

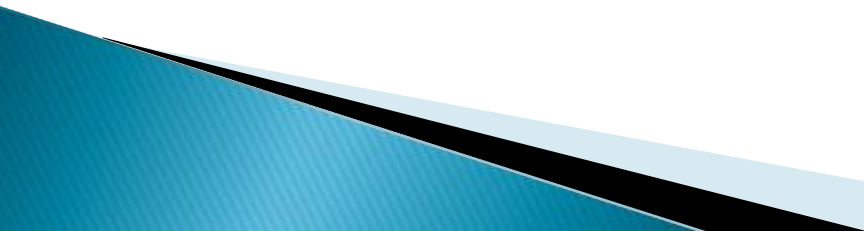
Anti-helminthic Drugs

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INTRODUCTION

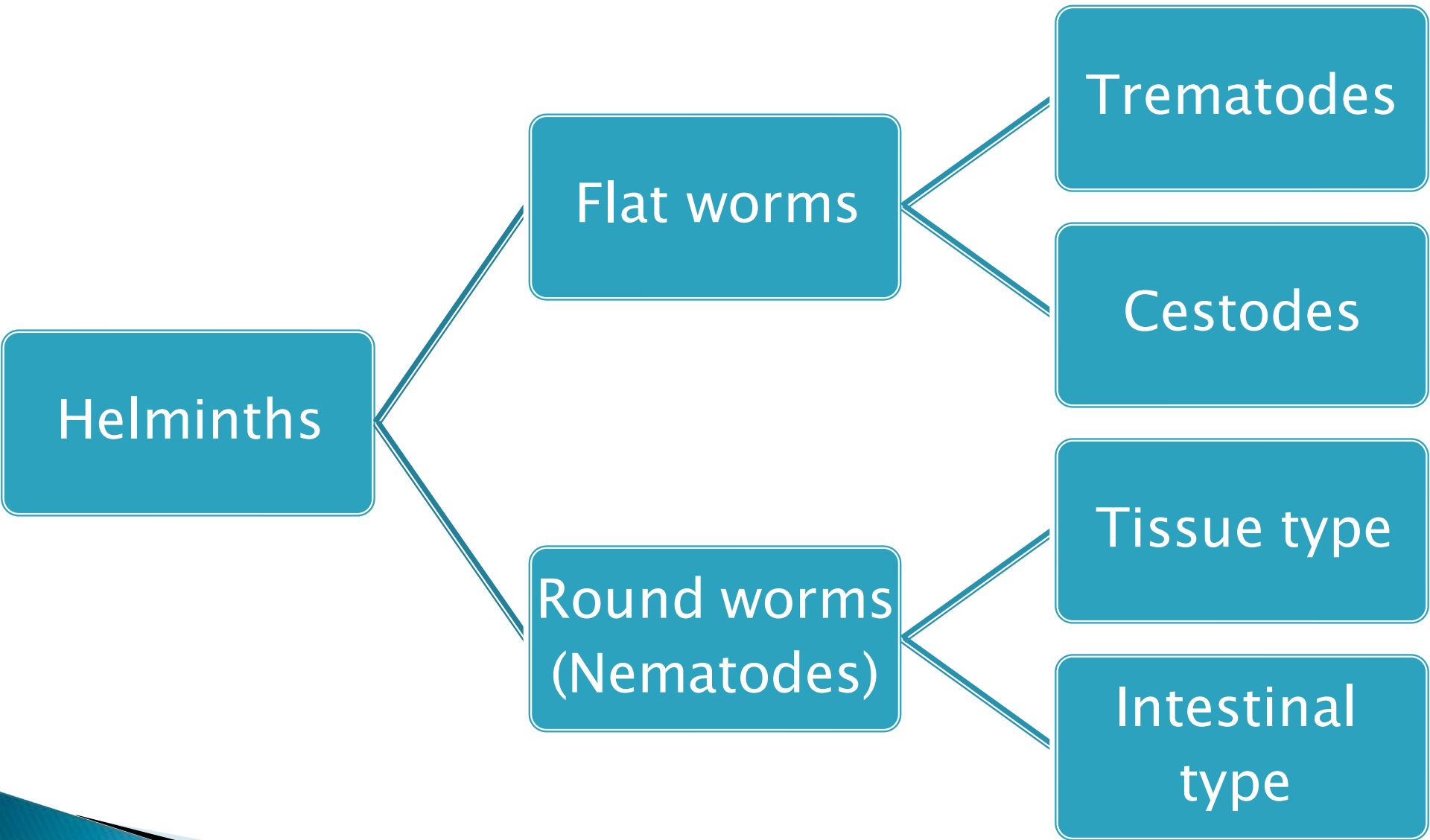
- ▶ Helminthiasis is prevalent globally but more common in developing countries
- ▶ Humans are the primary hosts for the most of helminthic infections.

