



Chapter 52

Introduction to Antiparasitic Drugs

Targets of antiparasitic chemotherapy

- Unique essential enzymes found only in the parasite;
- Similar enzymes found in both host and parasite but indispensable only for the parasite;
- Common biochemical functions found in both parasite and host but with different pharmacologic properties.

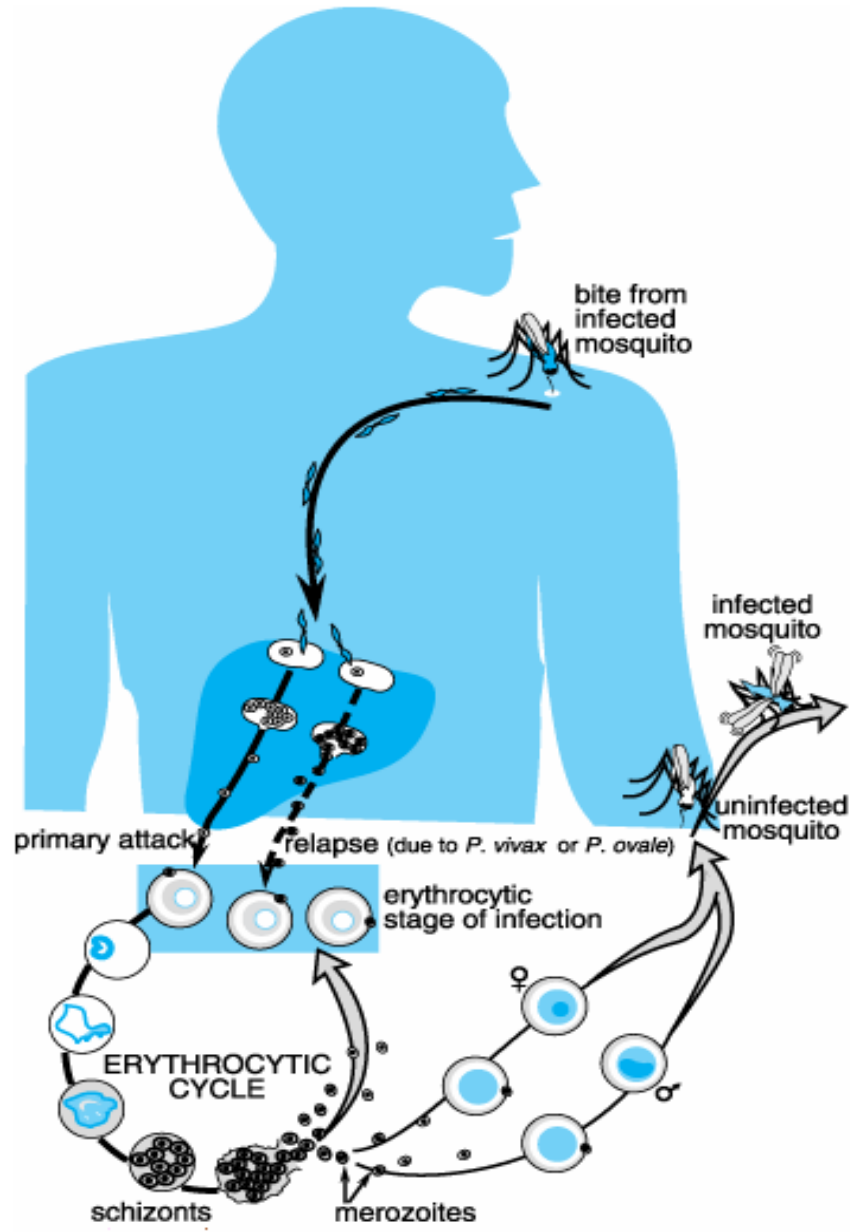
Classification of antiparasitic drugs

- Antiprotozoal Drugs-used against invasion of single celled parasites
 - used for treatment of malaria, amebiasis, giardiasis, toxoplasmosis and trichomoniasis
- Anthelmintic Drugs-used against invasion of parasitic worms (Helminthiasis)
 - Roundworms, pinworms, whipworms, hookworms and tapeworms

Malaria

- Four species of plasmodium cause human malaria:
 - *Plasmodium falciparum* → responsible for nearly all serious complications and deaths.
 - *P vivax*
 - *P malariae*
 - *P ovale*
- Transmitted by the Anopholes mosquito
- Antimalarials act at different stages in life cycle

Parasite life cycle



Drug classification

Tissue schizonticides: eliminate developing or dormant **liver** forms;

Blood schizonticides : act on **erythrocytic** parasites;

Gametocides : kill **sexual stages** and prevent transmission to mosquitoes.

