, urticaria, pruritus, fever).

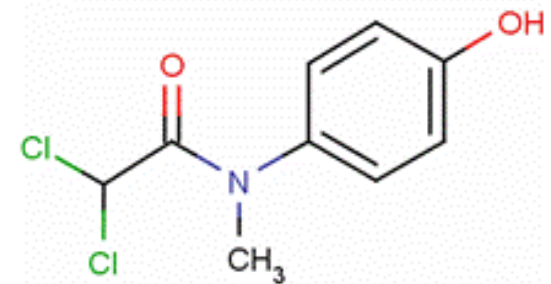
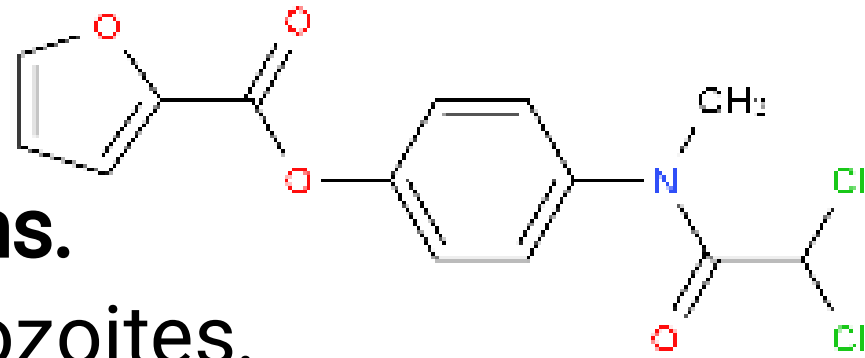


Diloxanide Furoate

Drug of choice for
asymptomatic luminal infections.

Not active against tissue trophozoites.

In the gut, it splits into **diloxanide**
and **furoic acid**; about 90% of the
diloxanide is rapidly absorbed.



The unabsorbed diloxanide is the active antiamebic

The mechanism of action is unknown.

Used with a tissue amebicide, usually **metronidazole**,
to treat serious intestinal & extraintestinal infections.

Adverse effects:

Flatulence is common, nausea & abdominal cramps
are infrequent & rashes are rare.

Paromomycin Sulfate

Aminoglycoside antibiotic that is not absorbed from the gastrointestinal tract.

It is used only as a **luminal amebicide** and has no effect against extraintestinal amebic infections.

Adverse effects

Occasional abdominal distress & diarrhea.

Parenteral paromomycin is now used to treat **visceral leishmaniasis**.



a sand fly



Post-kala-azar dermal leishmaniasis ,
a complication of visceral leishmaniasis.

Emetine & Dehydroemetine

Emetine, an alkaloid derived from ipecac.

Dehydroemetine, a synthetic analog.

Effective against **tissue trophozoites** of *E histolytica*,

Their use is limited to **severe amebiasis when metronidazole cannot be used.**

Used for the minimum period needed to relieve severe symptoms (3–5 days) and should be administered S. C. (preferred) or I.M.

Adverse effects

Pain, tenderness, and sterile abscesses at the injection site; diarrhea, nausea, and vomiting; muscle weakness and discomfort.

Serious toxicities include cardiac arrhythmias, heart failure, and hypotension.



ANTHELMINTIC DRUGS

Albendazole

Broad spectrum. Drug of choice for **hydatid disease** & **cystercercosis**.

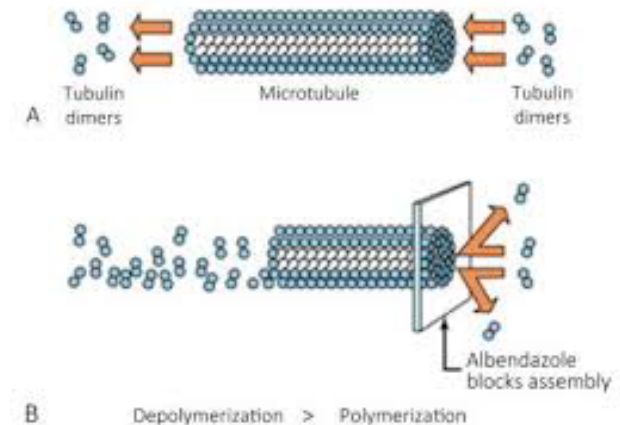
also used for (intestinal nematodes)

pinworm, hookworm

Mechanism of action:

inhibits microtubule synthesis in nematodes that irreversibly impairs glucose uptake, intestinal parasites are immobilized and die slowly.

orally , absorbed erratically, increased with fatty meal
metabolized in the liver to active metabolite
albendazole sulphoxide , half life of 8-12 hours



used on empty stomach for intraluminal parasites but with fatty meal when against tissue parasites.

