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Anthelmintics

Helminth

The helminths are macroscopic, multicellular organisms, having their own digestive, excretory, reproductive and nervous system.

Helminthiasis

- A disease in which part of the body is infested with one or more intestinal parasitic worms such as roundworm, tapeworms or flukes.
- The worms usually infest the intestine but sometimes. they may invade the other organs.

Types of Hilminth

They are of two types:

- Nematelminths (round bodied worms)
- Platyhelminths (flat-boddied worms)

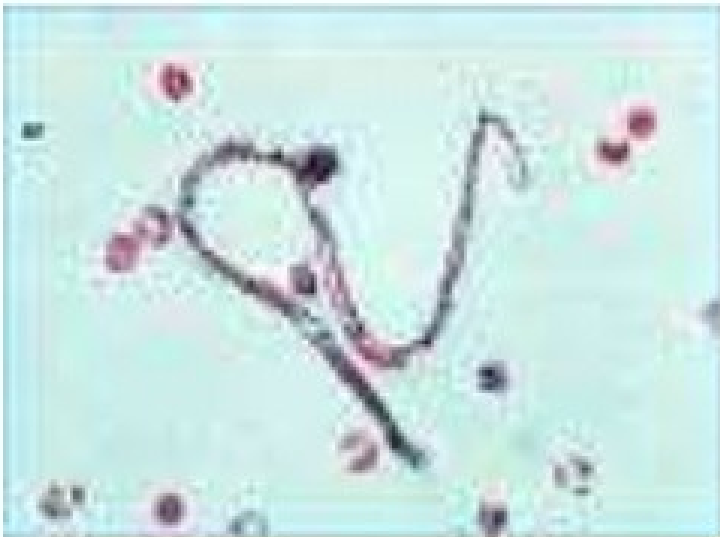
Nemathelminth



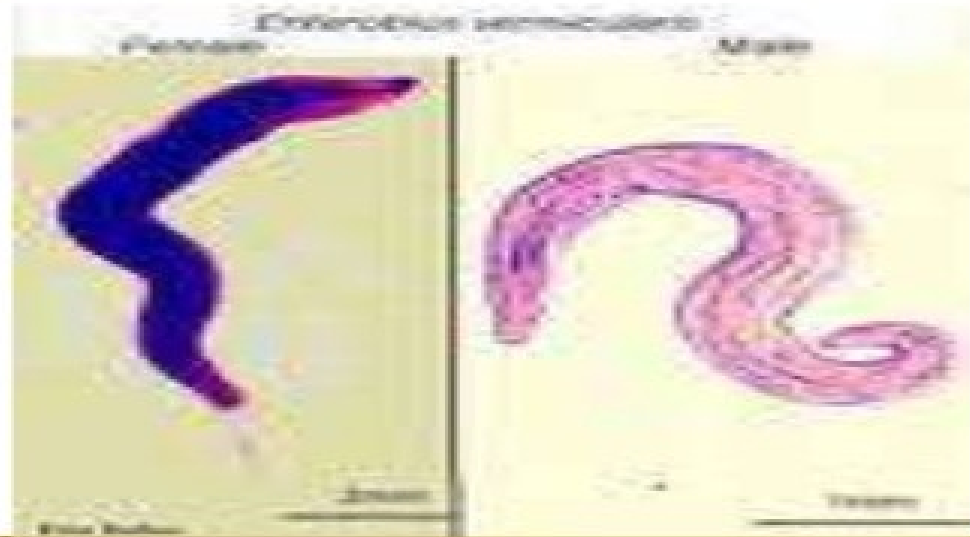
ROUND WORM



Hookworm



filariasis

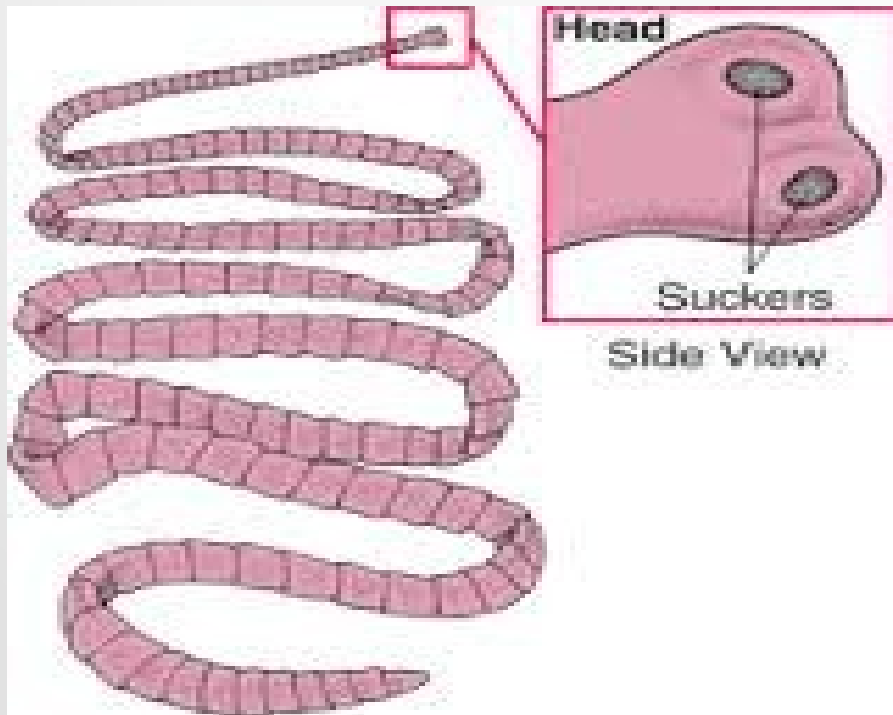


Pin worm male, female

Platyhelminth

These are of two types:

- Trematodes (flukes)
- Cestodes (tape worms)



Sub-Types

Trematodes include

- Blood flukes (schistosomiasis)
- Liver flukes (clonorchiasis)
- Intestinal flukes (fasciolopsiasis)
- Lung flukes (paragonimiasis)