Radical cure: eliminate both hepatic and erythrocytic stages. Not available.

Antimalarial drug---Chloroquine

Antimalarial Action

- ❖ Highly effective **blood** schizonticide.
- ❖ Moderately effective against **gametocytes** of *P vivax*, *P ovale*, and *P malariae* but not against those of *P falciparum*.
- ❖ Not active against liver stage parasites.

Mechanism of Action

Remains controversial, probably acts by concentrating in parasite **food vacuoles**, preventing the biocrystallization of the hemoglobin breakdown product, **heme**, into **hemozoin**, and thus eliciting parasite toxicity due to the buildup of free heme.

Clinical Uses

- Drug of choice in the treatment of nonfalciparum and sensitive falciparum malaria.
- It is still used to treat falciparum : safety, low cost, antipyretic properties, and partial activity.
- Does not eliminate dormant liver forms of *P vivax* and *P ovale*, and for that reason **Primaquine** must be added for the radical cure of these species.

Adverse Effects

Usually very well tolerated

Pruritus, GI disturbance, headache, malaise, blurring of vision, and urticaria

Rare : hemolysis in G6PD-deficient persons, impaired hearing, agranulocytosis, alopecia, bleaching of hair, hypotension,

Large IM injections or rapid IV infusions : severe hypotension and respiratory and cardiac arrest.

Other antimalarial drugs

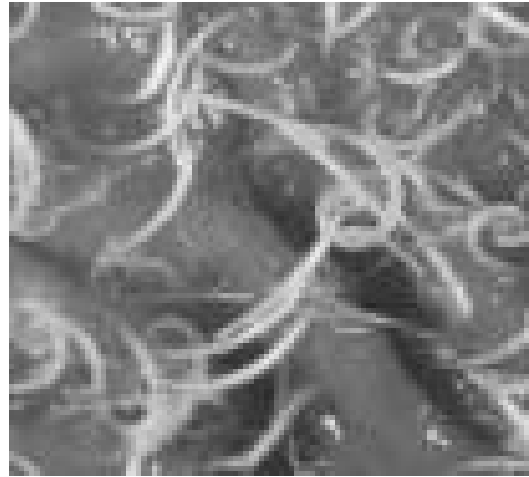
- Quinine & Quinidine- first-line therapies for falciparum malaria.
- Mefloquine- used in chloroquine-resistant strains of *P falciparum* and other species.
- Primaquine—used for the eradication of dormant liver forms of *P vivax* and *P ovale*
- Pyrimethamine--folic acid antagonist also used in prevention
- Atovaquone
- Antibiotics
- Halofantrine & Lumefantrine
- Artemisinin & its derivatives

Anthelmintic Drugs

- Used to treat parasitic worm infections: helminthic infections
- Unlike protozoa, helminths are large and have complex cellular structures
- Drug treatment is very specific to the organism



