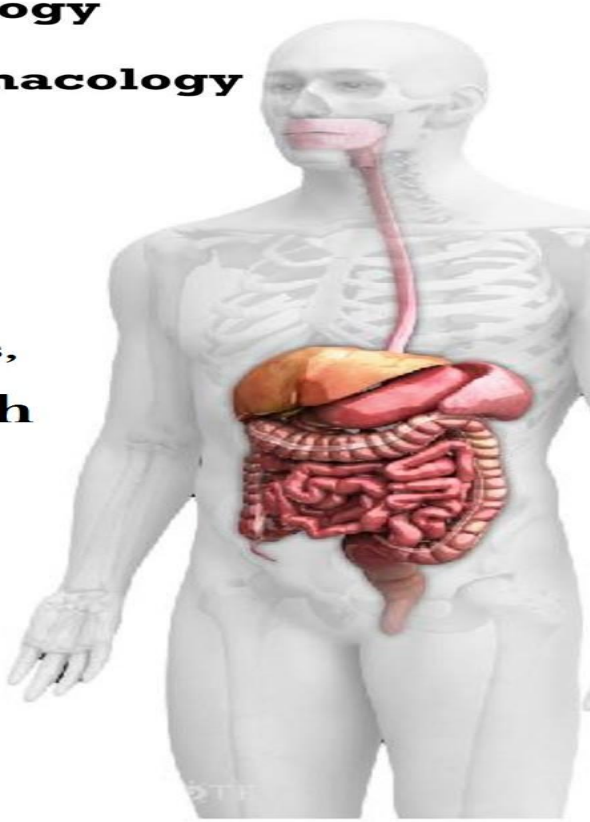
Digestive System

University of Jordan
Faculty of Medicine
Batch of 2013-2019

Medical Committee
The University of Jordan

◉ Slide ○ Sheet ○ Handout ○ Other

☐ Anatomy ☐ Embryology
☐ Physiology ☐ Histology
☐ Pathology ☒ Pharmacology
☐ Microbiology ☐ PBL



Slide # : 2

Antiamebic and Anthelmintic agents,

Doctor's name: Dr. Hamzeh

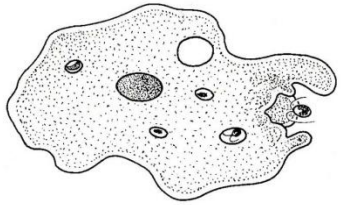
Done By:

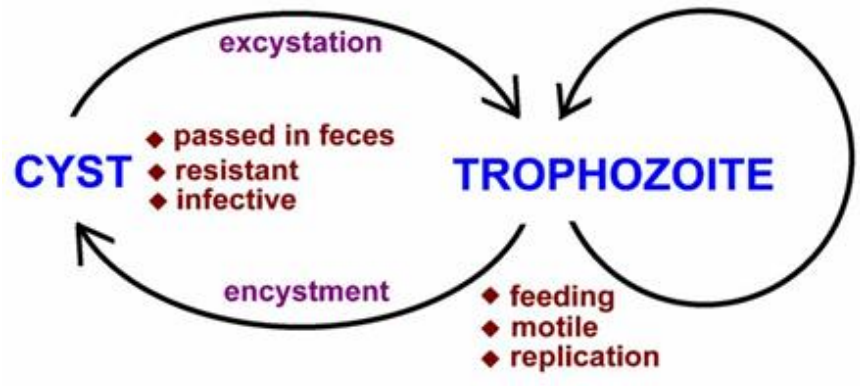
Date:

Price:

DESIGNED BY: TAMER ALTAMIMI "SMILE"

Amebiasis





Amebiasis is infection with ***Entamoeba histolytica***.

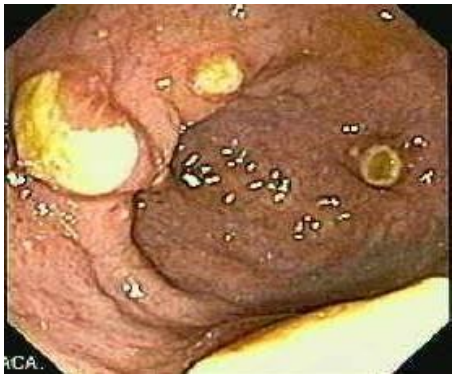
This organism can cause:

Asymptomatic intestinal infection.