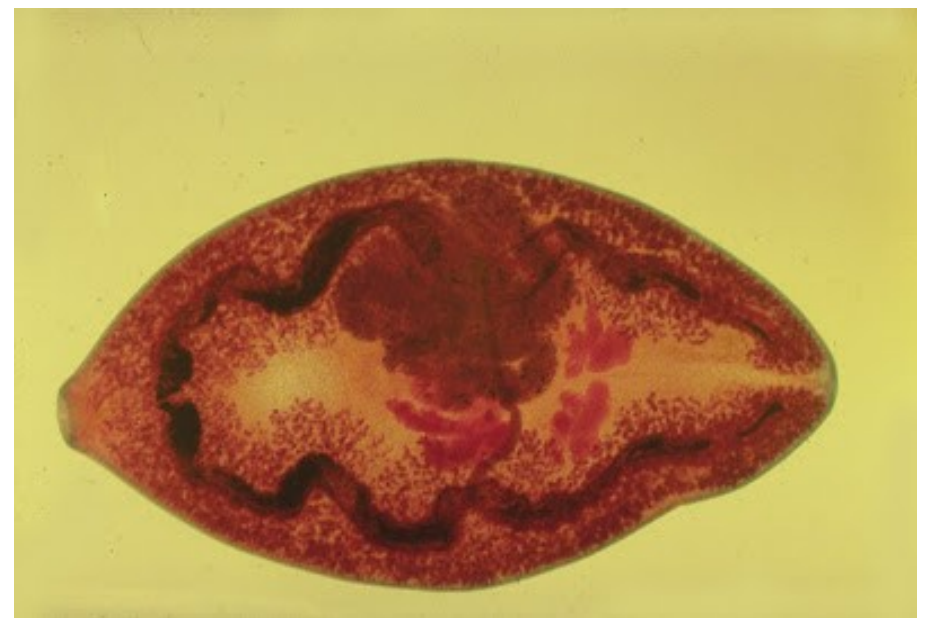
Blood Fluke



Liver fluke



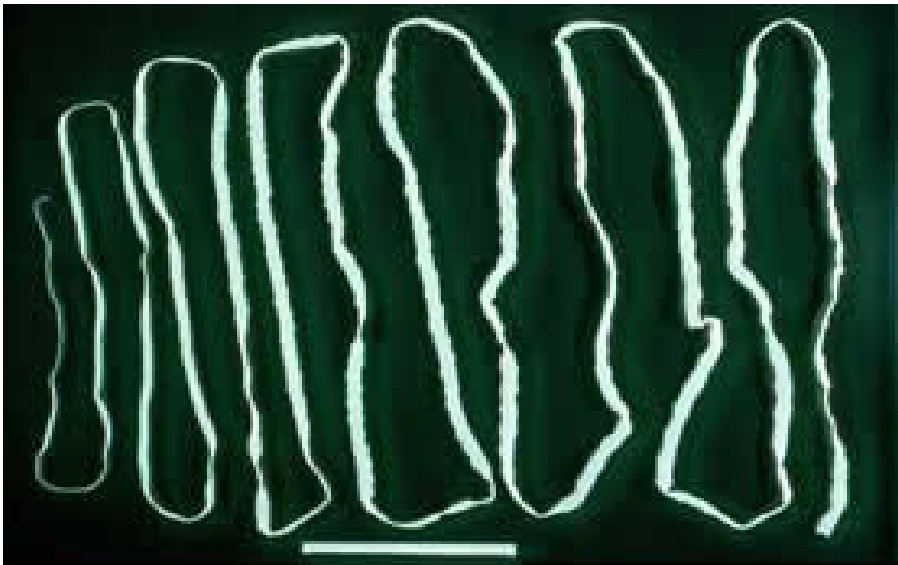
Intestinal fluke



Lung Fluke

Cestodes

- Beef tape worms (*taenia saginata*)
- Pork tape worms (*taenia solium*)
- Fish tape worms (*diphyllobothrium latum*)
- Dwarf tape worms (*hymenolepis nana*)



Source: Centers for Disease Control and Prevention

Beef Tapeworm



Pork tapeworm

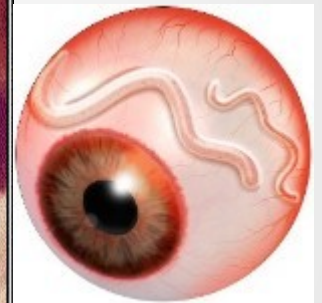
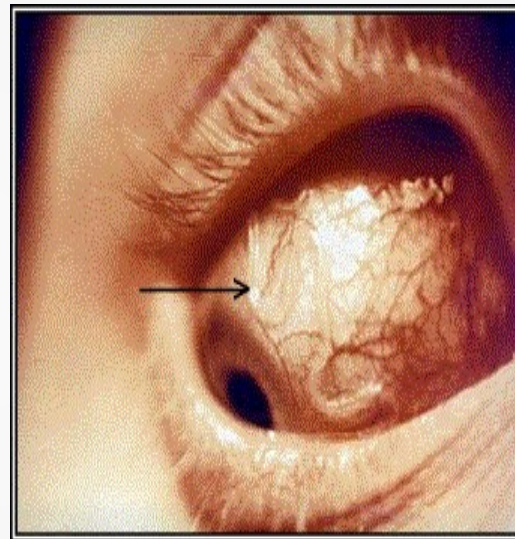