2. Hydated diseases: drug of choice ,400 mg twice with meals for 1 month

3. Neurocysticercosis: used along with corticosteroid to decrease the inflammation caused by dying organism

Adverse effects:

short term: use no significant adverse effects.

long term use : abdominal distress, headache ,fever , fatigue, alopecia , increased liver enzymes , pancytopenia. (low level of all blood cells produced by the bone marrow).

Not given during pregnancy & in hypersensitive people.

Mebendazole

Has wider spectrum and is more safe than albendazole

Mechanism of action:

inhibits microtubule synthesis, irreversibly impairs glucose uptake. Intestinal parasites are immobilized & die slowly.

kills hook worm, pin worm , ascariasis and trichuriasis.

Less than 10% of drug is absorbed

Absorption increases with fatty meal. converted to inactive metabolites rapidly in liver. half life of 2-6 hours

Given orally before or after meals, tablets should be chewed before swallowing.

Adverse effects and precautions:

short term therapy. Mild GI disturbance.

high dose Hypersensitivity reactions, agranulocytosis (rare) , alopecia ,elevation of liver enzymes .

13 caution under 2ys of age may cause convulsion.

Pyrantel Pamoate

Broad-spectrum antihelminthic, highly effective for **pinworm, ascariis & *Trichostrongylus orientalis*** infections and moderately effective against **hookworm**.

A neuromuscular blocker, causes paralysis of worms, which is followed by expulsion.

Effective in intestinal tract, not **in the tissues or the ova**

Given orally once with or without food.

For **pinworm**, the dose is repeated in 2 weeks.

For **ascariasis**, a single dose be repeated if eggs are found 2 weeks after treatment.

For **hookworm**, a single dose is effective against light infections. In heavy infections, a 3-day course.

A course of treatment can be repeated in 2 weeks.

Piperazine

Only recommended for the treatment of ascariasis.

Causes paralysis of ascaris by blocking ACh at the myoneural junction.

live worms are expelled by normal peristalsis.

readily absorbed orally and excreted unchanged in urine.

Given orally once daily for 2 days.

For heavy infections treatment is repeated after 1 wk.

Adverse effects: generally mild (5–30%)

nausea, vomiting, diarrhea, abdominal pain, dizziness, & headache.

Neurotoxicity & allergic reactions are rare.

Niclosamide

Used for the treatment of most tapeworm infections.

Niclosamide is a **salicylamide derivative**.

Minimally absorbed from the GIT.

Adult worms (but not ova) are rapidly killed, due to inhibition of oxidative phosphorylation or stimulation of ATPase activity.

Clinical Uses

2 g once, given in the morning on an empty stomach.

The tablets must be chewed thoroughly and then swallowed with water. Purgative needed.

Adverse effects:

Mild ,infrequent and transitory GI disturbance

Diethylcarbamazine Citrate

Drug of choice for filariasis, Loa loa & tropical eosinophilia.

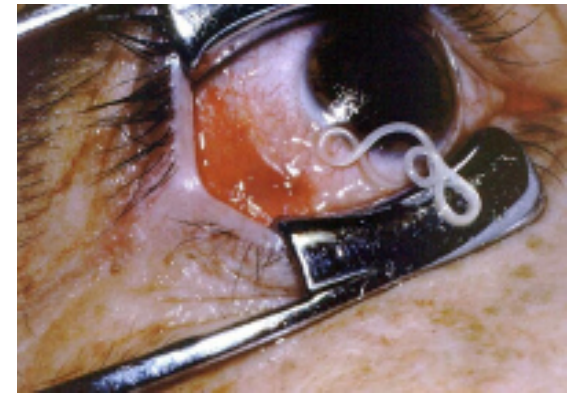
Rapidly absorbed from gut, half life of 2-3 hours , excreted in urine unchanged.

Mechanism of action:

immobilizes microfilariae and alters its surface structure ,making them susceptible to destruction by host defense mechanism.