Mild to moderate colitis.

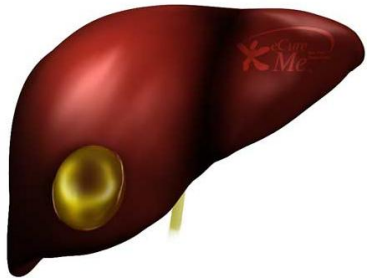
Severe intestinal infection (dysentery).

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



Ameboma

Liver abscess and other extraintestinal infection.



Treatment of Specific Forms of Amebiasis

Asymptomatic Intestinal Infection

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

Standard luminal amebicides are:

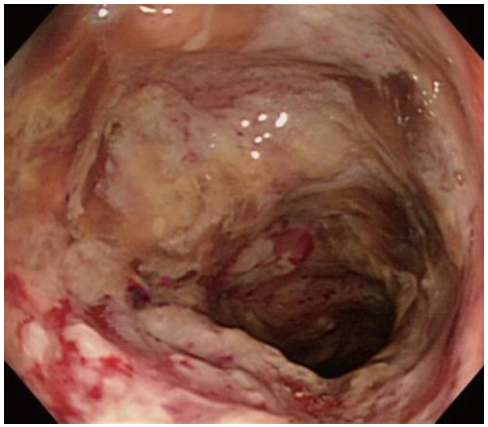
Diloxanide furoate, Iodoquinol, and Paromomycin.

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.

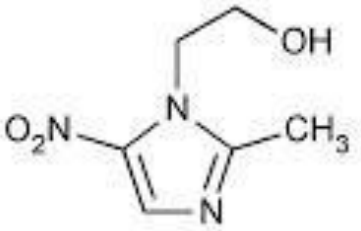
Tetracyclines and **erythromycin** are alternative drugs for moderate colitis but are not effective against extraintestinal disease.



Amebic Colitis

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

Metronidazole

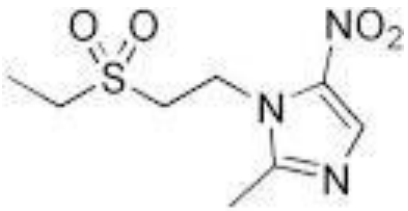


Drug of choice in the treatment of extraluminal amebiasis.

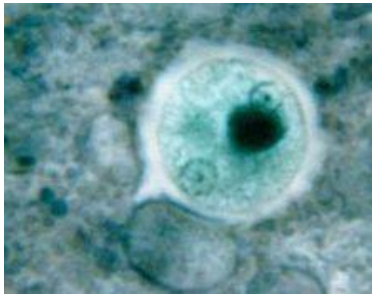
It kills trophozoites but not cysts of *E histolytica* and effectively eradicates intestinal & extraintestinal tissue infections.

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.

Reactive reduction products are responsible for antimicrobial activity.

The mechanism of tinidazole is the same

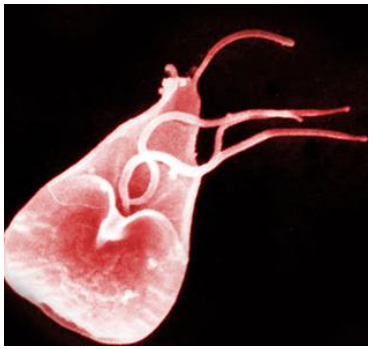
Clinical Uses

Amebiasis

Metronidazole or tinidazole

The drug of choice in the treatment of all tissue infections with *E histolytica*.

Not effective against luminal parasites and so **must be used with a luminal amebicide to ensure eradication of the infection**.