Fish Tapeworm

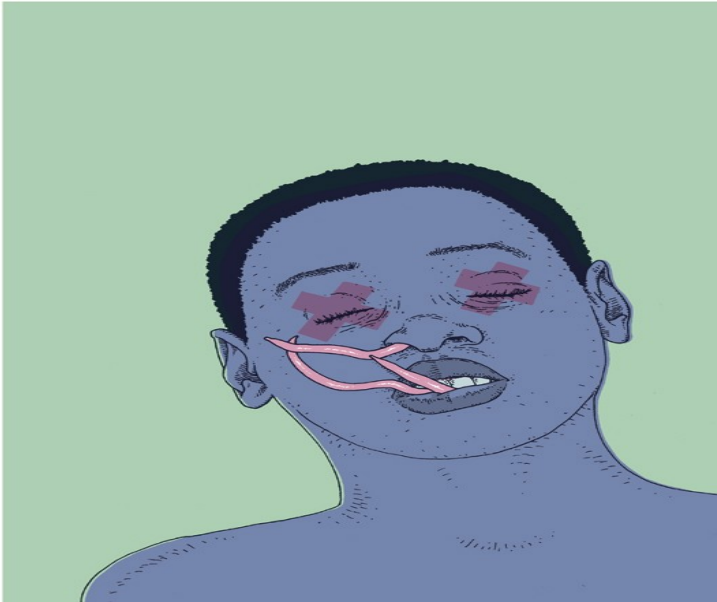


Dwarf Tapeworm

Diseases Caused By Worms:



River Blindness



Ascariasis



Trichinosis



Elephantiasis

Anthelmintic Drugs

- Drugs used to ***get rid of helminths*** are called anthelmintic drugs
- They may be:
 - Vermicide (*kill*)
 - Vermifuge (*expel*)

Mechanism of action

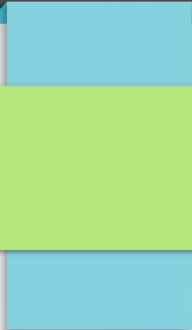
Based on mechanism of action in parasites

a. Drugs affecting energy production

- i. Inhibitors of fumarate reductase and glucose uptake, binding of tubulin in mitochondria.
- ii. Inhibitors of (mitochondrial) phosphorylation
- iii. Inhibitors of glycolysis

b. Drugs causing paralysis

- i. Cholinergic agents
- ii. GABA agonists
- iii. Muscle hyperpolarizer
- iv. Acetyl cholinesterase inhibitors
- v. Acetylcholine mimic



c. Other Actions

- i. Affecting permeability of the cell membrane
- ii. Vaculation of teguments

d. Unknown

Disruption of the teguments

Ideal anthelminths

- Orally effective in single dose
- Wide safety of margin with highest toxicity to worms
- Wide therapeutic index
- Broad spectrum activity
- Activity against mature and immature stages
- Single dose efficacy
- Ease of administration
- Economical
- Compatibility with other drugs

Drug Classification

Against:

- Nematodes
- Trematodes
- Cestodes
- Trematodes as well as cestodes

Drug Classification

- Nematodes:
 - Pyrantel pamoate
 - Levamisole
 - Piperazine
 - Ivermectin
 - Diethylcarbamazine
 - Thiabendazole
- Trematodes:
 - Metrifonate
 - Oxamniquine
 - Bithionol
 - Triclabendazole

Drug Classification

- Trematodes as well as cestodes
 - Praziquantel

- Cestodes
 - Niclosamide

Based on Chemical Structure

- i. Benzimidazoles
- ii. Imidathiazoles
- iii. Tetrahydropyrimidines
- iv. Organophosphates
- v. Piperazines
- vi. Macrolides
- vii. Unrelated Compounds

Benzimidazoles

- Inhibition of fumarate reductase system
- Glucose uptake

Members

- Thiabendazole
- Albendazole
- Cambendazole
- Fenbendazole
- Mebendazole
- Oxfendazole (R.T.L)
- Oxibendazole (R)
- Panbendazole

Benzimidazole pro-drugs

- Febental – Fenbendazole
- Netobimin - Albendazole

Imidathiazoles

- Nicotine like effect
- Immunomodulatory effect

Members

- Tetramisole (R)
- Levamisole (R)

Tetrahydropyrimidines

- Cholinergic effect

Members

- Morental (R)
- Pyrentel (R)
- Oxantel (R)

Organophosphorus Compounds

- Inhibit Cholinesterases and ali-esterases

Members

- Coumaphos (Asuntol)
- Dichlorvos
- Haloxon
- Napthalophos (Rametin)
- Trichlorphon (Neguvon)

Piperazines

- Hyperpolarization

Piperazine salts

- Phosphates
- Citrate
- Adipate
- Sulphate

Macrolides

- Avermectins
 - Ivermectin
 - Abamectin
 - Doramectin
- Milbemycins
 - milbemycin D
 - moxidectin
 - milbemycin oxime

