

Anthelmintic — Ivermectin, Praziquantel, Pyrantel Pamoate and More

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Infection caused by various helminths (worms) is among the most widespread of chronic infections and its occurrence is more common in developing regions with poor personal and environmental hygiene. In this article, we will study in detail the various anthelmintic (anti-parasitic) drugs, mechanism of action, adverse effects/toxicity and drugs of choice. Important therapeutic aspects of individual drugs will also be studied.



Definition of Anthelmintics

Anthelmintic, or antihelminthic, are the drugs that kill or expel **parasites** and are used for the treatment of various diseases caused by parasites.

Helminths are categorized as follows:

- **Nematodes** or roundworms.
- **Platyhelminthes** or flatworms.
- **Trematodes** or flukes.
- **Cestodes** or tapeworms.

Overview of Helminthiasis

Helminths have a **complex life cycle**, involving various host species and vectors in different stages of their life cycle. In most of the parasitic infections, a human acts as a host of the parasites.

There are several major causes of helminthiasis:

- Poor **hygiene**.
- Infection occurs due to the **consumption** of water and food contaminated with human or animal feces or undercooked meat (pork and fish).
- Some parasites enter the human body through **the skin** and **insect bites** (onchocerca volvulus, Wuchereria bancrofti).

Various Types of Helminths



Image: "Taenia Solium Scolex (x400)" by
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Tapeworms

Taenia saginata, *Taenia solium*, *Hymenolepis nana*

The intermediate hosts of the tapeworms (*T. saginata* and *T. solium*) are cattle and pigs.

Taenia solium (pork tapeworm) is most commonly found in Asia and Latin America. In the US, it is present in patients migrated from these countries. It causes **neurocysticercosis**. Its host is the pig and it can be acquired by a human by eating poorly cooked pork. Its eggs are generally ingested by oral-fecal contamination.

Taenia saginata, also called beef tapeworm, does not cause neurocysticercosis. Usually, humans get infected with *T. saginata* after consumption of undercooked beef. It causes **taeniasis** in the intestine and it is harmless. It mostly remains **asymptomatic**.

Echinococcus Species



Image: "Echinococcus Granulosus." by Ganímedes - Own work.
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E. granulosus, *E. multilocularis*, *E. vogeli*

The intermediate hosts for this infection are **sheep** and the primary host are **dogs**. Under certain conditions, humans can function as an intermediate host. As a consequence, the larvae develop into hydatid cysts within the tissues. They cause the **hydatid cysts**; the most affected part is the **liver** (two-thirds of the patients).

Flukes

Schistosoma haematobium, *Schistosoma mansoni*, *Schistosoma japonicum*

Flukes of genus *Schistosoma* cause **schistosomiasis**. It is also called **snail fever**. Different types of snails act as hosts of the genus *Schistosoma*. Complications arise due to **immunological reactions** towards trapped eggs of *Schistosoma* parasite in various tissues. Eggs reach **skin**, **brain**, **muscle**, adrenal glands and eyes. Eventually, **the excessive inflammatory process** causes **organ damage**.

Tissue roundworms

Trichinella spiralis, *Dracunculus medinensis* (guinea worm), *Wuchereria bancrofti*, *Loa loa*, *Onchocerca volvulus*, *Brugia malayi*



Image: "Wuchereria bancrofti Microfilaria of Wuchereria bancrofti, from a patient seen in Haiti." License: [Public Domain](#)

The adult filariae of these types of worms reside mainly in the lymphatic system, connective tissues or mesentery of the host and produce live embryos or **microfilariae**, which travel in the bloodstream through transmission from **mosquitoes or similar insects** when they feed.

After development within the secondary host, the larvae pass to the mouthparts of the insect and are re-injected into humans.

Common filarial diseases are **onchocerciasis** (the presence of microfilariae in the eye causing 'river blindness'), **loiasis** (the microfilariae causing inflammation in the skin and other tissues), **trichinosis** (the larvae from the viviparous female in the intestine migrate to the skeletal muscle, where they become encysted).



