

# Anthelmintics: Ivermectin, Praziquantel, Pyrantel Pamoate, and More

[See online here](#)

**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

Anthelmintics, or antihelminthics, are drugs that kill or expel **parasites**. They are used to treat various diseases caused by parasites, such as helminths.

**Helminths** are categorized as follows:

- **Nematodes** (roundworms)
- **Platyhelminthes** (flatworms)
- **Trematodes** (flukes)
- **Cestodes** (tapeworms)

# Overview of Helminthiasis

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

There are several major causes of helminthiasis:

- Poor **hygiene**.
- 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  
- Own work. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

## 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 occurs in immigrants from these countries. It causes **neurocysticercosis**. The main route of transmission to humans is through eating undercooked pork products. The tapeworm's eggs are ingested by oral-fecal contamination.

**Taenia saginata**, also called beef tapeworm, does not cause neurocysticercosis. Usually, humans get infected with *T. saginata* after eating 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.  
License: [CC BY-SA 4.0](https://creativecommons.org/licenses/by-sa/4.0/)

*E. granulosus*, *E. multilocularis*, *E. vogeli*

The intermediate hosts for this infection are **sheep**, and the primary hosts are **dogs**. Under certain conditions, humans can function as an intermediate host. The larvae may develop into hydatid cysts within the tissues, usually in 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** because different types of snails act as hosts of the genus *Schistosoma*. Infection can occur when a person's skin comes into contact with contaminated water. Complications arise when the body produces **immunological reactions** towards the *Schistosoma* parasite's trapped eggs in various tissues. Eggs reach the **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 the host's mesentery. They produce live embryos, called **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 cause 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 patients, but it can cause **pulmonary complications** (cough, wheezing) and **intestinal obstruction** in severe cases. 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 **neurocysticercosis activity, echinococcosis, ascariasis, hookworm, and trichuriasis**. The drug acts by inhibiting **helminth  $\beta$ -tubulin polymerization**, thus interfering with microtubule-dependent functions, such as glucose uptake, in the helminths.

Albendazole's bioavailability is less than 5% when taken on an empty stomach. Patients should be advised to take the drug with **fatty foods** to enhance absorption. **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 treating multiple infestations and is more efficacious than albendazole against trichuriasis.

The site of action of the drug is the **microtubular protein  $\beta$ -tubulin** of the parasite. It binds to  $\beta$ -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 provides symptomatic relief in **cutaneous larva migrans** cases. It also alleviates the skeletal muscle symptoms produced when ***Trichinella spiralis* larvae** migrate to muscles.

Thiabendazole's action mechanism is similar to albendazole's. 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)

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

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

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

## Praziquantel

Praziquantel is active against **schistosomes**, **cestodes**, and their larval forms, but not nematodes. It causes intracellular calcium to leak from the parasites' cell membranes, producing contracture and paralysis. The paralyzed tapeworms are dislodged from the intestinal mucosa and are expelled from the intestine. **Flukes** and **schistosomes** are also cleared from 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.

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

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

## Piperazine

Piperazine is highly active against **Ascaris and Enterobius infections**, with cure rates of 90–100%. It causes hyperpolarization of worm muscles by opening chloride channels, thus causing relaxation and depressing responsiveness to ACh's contractile action. Flaccid paralysis occurs, and the worms are expelled alive. Piperazine is safe and well-tolerated. The occasional side effects include nausea, vomiting, abdominal discomfort, and urticaria.

## Pyrantel pamoate

This drug is effective against the following helminths:

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

It is a depolarizing neuromuscular blocking agent that causes paralysis in the parasite. It also inhibits 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*, *Diphyllobothrium latum*, and *Hymenolepis nana*, as well as threadworm. The drug inhibits oxidative phosphorylation in the mitochondria and interferes with the anaerobic generation of ATP in the tapeworm. Thus, organisms die from ATP deficiency. However, niclosamide does not kill the ova/larva. It should be used with caution in *T. solium* cases because of an increased risk of visceral cysticercosis.

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



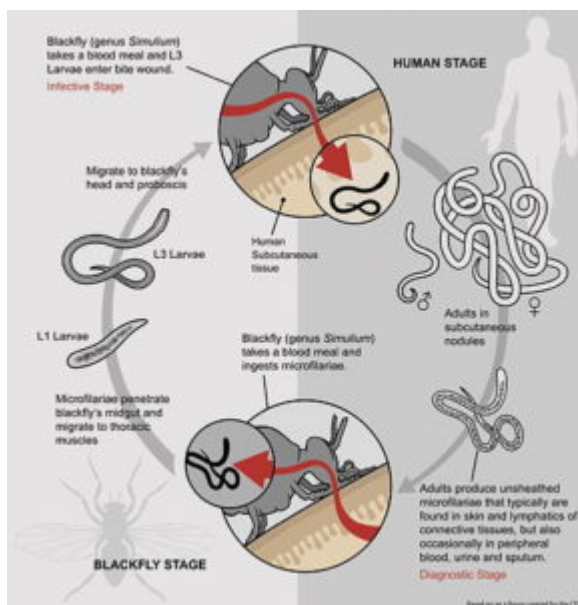
## Levamisole

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. Side effects are unusual but may include nausea, abdominal pain, giddiness, fatigue, drowsiness, or insomnia.

## Ivermectin

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

**Important:** Ivermectin is only effective during 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 against 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 one week of treatment. However, the therapy needs to be continued for **10-12 years** (throughout the parasite's lifespan) to kill the parasite. It has a long half-life of 48-60 hours.

Adverse effects are usually caused by the deaths 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 usually 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 to manage 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 (**fasciola hepatica**). The mechanism of action is unknown.

## 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
- **Cysticercosis:** Albendazole
- **Diphyllobothrium latum:** Praziquantel or Niclosamide
- **Echinococcus granulosus:** Albendazole
- **Loiasis:** DEC

# References

Berger, S. A., & Marr, J. (2006). Human parasitic diseases sourcebook. Jones & Bartlett Learning. PP 465.

Brunton, Laurence L., Bruce Chabner, and Björn C. Knollmann, eds. Goodman & Gilman's the pharmacological basis of therapeutics. Vol. 12. New York: McGraw-Hill Medical, 2011. pp 1468-1484.

Drugbank. [Diethylcarbamazine](#) via drugbank.ca

Howland RD, Mycek MJ, Harvey RA, Champe PC. Lippincott's illustrated reviews: Pharmacology. Philadelphia: Lippincott Williams & Wilkins; 2006.

Medscape. [Albendazole](#) via medscape.com

Medscape. [Ascariasis](#) via medscape.com

Medscape. [Schistosomiasis](#) via medscape.com

Rang, H. P., Ritter, J. M., Flower, R. J., & Henderson, G. (2016). Rang & Dale's Pharmacology. 8<sup>th</sup> Edition. Elsevier Health Sciences.

Stanford. [Glutamate-gated chloride channel – Mechanism of Action](#) via stanford.edu

Tripathi KD. Essentials of Medical Pharmacology, 6<sup>th</sup> Edition. Jaypee Brothers Medical Publishers (P) Ltd. (2008).

Uptodate. [Antihelminthic therapies](#) via uptodate.com

Wolstenholme, A. J. (2012). [Glutamate-gated chloride channels](#). Journal of Biological Chemistry, 287(48), 40232-40238. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23038250>

**Legal Note:** Unless otherwise stated, all rights reserved by Lecturio GmbH. For further legal regulations see our [legal information page](#).

Notes