Clinical Types

1. Worms live in hosts alimentary canal.
2. Worms or larvae live in other tissues of host body like muscles, viscera , meninges, lungs, subcutaneous tissues.

Anti-helminthics

- ▶ Helminthics harm the host by depriving them of food, causing blood loss, injury to organs, intestinal or lymphatic obstruction and by secreting toxins
- ▶ Major cause of ill health
- ▶ Anthelmintics
 - Kill (Vermicide)
 - Expel (Vermifuge)
- ▶ Choice based on efficacy, lack of toxicity, ease of administration, low cost



1. ROUND WORMS

A) INTESTINAL ROUND WORMS (NEMATODES)

- ▶ *Ascaris lumbricoides* (Round worm)



- ▶ *Enterobius vermicularis* (pin worm)



ROUND WORMS

A) **INTESTINAL ROUND WORMS (NEMATODES)**

- ▶ Trichuris trichuria (whip worm)



- ▶ Strongyloids stercoralis (thread worm)



- ▶ Ankylostoma duodenale (hook worm)



1. ROUND WORMS (B. Tissue Types)

FILARIAE

Lymphatic filariasis:

- ▶ *Wuchereria bancrofti*
- ▶ *Brugia malayi*



Filariasis

Subcutaneous filariasis:

- ▶ *Loa loa*
- ▶ *Onchocerca volvulus*



Onchocerciasis

Filariae

- ▶ Adult filariae live in the lymphatics
- ▶ cause lymphadenitis and swelling of limb connective tissue or mesentery of host
- ▶ produce live embryos or microfilariae, which goes to blood stream.



elephantiasis

**Wuchereria or Brugia obstructs lymphatic vessels
producing elephantiasis**

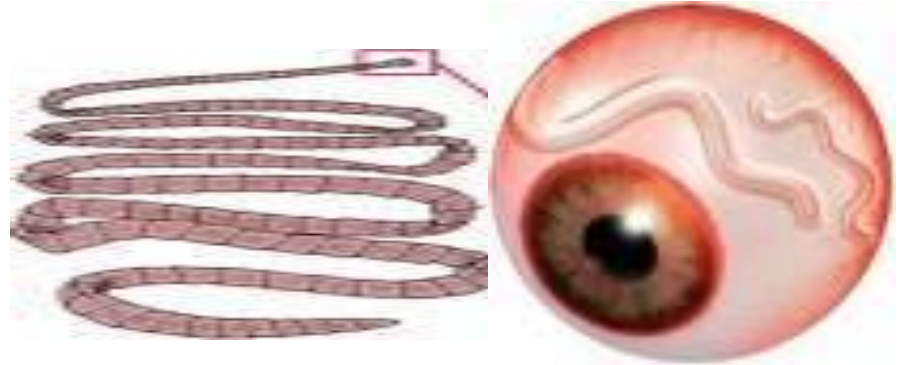


elephantiasis

2. FLAT WORMS (Intestinal tape worms)

A) TAPE WORMS (CESTODES)

- ▶ Taenia saginata (Beaf)
- ▶ Taenia solium (Pork)
- ▶ Neurocysticercosis



Tapeworm

Cysticercosis

In some conditions this larvae may develop in humans resulting in cysticercosis (i.e. larvae gets encysted in the muscle and viscera or more seriously in the brain or eye.)