Image: "An infection in the leg by Wuchereria bancrofti." by Unknown. License: [CC BY-SA 3.0](#)

Roundworms

Ascaris Lumbricoides, *Toxocara canis*

Ascariasis is the most common intestinal nematode infection. It remains **asymptomatic** in most of the patients. However, it can cause **pulmonary complications** ([cough](#), [wheezing](#)) and **intestinal obstruction** when a person is heavily infected. It is usually prevalent in the areas of poor sanitation and hygiene.

Hookworm

Ancylostoma duodenale, Necator americanus

The reason for the infection is **larval penetration through the skin**. After reaching the [lung](#), the larvae migrate to the oral cavity and are swallowed, the hookworm attaches to the **intestinal mucosa** and feeds through the host.

Anthelmintic Drugs

Albendazole

The drug has a broad range of activity in **neurocysticercosis, echinococcosis, ascariasis, hookworm, and trichuriasis**. The drug acts by inhibiting the **polymerization of helminth β -tubulin**, thus interfering with microtubule-dependent functions such as glucose uptake in the helminths.

Bioavailability of albendazole is less than 5 % when taken on an empty stomach. Absorption of the drug is enhanced by administering it with **fatty foods**.

Side effects include abdominal pain, nausea, vomiting, and increased hepatic **transaminases**; these are generally transient and usually do not require discontinuation of the drug. **LFT's** should be monitored during therapy with albendazole.

Mebendazole

The drug is effective against a spectrum of intestinal and tissue nematode infections, including **ascariasis, hookworm, enterobiasis, and trichuriasis**. Mebendazole is the preferred drug for the treatment of multiple infestations and is more efficacious than albendazole in trichuriasis.

The site of action of the drug is the **microtubular protein β -tubulin** of the parasite. It binds to β -tubulin of the worm with high affinity and inhibits its polymerization. It also blocks glucose uptake in the helminths.

Albendazole and mebendazole are effective against the following parasites:



Image: "Trichinella Spiralis in Muscle Tissue." by Doc. RNDr. Josef Reischig, CSc. - Author's archive. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

- *Ascaris lumbricoides*
- *Necator americanus*
- *Trichinella spiralis*
- *Enterobius vermicularis*
- *Trichuris trichiura*
- *Echinococcus*
- *Strongyloides stercoralis*
- *Taenia solium*
- Microsporidia

Thiabendazole

Thiabendazole is an older benzimidazole derivative and, apart from the therapeutic response against various helminths, it has symptomatic relief in **cutaneous larva migrans** and skeletal muscle symptoms produced by the migration of **Trichinella spiralis larvae** to muscles.

The mechanism of action of thiabendazole is similar to albendazole. Thiabendazole has **anti-inflammatory, analgesic and antipyretic actions**. Adverse reactions include dizziness, nausea, vomiting, drowsiness, pruritus, headache, neuropsychiatric disturbances, hepatitis and hypersensitivity reactions including **Stevens-Johnson syndrome**. A topical suspension of thiabendazole is used for cutaneous larva migrans.

Diethylcarbamazine (DEC)

It is a piperazine derivative that is effective against **lymphatic filariasis, loiasis, and visceral larva migrans**. Diethylcarbamazine is only effective on **the microfilaria (larvae)** stage of various parasites. It does not kill the adult parasite (**microfilaria**).

It may act by changing the parasite such that it becomes susceptible to the host's normal immune responses (**phagocytosis**). However, the exact mechanism of action is unclear. It may also interfere with **helminth arachidonate metabolism**.

It is a **drug of choice for loiasis**. It is also the **drug of choice for filariasis** caused by **Wuchereria bancrofti and Brugia malayi**. Nausea, loss of appetite, headache, weakness, and dizziness are common side effects.

Praziquantel

It has activity against **schistosomes**, **cestodes**, and their larval forms, but not nematodes. It acts by causing leakage of intracellular calcium from the cell membranes of parasites producing contracture and paralysis. The paralyzed tapeworms are dislodged from the attached intestinal mucosa and are expelled from the intestine. **Flukes** and **schistosomes** are also cleared in tissues and veins.