Pinworms



whipworms



threadworms



Ascaris

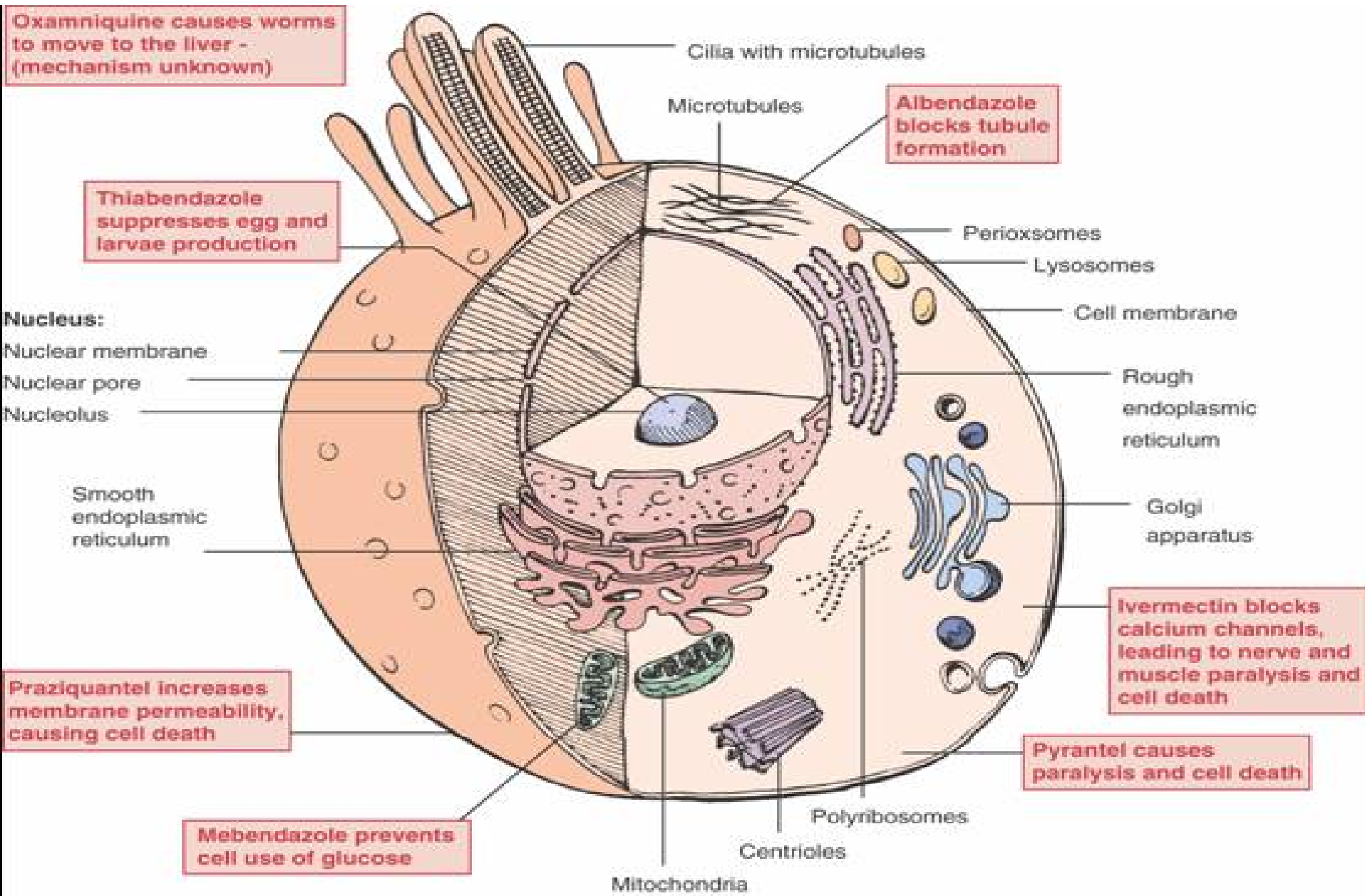


hookworms



tapeworms

Sites of Action of Anthelmintic Drugs



Action of Anthelmintic Drugs

- Affect metabolic processes that are either different in worms than in human hosts or are not found in humans
- Cause death of the worm by interfering with normal functioning

Albendazole (*Albenza*)

- Treats active lesions caused by pork tapeworm and cystic disease of the liver, lungs, and peritoneum caused by dog tapeworm
- Serious adverse effects
- Should be used only after causative worm is identified
- Poorly absorbed from the GI tract; reaches peak levels in about 5 hours
- Metabolized in the liver and primarily excreted in urine
- Should not be used during pregnancy or lactation

Clinical Uses

- A. ASCARIASIS, TRICHURIASIS, AND HOOKWORM, AND PINWORM INFECTIONS.
- The treatment is a single dose of 400mg orally (repeated for 2-3 days for heavy ascaris infections and in 2 weeks for pinworm infections)

Clinical Uses

- B. HYDATID Disease
- Albendazole is the treatment of choice for medical therapy and is useful adjunct to surgical removal or aspiration of cysts.