Cestodes

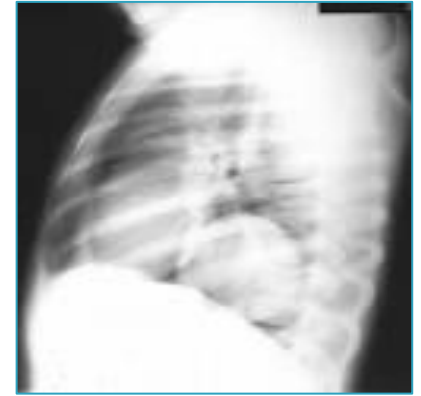


- ▶ Humans become infected by eating raw or under cooked meat containing larvae of infected cattle or pig which has encysted in the animal muscle tissue.
- ▶ In some conditions this larvae may develop in humans resulting **cysticercosis** (i.e. larvae gets encysted in the muscle and viscera or more seriously in the brain or eye.)

2. FLAT WORMS (Cestodes)

Hydatid tape worm

- ▶ These are cestodes, primary in canines and sheep as intermediate host.



Hydateid cyct

- ▶ Humans can act intermediate host in which larvae develop to hydatid cyst with in tissue.

Hymenolepis nana (Dwarf)

2. FLAT WORMS (Trematodes)

TISSUE TYPES

- ▶ Schistosoma haematobium
- ▶ Schistosoma Japonicum
- ▶ Adult worms live in the **gut wall** or the **bladder**
- ▶ Eggs pass into the bladder or gut and produce inflammation of these organs, resulting in haematuria or loss of blood in feces.



Fasciola hepatica

Helminthics

S. no	Common Name	Worms
1	Round Worm	Ascaris lumbricoides
2	Hook Worm	Ancylostoma duodenale
3	Pin Worm	Enterobius vermicularis
4	Thread Worm	Strongyloides stercoralis
5	Whip Worm	Trichuris trichiura
6	Filaria	Wuchereria bancrofti Brugia malayi
7	Tape Worms	Tenia saginata Tenia solium H. Nana Neurocysticercosis

Anti-Helminthic Drugs

BENZIMIDAZOLES: Thiabendazole, Mebendazole, Albendazole,

- ▶ It is a broad spectrum (Round worm, Pin worm, Hook worm, Trichuris, Strongyloides, Trichineella spiralis)
- ▶ Mechanism of action:
 - inhibits microtubule synthesis in nematodes: intestinal parasites are immobilized and die slowly
 - irreversibly impairs glucose uptake
- ▶ Inhibits development of **eggs** of worms and kills **larve**
- ▶ Possesses anti-inflammatory actions

Mebendazole

- ▶ Retains the broad spectrum anti-helminthic activity but not the toxicity of thiabendazole
- ▶ **Pharmacokinetics:** Absorption of mebendazole is minimum
 - 75-90 % passed in faeces
- ▶ **ADR:**
 - Nausea, vomiting, abdominal pain, diarrhoea, giddiness, itching
- ▶ **Preparations:**
 - 100 mg tab, 100 mg/5 ml suspension

Doses of Mebendazole

Round Worm

Hook Worm

Whip Worm

• 100 mg BD for 3 days

Pin Worm

• 100 mg single dose

Albendazole

- ▶ Retains the broad spectrum anti-helminthic activity
- ▶ Advantage: Single dose administration
- ▶ **Pharmacokinetics:** Absorption is enhanced by fatty diet
- ▶ Converted to its sulfoxide metabolite ($t_{1/2}$ 8.5 hours)
Wide distribution in the body
- ▶ **Preparations:** 400 mg tab, 200 mg/5 ml suspension
- ▶ **Side effects:** GIT side effects, prolonged use: headache, fever, alopecia, jaundice