Unrelated individual entities

- Phenothiazine (R)
- Diethylcarbamazine (R)
- Bunamidine (T)
- Niclosamide (T)
- Praziquantel (T)
- Oxyclozanide (L)
- Rafoxanide (L)
- Nitroxynil (L)
- Closantel (L)
- Clorsulon (L)

Mebendazole (Prototype)

- Synthetic benzimidazole derivative
- 75% effective for tape worms but not for *H. nana*
- Drug of choice for treatment of:
 - Round worms
 - Whip worms
 - Hook worms
- Alternative for treatment of:
 - Trichinosis
 - Visceral larva migrans

ADRs

- No adverse effects with short term therapy, mild GIT disturbances – nausea, diarrhoea and abdominal pain
- Allergic reaction, loss of hair and elevation of liver enzymes
- Contra-indications:
 - In pregnancy
 - In liver cirrhosis

Pyrantel Pamoate

- **Mechanism of action**
 - Activation of nicotinic cholinergic receptors
 - Persistent depolarization leading to contracture and spastic paralysis – expelling of worms
 - Inhibition of acetylcholinesterase
- **Clinical uses**
 - Originally for thread worms but extended to round worms and hook worms as well
 - Less active against necator and strongyloides
 - Inactive against trichuris
- **ADRs**
 - Free from ADRs
 - Mild GIT disturbance
 - Headache, dizziness and drowsiness

Piperazine

- **MOA**
 - Hyperpolarization of Ascaris muscles GABA agonistic action of Cl⁻ channel opening
 - Decreased responsiveness to Ach contractile response – flaccid paralysis
- **Clinical uses**
 - Used for treatment of ascariasis and enterobios (as alternative)
- **ADRs**
 - Nausea, vomiting, abdominal pain and headache
 - Neurotoxic and allergic reactions are rare
- **Contra-indications**
 - Renal insufficiency
 - Epileptics

DEC

- **MOA**
 - Alteration of MF membrane – to be readily phagocytosed by tissue monocytes
 - Since piperazine derivative – hyperpolarization and muscle weakness
- **Clinical uses**
 - Filariasis
 - Tropical eosinophilia
- **ADRs**
 - Nausea, anorexia, lethargy, febrile reaction
 - At times, renal haemorrhage and encephalopathy

Ivermectin

- **MOA**

- Acts via special type of glutamate gated Cl-channel found only in invertebrates
- Potentiation of GABA activity – paralysis of muscles of worms

- **Clinical uses**

- Drug of choice for onchocerciasis
- In strongyloidiasis
- in pediculosis
- In treatment of cutaneous larva migrans

- **ADRs**

- Pruritus, postural hypertension, ecg changes, giddiness, arthralgia, lymphadenopathy

Niclosamide

- **MOA**
 - Inhibition of oxidative phosphorylation in mitochondria and interference of anaerobic generation of ATP
- **Clinical uses**
 - Against tape worms – saginata, solium, latum and nana
- **ADRs**
 - Well tolerated
 - No systemic toxicity
 - Can be given in pregnancy

Praziquantel

- **MOA**

- Rapidly taken up by worms
- Leakage of intracellular Ca^{++} causing paralysis
- Worms lose grip on intestinal wall including tissues and veins
- Acts against all stages of worms including larvae
- Other MOA – vacuolization of membrane and release of contents of tape worms

- **Clinical uses**

- Mainly on schistosomiasis and other trematodes, cestodes but not nematodes

- **ADRs**

- Drowsiness
- Dizziness
- Urticaria

Praziquantel

- **Contra-indication**
 - Inocular cysticercosis

Bithionol

- **MOA**
 - Uncouples parasites specific oxidative phosphorylation. By blocking ATP synthesis, inhibits energy derived by helminth by anaerobic metabolism
- **Clinical Uses**
 - Drug of choice for fascioliasis and paragonimiasis
- **ADRs**
 - GIT disturbances
 - Skin rashes
 - Urticaria
- **Contra-indications**
 - Avoided in children below 8 years of age



Thank you