Giardia lamblia

Giardiasis

Metronidazole is the treatment of choice

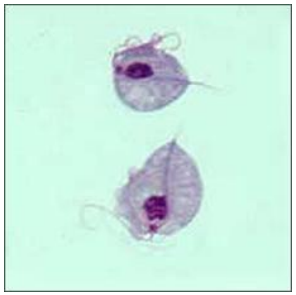
Efficacy after a single treatment is about 90%

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:

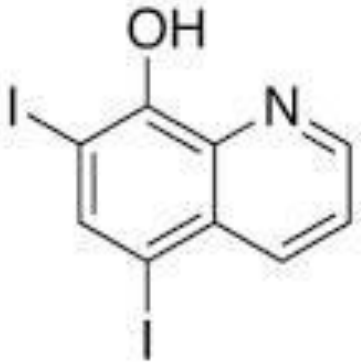
Pancreatitis and severe central nervous system toxicity (ataxia, encephalopathy, seizures)

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:

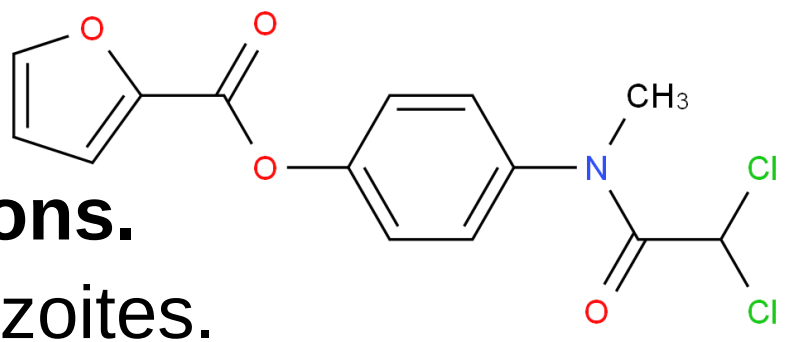
Diarrhea , anorexia, nausea, vomiting, abdominal pain, headache, rash, and pruritus.

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

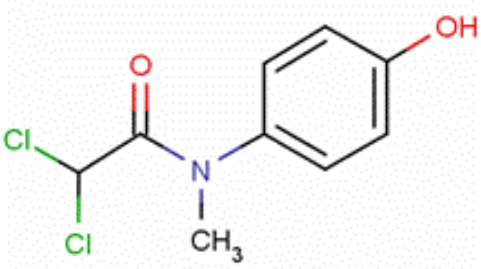


Drug of choice for

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.

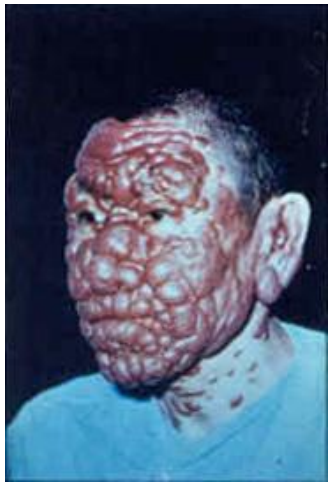
It is used only as a luminal amebicide and has no effect against extraintestinal amebic infections.

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.**

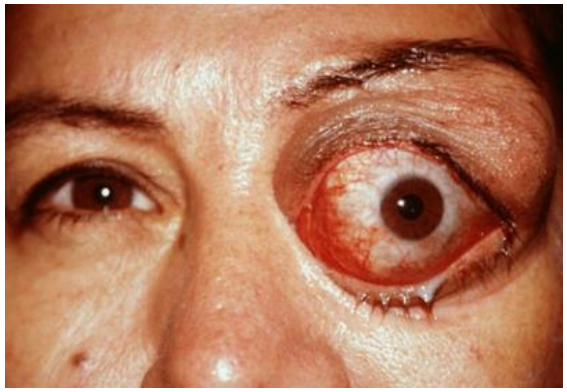
Used for the minimum period needed to relieve severe symptoms (3–5 days) and should be administered S.C. (preferred) or I.M.

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 Agents.



Albendazole

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

also used for (intestinal nematodes) **pinworm, hookworm**

Mechanism of action:

inhibits microtubule synthesis 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.

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 (reduction in the number of erythrocytes, white blood cells, and blood platelets in the blood).

Mebedazole

Wider spectrum and is more safe than albendazole indicated for the treatment of nematode infestations, whipworm,threadworm,pinworm. roundworm, hookworm,

Mechanism of action: inhibits microtubule synthesis

Pharmacokinetics:

less than 10% of orally administered drug is absorbed Absorption increases with fatty meal.

converted to inactive metabolites rapidly in liver.

half life of 2-6 h

Taken orally before or after meal, tablets should be chewed before swallowing.

Adverse effects :

Relatively free of toxic effects, although patients may complain of abdominal pain and diarrhea.