Doses of Albendazole

Round Worm, Pin
Worm, Hook Worm
Whip Worm

• 400 mg single dose

Tape Worm
Strongyloidosis

• 400 mg for 3
consecutive days

Neurocysticercosis

• 400 mg BD for 8–15
days

Doses of Albendazole

Hydatid disease

- 400 mg BD for 4 weeks

Filariasis

- Added to DEC/
Ivermectin

PYRANTEL PAMOATE

- ▶ Introduced in 1969 for pin worm infestation in children
- ▶ Use soon extended to roundworm and hookworm
- ▶ Efficacy against *Ascaris*, *Enterobius* and *Ancylostoma* (10 mg/kg) is comparable to Mebendazole
- ▶ **Pharmacokinetics:** It is poorly absorbed orally,
- ▶ Half of the drug is excreted unchanged in the feaces.
- ▶ **Mechanism of action:** activation of **nicotinic cholinergic receptors** in the worms: persistent depolarization.
Spastic paralysis

PYRANTEL PAMOATE

Adverse Effects

- ▶ Infrequent mild transient GI disturbance
- ▶ drowsiness, headache, insomnia.
- ▶ Rash, fever

Contra-indications

- ▶ Should not be used in liver diseases.
- ▶ Pregnancy
- ▶ Child under 2 years of age

PIPERAZINE

- ▶ Introduced in 1950, highly active against *Ascaris* and *Enterobius* (90-100 % cure rates)
- ▶ Considered as second choice drug
- ▶ **Mechanism of action: GABA agonistic actions**, flaccid paralysis, Worms are expelled alive
- ▶ Purgative is administered with it
- ▶ **ADR:** Abdominal discomfort, urticaria, convulsions, neurotoxicity
- ▶ Safe in pregnancy

Drugs used for treating human intestinal nematodes (single dose unless otherwise stated)

	Ascariasis	Hookworm	Enterobius	Tricuris	Strongloides
Piperazine	++	+	++	-	-
Pyrantal pamoate	++	++	++	-	-
Albendazole	++	++	++	+	+
Mebendazole	++	++	++	+	+
Thiabendazole	n/a	n/a	n/a	n/a	++

Diethyl Carbamazine

- ▶ Drug of choice for the treatment of filariasis caused by *Wuchereria bancrofti* (90 % cases) and *Brugia Malayi*

Pharmacokinetics:

- ▶ It is synthetic peprazine derivative
- ▶ Rapidly absorbed from gut
- ▶ It has a half life of 2-3 hours which increases in alkaline urine to 10 hours.
- ▶ It is excreted in urine unchanged.
- ▶ Dosage is reduced in urinary alkalosis and renal impairment.

Diethyl Carbamazine

Mechanism of action:

- ▶ It **immobilizes microfilariae** and alters its surface structure making them susceptible to destruction by host defense mechanisms
- ▶ It is not teratogenic
- ▶ It is a drug of choice for the treatment of *W. bancrofti*, *B. malayi*, *loa loa*
- ▶ Microfilariae are rapidly killed. Adult worms are killed slowly requiring several course of treatment

Diethyl Carbamazine

Filariasis

- 2 mg/kg TDS (12 days to 3 weeks)

Tropical
pulmonary
eosinophilia

- 2 mg/kg TDS (2 to 3 weeks)

Loa loa and
O. volvulus

- Test dose (25-50 mg)
1 mg /kg 5-6 days

Diethyl Carbamazine

- ▶ Fever, loss of appetite, headache, weakness, dizziness are the usual complaints

Reactions induced by Dying parasites:

- ▶ Febrile reaction with rash, pruritis, enlargement of lymph nodes, bronchospasm, hypotension
- ▶ Start with low dose (0.5 mg/kg)
- ▶ Anti-histaminics and corticosteroids administered