Microfilariae are rapidly killed. Adult worms are killed slowly requiring several courses of treatment.

The mode of action against adult worms is unknown.



Adverse Reactions

generally mild and transient, include headache, malaise, anorexia, weakness, nausea, vomiting, and dizziness.

Adverse effects also occur as a result of the **release of proteins from dying microfilariae or adult worms**.

Reactions include fever, malaise, papular rash, headache, gastrointestinal symptoms, cough, chest pain, and muscle or joint pain.

Leukocytosis is common (**white blood cell count above the normal range in the blood**).

Eosinophilia (**abnormally high amounts of eosinophils**).

Proteinuria may also occur.

Caution when using diethylcarbamazine in patients with hypertension or renal disease.

Doxycycline

Has macrofilaricidal activity against *Wuchereria bancrofti* (lymphatic filariasis), and better activity than any other available drug against **adult worms**.

Active also against **onchocerciasis** (river blindness)



Doxycycline acts indirectly, by killing *Wolbachia*, an **intracellular bacterial symbiont of filarial parasites**.

It may be used for **filariasis**, both for treatment of active disease and in mass chemotherapy campaigns.

Ivermectin

Drug of choice for the treatment of **onchocerciasis** (river blindness) and for **strongyloidiasis**.

Strongyloidiasis:

A GABA agonists. Paralyzes nematodes, causing a flaccid paralysis in the worm. Does not cross the blood brain barrier in humans (therefore little CNS effects). .

Onchocerciasis:

Microfilaricidal. It does not kill adult worms but blocks the release of microfilariae.

After a single dose, microfilariae in the skin diminish rapidly within 2–3 days .

Microfilariae in the anterior chamber of the eye decrease slowly over months. Repeated doses have a low microfilaricidal action and permanently reduce microfilaria production.

Adverse Reactions:

In strongyloidiasis:

fatigue, dizziness, nausea, vomiting, abdominal pain, and rashes.

In onchocerciasis

Occurs in 5–30% ,generally mild due to the killing of microfilariae.

A more intense reaction in **1–3%**

A severe reaction in **0.1%**, including high fever, hypotension, and bronchospasm.

Swellings and abscesses occasionally occur at 1–3 weeks at sites of adult worms.

Corneal opacities & eye lesions may develop several days after treatment.

Bithionol

The drug of choice in the treatment of sheep liver fluke (*Fasciola hepatica*) and the second drug of choice in lung fluke (*Paragonimus westermani*).

Mechanism of action:

Unknown, bithionol may work by uncoupling oxidative phosphorylation, thus reducing the production of ATP in the helminthes.

Adverse Reactions:

generally mild (40% of patients) and include:

diarrhea, abdominal cramps, anorexia, nausea, vomiting, dizziness, and headache.

Skin rashes may occur, a reaction to antigens released from dying worms.

Praziquantel

Effective in **schistosoma infections** of all species & most other trematode & cestode infections, including cysticercosis.

safe and effective as a single oral dose.

Useful in mass treatment of several infections.

Plasma concentrations of praziquantel increase when the drug is taken with a **high-carbohydrate meal**.

It increases the permeability of cell membranes to calcium, resulting in paralysis, dislodgement, and death.

Mild and transient adverse effects, except for **Neurocysticercosis** due to inflammatory reactions around dying parasites.



Brain parenchymal cysticercosis.

Metrifonate

Safe, low-cost alternative drug for *Schistosoma haematobium* infections.

Not active against *S mansoni* or *S japonicum* .

Organophosphate cholinesterase inhibitor temporarily paralyzes the adult worms, resulting in their shift from the bladder venous plexus to small arterioles of the lungs, where they are trapped, encased by the immune system, and die.

Given three times orally at 14-day intervals.

A prophylactic agent when given monthly to children

Used in mass treatment programs.

Oxamniquine

Alternative to praziquantel for the treatment of *S mansoni* infections.

Used extensively for mass treatment.

Not effective against *S haematobium* or *S japonicum*.

Active against both mature and immature stages.

The mechanism of action is unknown.

Contraction and paralysis of the worms results in detachment from terminal venules in the mesentery and transit to the liver, where many die.

Surviving females return to the mesenteric vessels but cease to lay eggs.

In mixed schistosome infections, it has been used in combination with metrifonate.