Common side-effects are appetite loss, dizziness, drowsiness, headache, malaise, abdominal pain, nausea, vomiting, and diaphoresis. Undesirable effects are usually transitory and rarely of clinical importance.

It is a drug of choice to treat the **cysticercosis** caused by *T. solium*. Side effects are prominent in patients with a heavy parasite load because of products released from the dead worms.

Praziquantel is contraindicated in the treatment of **ocular cysticercosis**, as the destruction of the organism can cause permanent damage to the eyes. Praziquantel is considered safe for pregnant and [lactating women](#) (category B drug).

Piperazine

It is highly active against **Ascaris and Enterobius infections** with cure rates of 90–100 %. It causes hyperpolarization of worm muscle by opening chloride channels that cause relaxation and depresses responsiveness to the contractile action of ACh. Flaccid paralysis occurs and worms are expelled alive. Piperazine is safe and well tolerated. Nausea, vomiting, abdominal discomfort and urticaria are occasional.

Pyrantel pamoate

It is effective against the following helminths:

- *Ascaris lumbricoides*
- *Necator americanus*
- *Enterobius vermicularis*

It is a depolarizing neuromuscular blocking agent and it causes paralysis in the parasite. It also inhibits the cholinesterase. It is poorly absorbed by the GI tract.

Important: It is most effective against intestinal parasites. Caution should be taken while treating the patient with liver dysfunctions.

Niclosamide

It is active against *T. saginata*, *T. solium*, *Diphyllobothrium latum*, and *Hymenolepis nana*, as well as threadworm. The drug acts by inhibiting oxidative phosphorylation in mitochondria and interfering with the anaerobic generation of ATP in the tapeworm; thus, organisms are killed due to the unavailability of ATP. It does not kill ova/larva.

It is minimally absorbed from the GI tract and no systemic toxicity occurs. It is well tolerated; **minor abdominal symptoms** are produced occasionally. Malaise, pruritus, and lightheadedness are rare. Niclosamide is safe during pregnancy and in patients with poor health.

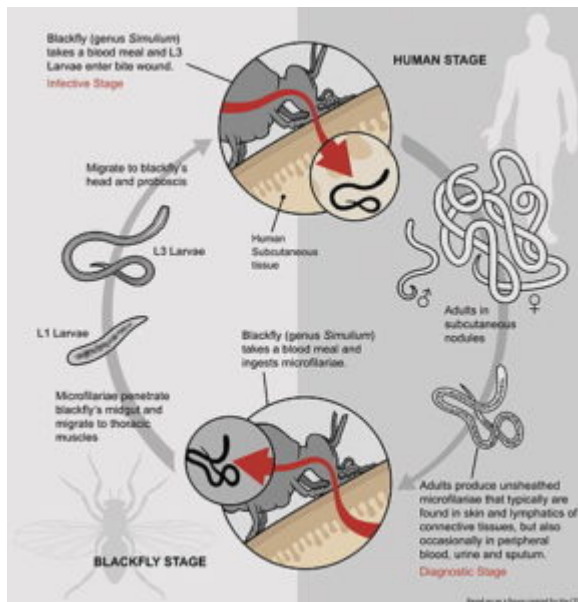
Levamisole

Levamisole is effective in common roundworm (***A. lumbricoides***). It has a nicotine-like action stimulating and blocking the **neuromuscular junctions**. Consequently, it causes the paralysis of parasites and they are expelled from the body through feces. Low incidences of side effects are nausea, abdominal pain, giddiness, fatigue, drowsiness or insomnia.

Ivermectin

It is obtained from ***Streptomyces avermitilis***. Ivermectin acts on the glutamate-gated chloride channels (**GluCl_s**) present in the protostome invertebrates. They control the locomotion and feeding in the parasites. Ivermectin causes the hyperpolarization of the **GluCl_s**, resulting in the paralysis and death of the parasite.

Important: Ivermectin is only effective on the **larvae** stage of various parasites. It does not kill the adult parasite.