Clinical Uses

- C. NEUROCYSTICERCOSIS
- Indication for medical therapy for neurocysticercosis are controversial, as anthelmintic therapy is not clearly superior to therapy with corticosteroids alone and may exacerbate neurologic disease.

Adverse Reactions

- When used for 1-3 days, albendazole is nearly free of significant adverse effects (mild and transient epigastric distress, diarrhea, headache, nausea, dizziness, lassitude, and insomnia).
- In long-term use, it can cause abdominal distress, headache, fever, fatigue, alopecia, and pancytopenia.

Ivermectin (*Stromectol*)

- Effective against the nematode that causes onchocerciasis, or river blindness
- Used to treat threadworm disease or strongyloidiasis
- Readily absorbed from GI tract; reaches peak plasma levels in 4 hours
- Completely metabolized in the liver with a half-life of 16 hours; excreted through the feces
- Should never be taken during pregnancy; used with caution during lactation

Clinical Uses

- A. ONCHOCERCIASIS

- Treatment is with a single oral dose of ivermectin(150mcg/kg), with water on an empty stomach. Dose are repeated; regimes vary from monthly to less frequent (every 6-12 months) dosing schedules.

- B. STRONGYLOIDIASIS

- Treatment consists of two daily doses of 200mcg/kg.

Clinical Uses

- C. OTHER PARASITES
- Ivermectin reduces microfilariae in *Brugia malayi* and *M ozzardi* infections but not in *M perstans* infections. It dose not kill adult worms.
- Ivermectin is also effective in controlling scabies, lice and cutaneous larva migrans and in eliminating a large proportion of ascarid worms.

Adverse Reactions

- Mazotti reaction
due to killing of microfilariae. The reaction includes fever, headache, dizziness, somnolence, weakness, rash, increased pruritus, muscle pains. This reaction starts on the first day and peaks on the second day after treatment. The Mazotti reaction diminishes with repeated dosing.

Mebendazole (*Vermox*)

- Most commonly used of all of the anthelmintics
- Effective against pinworms, roundworms, whipworms, and hookworms
- Available in the form of a chewable tablet
- Has few adverse effects
- Is not metabolized in the body, and most is excreted unchanged in the feces
- Should not be used during pregnancy

Clinical Uses

- Pinworm infection

the dose is 100mg once, repeated at 2 weeks.

Ascariasis, trichuriasis, hookworm, and trichostrongylus infections, a dosage of 100mg twice daily for 3 days.

For intestinal capillariasis, is used at a dosage of 400mg/d in divided doses for 21 or more days.

Adverse Reactions

- Short-term mebendazole therapy is nearly free of adverse effects. Rare side effects, usually with high-dose therapy, are hypersensitivity reactions.

Praziquantel (*Biltricide*)

- Very effective in the treatment of a wide number of schistosomes or flukes
- Taken in a series of three doses at 4- to 6-hour intervals
- Has relatively few adverse effects
- Rapidly absorbed from the GI tract; reaches peak plasma levels within 1 to 3 hours
- Metabolized in the liver with a half-life of 0.8 to 1.5 hours
- Excreted primarily through the urine

Clinical Uses

- A. SCHISTOSOMIASIS

Praziquantel is the drug of choice for all forms of schistosomiasis. The dosage is 20mg/kg for two or three doses at intervals of 4-6 hours.

Clinical Uses

- B. CLONORCHIASIS, OPISTHORCHIASIS, AND PARAGONIMIASIS
- C. TAENIASIS AND DIPHYLLOBOTHRIASIS
- D. NEUROCYSTICERCOSIS
- E. HNANA
- F. HYDATID DISEASE
- G. OTHER PARASITES

Contraindications to the Use of Anthelmintic Drugs

- Presence of known allergy to any of these drugs
- Lactation
- Pregnancy (in most cases)
- Caution should be used in the presence of renal or hepatic disease or severe diarrhea and malnourishment

Other anthelmintic drugs

- Diethylcarbamazine
- Levamisole
- Niclosamide
- Piperazine
- Pyrantel pamoate
- Thiabendazole