Pyrantel Pamoate

Broad-spectrum antihelminthic.

highly effective for **pinworm, ascaris** & ***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**

Poorly absorbed, given orally once with or without food.

Adverse Effects

transient GI disturbance, drowsiness , headache ,insomnia, rash ,fever

Piperazine

Only recommended for the treatment of ascariasis.

Mechanism of action:

causes paralysis of ascaris by blocking A.ch at myoneural junction, expelling the live worm by normal peristalsis.

pharmacokinetics :

readily absorbed orally and excreted unchanged in urine.

Adverse effects: generally mild (5–30%)

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

Neurotoxicity & allergic reactions are rare.

Niclosamide

Used for 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.

not effective against cysticercosis or hydatic disease.

Clinical Uses

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

The tablets must be chewed thoroughly and then swallowed with water. A laxative is given prior to oral administration of niclosamide to purge the bowel of all dead segments and so preclude digestion and liberation of the ova, which may lead to cysticercosis.

Diethylcarbamazine

Effective in the treatment of **Wuchereria bancrofti,**

Loa loa & **Brugia malayi** infections.

used in the treatment of **filariasis** because it

immobilizes microfilariae and render them susceptible to host defense mechanisms.

Rapidly absorbed following oral administration with meals and is excreted primarily in urine.

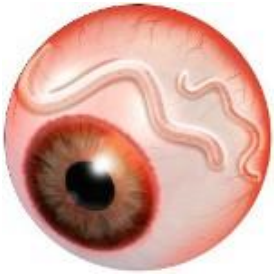
Adverse effects

Primarily caused by host reactions to the killed organisms.

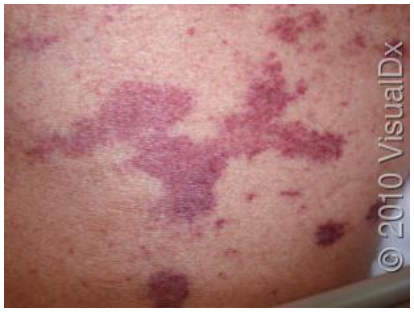
fever, malaise, rash, myalgias, arthralgias, and headache, and their severity is related to parasite load.

Most patients have leukocytosis. WBC count above the normal range. Steroids may be given to ameliorate the symptoms.

Ivermectin



Drug of choice for the treatment of **onchocerciasis** (river blindness) and for cutaneous larva migrants and **strongyloidiasis** (threadworm).



Mechanism

intensifies GABA –mediated transmission of signals in peripheral nerves causing paralysis of the worm.
Given orally. It does not cross the blood-brain barrier.

The killing of the microfilaria can result in a **Mazotti-like reaction** (fever, headache, dizziness, somnolence and hypotension).

Praziquantel

Effective in **schistosome infections** of all species & most other trematode & cestode infections (Tapeworm) including **cysticercosis**.

safe and effective as a single oral dose,

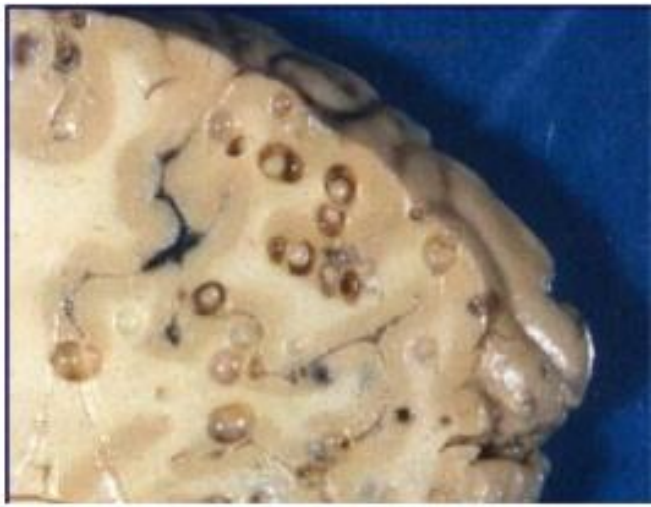
Useful in mass treatment of several infections.

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.

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



Brain parenchymal cysticercosis.

Bithionol

Used for the treatment of **fascioliasis** (sheep liver fluke)

& **pulmonary paragonimiasis** (Lung Fluke).

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.