Anthelmintic drugs

✓ Worms that infect humans.
  o Nematodes (roundworms)
  o Trematodes (flukes)
  o Cestodes (tapeworms)

▪ Most anthelmintics target:
  ✓ Eliminating the organisms from the host.
  ✓ Controlling spread of infections.

CHEMOTHERAPY OF HELMINTIC INFECTIONS: FOR NEMATODES
- Diethylcarbamazine BANOCIDE
- Ivermectin STROMECTOL
- Mebendazole VERMOX
- Pyrantel pamoate PIN-X
- Thiabendazole MINTEZOL

CHEMOTHERAPY OF HELMINTIC INFECTIONS: FOR TREMATODES
- Praziquantel BILTRICIDE

CHEMOTHERAPY OF HELMINTIC INFECTIONS: FOR CESTODES
- Albendazole ALBENZA
- Niclosamide
Drugs for the treatment of nematodes

• Nematodes are elongated roundworms

• Possess a complete digestive system.

• They cause infections of the:
  ▪ Intestine
  ▪ Blood
  ▪ Tissues
Drugs for the treatment of nematodes

- **Mebendazole**
  
  ✓ Acts by inhibiting the assembly of the microtubules in the parasite.
  
  ✓ Irreversibly blocking glucose uptake.
  
  ✓ Affected parasites are expelled in the feces.
  
  ➢ **Adverse effects**: include abdominal pain and diarrhea.
  
  • Mebendazole **should not** be used in pregnant women.
Pyrantel pamoate

- Pyrantel pamoate is poorly absorbed orally
- Exerts its effects in the intestinal tract.
- It acts as a depolarizing, neuromuscular-blocking agent,
- Causing release of acetylcholine
- Inhibition of cholinesterase
- leading to paralysis of the worm.
- The paralyzed worm releases its hold on the intestinal tract and is expelled.

- Adverse effects are mild and include nausea, vomiting, and diarrhea.
Ivermectin

- Targets the glutamate-gated chloride channel receptors.
- Chloride influx is enhanced, and hyperpolarization occurs, resulting in paralysis and death of the worm.
- The drug is given orally and does not readily cross the blood–brain barrier.
- Ivermectin **should not** be used in pregnancy.
- The killing of the microfilaria in onchocerciasis can result in a dangerous Mazzotti reaction (fever, headache, dizziness, hypotension).
- **The severity of this reaction is related to parasite load.**
- Antihistamines or steroids may be given to ameliorate the symptoms.
Diethylcarbamazine

- Diethylcarbamazine is the drug of choice for filariasis.
- It kills the microfilariae and has activity against adult worms.
- Diethylcarbamazine is rapidly absorbed following oral administration with meals and is excreted mainly in the urine.
- **Adverse effects:**
  - include fever, nausea, vomiting, arthralgia, and headache.
  - Diethylcarbamazine can accelerate blindness and cause severe Mazzotti reactions in patients with onchocerciasis.
  - It should be avoided in patients with this disorder.
Avoid in pregnancy

Albendazole
Ivermectin
Mebendazole
Thiabendazole
Characteristics of and therapy for commonly encountered nematode infections

**Onchocerciasis (River Blindness)**
- **Causative agent:** Onchocerca volvulus.
- Common in areas of Mexico, South America, and tropical Africa.
- Characterized by subcutaneous nodules, a pruritic skin rash, and ocular lesions often resulting in blindness.
- **Therapy:** Ivermectin.

**Trichuriasis (Whipworm Disease)**
- **Causative agent:** Trichurus trichiura.
- Infection is usually asymptomatic; however, abdominal pain, diarrhea, and flatulence can occur.
- **Therapy:** Mebendazole.

**Enterobiasis (Pinworm Disease)**
- **Causative agent:** Enterobius vermicularis.
- Most common helminthic infection in the United States.
- Pruritus ani occurs, with white worms visible in stools or perianal region.
- **Therapy:** Mebendazole or pyrantel pamoate.

**Ascariasis (Roundworm Disease)**
- **Causative agent:** Ascaris lumbricoides.
- Second only to pinworms as the most prevalent multicellular parasite in the United States; approximately one-third of the world's population is infected with this worm.
- Ingested larvae grow in the intestine, causing abdominal symptoms, including intestinal obstruction; roundworms may pass to blood and infect the lungs.
- **Therapy:** Pyrantel pamoate or mebendazole.

**Hookworm Disease**
- **Causative agents:** Ancylostoma duodenale (Old World hookworm), Necator americanus (New World hookworm).
- Worm attaches to the intestinal mucosa, causing anorexia, ulcer-like symptoms, and chronic intestinal blood loss that leads to anemia.
- **Therapy:** Pyrantel pamoate or mebendazole.

**Strongyloidesis (Threadworm Disease)**
- **Causative agent:** Strongyloides stercoralis.
- Relatively uncommon compared with other intestinal nematodes; a relatively benign disease in normal individuals that can progress to a fatal outcome in immune-compromised patients.
- **Therapy:** Ivermectin.

**Filariasis**
- **Causative agents:** Wuchereria bancrofti, Brugia malayi.
- Worms cause blockage of lymph flow. Ultimately, local inflammation and fibrosis of the lymphatics occurs.
- After years of infestation, the arms, legs, and scrotum fill with fluid, causing elephantiasis.
- **Therapy:** A combination of diethylcarbamazine and albendazole.