[Image:](#) "The life cycle of *O. volvulus*." by Giovanni Maki, derived from a CDC image at <http://www.dpd.cdc.gov/dpdx/HTML/Filariasis.htm> - Basáñez M-G, Pion SDS, Churcher TS, Breitling LP, Little MP, et al. (2006) River Blindness: A Success Story under Threat? PLoS Med 3(9): e371. doi:10.1371/journal.pmed.0030371 (image link). License: [CC BY 2.5](#)

Ivermectin is active on the following parasites:

- *Onchocerca volvulus*
- *Strongyloides stercoralis*
- *Ascaris lumbricoides*
- *Trichuris trichiura*
- *Enterobius vermicularis*
- Filariasis

Onchocerciasis is caused by ***Onchocerca volvulus*** - the vector is a **black fly** (*Simulium* genus). Humans are the hosts of *Onchocerca volvulus*. The disease is also called **river blindness**. It is most common in **West African savanna** areas and it usually causes blindness by the age of 40–50 years in the affected individuals.

Ivermectin (150 mcg/kg, OD oral route) kills 90 % of the **microfilaria** within 1 week of treatment. However, the therapy needs to be continued for **10–12 years** (throughout the lifespan of the parasite) to kill the parasite. It has a long half-life of 48–60 hours.

Adverse effects are usually the result of the death of the **parasites**. These include fever, headache, mild-pruritus, giddiness, weakness, rash, nausea, abdominal pain, constipation, lethargy joint/muscle pain, **hypotension, tachycardia**, and **edema**. These reactions are mild and last for two days after treatment.

In some patients (1–3 %), the reaction could be severe due to high fever, hypotension, and **bronchospasm**. **Corticosteroids** are given in such cases for the management of adverse effects. Ivermectin is contraindicated in **pregnant and lactating women**.

Bithionol

It is given with triclabendazole to treat the infections (**fascioliasis**) caused by sheep fluke. Mechanism of action is unknown. Fascioliasis is caused by **Fasciola hepatica**.

Drug of Choice for the Treatment of Helminthic Infections

Roundworms (Nematodes)

- **Ascaris lumbricoides:** (mnemonics: PAM) Pyrantel pamoate, Albendazole, Mebendazole
- **Necator americanus:** (PAM) Pyrantel pamoate, Albendazole, Mebendazole
- **Trichuris trichiuria:** Albendazole, Mebendazole
- **Strongyloides stercoralis:** Ivermectin
- **Enterobius vermicularis:** Pyrantel pamoate, Mebendazole
- **Trichinella spiralis:** Mebendazole or Albendazole
- **Cutaneous larva migrans:** Albendazole, Ivermectin
- **Wucheria bancrofti and Brugia malayi:** DEC (Diethylcarbamazine)
- **Onchocerca volvulus:** Ivermectin

Flukes (Trematodes)

- **Schistosoma haematobium:** Praziquantel
- **Schistosoma mansoni:** Praziquantel
- **Schistosoma japonicum:** Praziquantel
- **Paragonimus westermani:** Praziquantel
- **Fasciola hepatica:** Bithionol or Triclabendazole
- **Fasciolopsis buski:** Praziquantel or Niclosamide

Tapeworms (Cestodes)

- **Taenia saginata:** Praziquantel or Niclosamide
- **Taenia solium:** Praziquantel or Niclosamide
- **Cysticercosis:** Albendazole
- **Diphyllobothrium latum:** Praziquantel or Niclosamide
- **Echinococcus granulosus:** Albendazole
- **Loa loa:** DEC

Review Questions

The correct answers can be found below the references.

1. Which of the following is the drug of choice for the treatment of loiasis?

- A. Albendazole
- B. Diethylcarbamazine (DEC)
- C. Praziquantel
- D. Ivermectin
- E. Levamisole

2. Which of the following is the drug of choice for the treatment of filariasis?

- A. Pyrantel pamoate
- B. Diethylcarbamazine (DEC)
- C. Praziquantel
- D. Ivermectin
- E. Levamisole

3. Which of the following parasites cause neurocysticercosis?

- A. Taenia saginata
- B. Taenia solium
- C. Echinococcus granulosus
- D. Wuchereria bancrofti
- E. Onchocerca volvulus

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Correct answers: 1B, 2B, 3B

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