Ivermectin

- ▶ Obtained from *Streptomyces avermitilis*
- ▶ DOC for single dose treatment of onchocerciasis and strongyloidosis (thread worm)
- ▶ Add on therapy to albendazole/mebendazole in heavy trichuriasis (Whip worm)
- ▶ **MAO:** Glutamate gated Cl⁻ channel : tonic paralysis
 - In onchocerciasis it is microfilaricidal
 - It does not kill adult worm
- ▶ It has a half life of 16 hrs

Ivermectin

Clinical uses:

- ▶ **Onchoceriasis:** used in river blindness control program of WHO in Africa and Latin America
- ▶ a single dose of 150 mg/kg, repeated after every 3 months for one year,
- ▶ after this it is repeated yearly untill adult worm dies which may take a year or more
- ▶ **Thread Worm:** 0.2 mg/kg highest cure rate (single)

Ivermectin

- ▶ **Adverse effects:**

Fatigue, dizziness, GI disturbance

- ▶ **In onchocerciasis:**

Mazotti reaction i.e. fever, headache, dizziness, somnolence, weakness, rash, diarrhea, arthralgia, hypotension, lymphadenitis, peripheral edema due to killing of microfilariae

- ▶ Swelling and abscess at site of adult worm

- ▶ Corneal opacities.

Praziquantel

- ▶ Wide activity against Schistosomes, trematodes, cestodes
- ▶ **MAO:** leakage of **intracellular calcium**, from the membrane contracture and paralysis
- ▶ Loose grip of GIT and are expelled
- ▶ Effective against adult, juvenile and larval stages of tapeworm
- ▶ **PK:** crosses BBB, $t_{1/2}$ 1.5 hrs

Uses

Tapeworms

- 10 mg/kg single dose in morning

Neurocysticercosis

- 50 mg/kg in three divided doses for 25-30 days

Flukes

- 75 mg/kg fasciola hepatica

Neurocysticercosis

- ▶ Migration of *T. solium* larvae to various tissues via blood stream
 - ▶ Larvae dies and produces an intense focal reaction
 - ▶ Anthelmintics kills the larve and may ppts the reaction resulting in meningeal irritation, rise in intracranial pressure, seizures, neurological phenomena
 - ▶ Decision depends on number, location and viability of cysts
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Neurocysticercosis (Albendazole Vs Praziquantel)

- ▶ Treatment shorter (8-15 days) with **Albendazole** compared to praziquantel (15-30 days)
 - ▶ Cure rates higher with **Albendazole** (75-85 %) Vs Praziquantel (50 -60 %)
 - ▶ Corticosteroids enhance the absorption of albendazole but lower the blood levels of praziquantel
 - ▶ Albendazole is cheaper
 - ▶ **Rx:** Prednisolone 40 -60 mg/day or dexamethasone 8 -12 mg/day started 2 day prior and continued for 2 weeks after
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Choice of drugs for helminthiasis

Common Name	Worms	Drugs
Round Worm	<i>Ascaris lumbricoides</i>	Albendazole, Mebendazole, Pyrantel
Hook Worm	<i>Ancylostoma duodenale</i>	Albendazole, Mebendazole, Pyrantel
Pin Worm	<i>Enterobius vermicularis</i>	Albendazole, Mebendazole, Pyrantel
Thread Worm	<i>Strongyloides stercoralis</i>	Ivermectin
Whip Worm	<i>Trichuris trichiura</i>	Albendazole, Mebendazole
Filaria	<i>Wuchereria bancrofti</i> <i>Brugia malayi</i>	Diethyl carbamazine, Ivermectin
Tape Worms	<i>Tenia saginata</i> <i>Tenia solium</i> H. Nana Neurocysticercosis	Praziquantel Praziquantel Praziquantel Albendazole
Hydatid Disease	<i>Echinococcus granulosus</i>	Albendazole

Must Know

- ▶ Albendazole/Mebendazole
 - ▶ DEC
 - ▶ Rx of Neurocysticercosis
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