**Trichinosis**
- **Causative agent:** Trichinella spiralis.
- Usually caused by consumption of insufficiently cooked meat, especially pork.
- **Therapy:** Albendazole or mebendazole.
Drugs to treat trematodes

• The trematodes (flukes) are leaf-shaped flatworms.
• Characterized by the tissues they infect:
  o liver
  o lung
  o Intestinal
  o Blood.
Drugs to treat trematodes

- **Praziquantel**
  - Praziquantel is an agent of choice for the treatment of all forms of schistosomiasis, other trematode infections,
  - Cestode infections such as taeniasis.
- Permeability of the cell membrane to calcium is increased, causing contracture and paralysis of the parasite.
- Praziquantel should be taken with food and not chewed due to a bitter taste.
- It is rapidly absorbed after oral administration and distributes into the cerebrospinal fluid (CSF).
- The drug is extensively metabolized, and the inactive metabolites are excreted primarily in the urine.
- Common adverse effects include dizziness, malaise, and headache as well as gastrointestinal upset.
- Praziquantel is contraindicated for the treatment of ocular cysticercosis, because destruction of the organism in the eye may cause irreversible damage.
Characteristics of and therapy for commonly encountered trematode infections

**Paragonimiasis**
- This disease is caused by *Paragonimus westermani* (lung fluke). The organisms move from the gastrointestinal tract to the lung, which is the primary site of damage. Secondary bacterial infections can result in a cough that produces bloody sputum.
- The disease is transmitted by eating raw crab meat.
- Paragonimiasis is diagnosed by identifying eggs in the sputum and stool.
- Therapy: *Praziquantel*.

**Schistosomiasis (New World)**
- This disease is caused by *Schistosoma mansoni* and *Schistosoma japonicum*. The primary site of infection is the gastrointestinal tract. Damage to the intestinal wall is caused by the host's inflammatory response to eggs deposited at that site. The eggs also secrete proteolytic enzymes that further damage the tissue.
- Clinical presentation includes GI bleeding, diarrhea, and liver damage.
- The disease is transmitted by direct skin penetration.
- This form of schistosomiasis is diagnosed by identification of characteristic eggs in the stool.

**Clonorchiasis**
- This disease is caused by *Clonorchis sinensis* (Oriental liver fluke). The primary site of infection is the biliary tract, where the resulting inflammatory response can cause fibrosis and hyperplasia.
- The disease is transmitted by eating raw freshwater fish.
- Clonorchiasis is diagnosed by identifying eggs in the stool.
- Therapy: *Praziquantel*.

**Schistosomiasis (Old World)**
- This disease is caused by *Schistosoma haematobium*. The primary sites of infection are veins of the urinary bladder, where the organism's eggs can induce fibrosis, granulomas, and hematuria.
- The disease is transmitted by direct skin penetration.
- This form of schistosomiasis is diagnosed by identifying characteristic eggs in the urine or bladder wall.
- Therapy: *Praziquantel*. 
Drugs to treat cestodes

• The cestodes, or “true tapeworms,” typically have a flat, segmented body and attach to the host’s intestine.

• Like the trematodes, the tapeworms lack a mouth and a digestive tract throughout their life cycle.
Drugs to treat cestodes

Niclosamide

- It inhibits the mitochondrial phosphorylation of adenosine diphosphate (ADP) in the parasite, making it lethal.
- Anaerobic metabolism may also be inhibited.
- A laxative is administered prior to oral administration to purge the bowel of all dead segments and to enhance digestion and liberation of the ova.
Characteristics of and therapy for commonly encountered cestode infections.

**Echinococcosis**
- This disease (also called hydatid disease) is caused by Echinococcus granulosus (dog tapeworm). Infection produces large, hydatid cysts in the liver, lung, and brain. Anaphylactic reaction to worm antigens can occur if the cyst ruptures.
- The disease follows ingestion of eggs in dog feces. Sheep often serve as an intermediate host.
- Echinococcosis is diagnosed by CT scan or biopsy of infected tissue and is treated by surgical excision of cysts.
- Therapy: Praziquantel, albendazole, and/or surgery.

**Cysticercosis**
- This disease is caused by Taenia solium larvae. Infection produces cysticerci in the brain (causing seizures, headache, and vomiting) and in the eyes.
- The disease follows ingestion of eggs from human feces.
- Cysticercosis is diagnosed by CT scan or biopsy.
- Therapy: Praziquantel, albendazole, and/or surgery.

**Taeniasis**
- This disease is caused by the larval form of Taenia saginata (beef tapeworm). The organism primarily infects the intestines and does not produce cysticerci. Most infected individuals are asymptomatic.
- The disease is transmitted by larvae in undercooked or raw beef.
- Taeniasis is diagnosed by detection of proglottids in stools.
- Therapy: Albendazole.

**Diphyllobothriasis**
- This disease is caused by Diphyllobothrium latum (fish tapeworm). The adult worm in a host's intestine can be as long as 15 meters.
- The disease is transmitted by larvae in raw or undercooked fish.
- Diphyllobothriasis is diagnosed by detection of characteristic eggs in stools.
- Therapy: Praziquantel or niclosamide.
Albendazole

• Absorbed after oral administration.
• Absorption is enhanced by a high-fat meal.
• The drug distributes widely, including the CSF.
• It undergoes extensive first-pass metabolism, including formation of an active sulfoxide.