

No.6



Pharmacology

| Modified slides

Writer: Sara Haroon

Corrector: Alaa Bany Amer

Doctor: Munir Gharaibeh

Pancreatic Enzymes

As you know pancreas releases many digestive enzymes such as lipases to digest lipids, amylase to digest starch or carbs and proteases for proteins digestion. In chronic diseases of the pancreas or after surgical removal of the pancreas we will need to replace these enzymes because deficiency of them would lead to indigestion.

- **These medications contain digestive enzymes to help break down and digest fats, starch, and proteins in food.**
- **Extracts of hog pancreas.** They're not synthetic compounds
- **Used in conditions where the pancreas cannot make or does not release enough digestive enzymes into the small intestines to digest the food (e.g., chronic pancreatitis, cystic fibrosis, cancer of the pancreas, post-pancreatectomy, post-gastrointestinal bypass surgery).**

Pancrelipase

- **Available in sizes with different amounts of lipase, amylase and protease.** So we can adjust the amount of these enzymes according to the patient's need
- **Dose should be adjusted according to age, weight, degree of pancreatic insufficiency** some patients have partial pancreatic insufficiency not 100% so dosage should be adjusted otherwise there will be many side effects , **and the amount of dietary fat intake.**

Pancrelipase

- **Taken with plenty of fluids.**
- **Used regularly to get the most benefit from it.**
- **Taken with every meal or snack.**

Pancrelipase

- **Side Effects:**
- **Diarrhea**(when the amount of lipase is high) , **constipation, headache, abdominal pain/cramps/bloating**
(because they work locally so we expect these side effects), **gas, dizziness, cough, nausea, or vomiting.**
- **May cause mucositis if not swallowed quickly.**
- They will start digesting tissues of the oral cavity, pharyngeal cavity, esophagus and stomach because they have proteases and tissues mostly consist of proteins so they might cause mycositis or inflammation of the epithelial lining of the GI tract.

Bile Acid therapy for Gallstones

- **Ursodiol:**

- **Naturally occurring bile acid, from bears.**
- **Absorbed in the g.i.t. and conjugated in the liver with glycine or taurine, and excreted in the bile.**
- **Blocks hepatic cholesterol synthesis and thereby decreases secretion of cholesterol by the liver and the amount of cholesterol in bile, eventually formation of gallstones will be decreased**
- **Also, stabilizes hepatocyte canalicular membranes.**

In certain conditions of the gallbladder like gallbladder stones which are usually formed by cholesterol crystals and we might need to dissolve these crystals. Of course the best treatment is surgical removal of gallbladder, cholecystectomy used to be a major surgery with very long incision, but nowadays cholecystectomy is performed easily through 3 small incisions (laparoscopic surgery) and another method is to dissolve these gallstones by bile acid therapy

Ursodiol

• Clinical Uses:

- **To dissolve small cholesterol gallstones in patients who refuse cholecystectomy or who are poor surgical candidates.** They might help a bit but again standard treatment for gallstones nowadays is cholecystectomy.
- **Mild cases**
- **Prevention of gallstones in obese patients.** Obese patients are viable for forming gallstones, so we can use this drug as a prophylactic treatment
- **Early stage biliary cirrhosis.**
- **Free of side effects.**

Risk factors for developing gallstones (5fs):

- Forty
- Fatty
- Female
- Fertile
- Fair (gallstones more common in Caucasians) [this one wasn't mentioned by the doctor]

Antiprotozoal Agents

Metronidazole(Flagyl) **Tinidazole**

Penetrate protozoal and bacterial cells but not mammalian cells.

Work as an electron sink, so, reduced at 5-nitro group by the enzyme Nitroreductase, which is only found in anaerobic organisms.

The reduced molecule disrupts replication and transcription and inhibits DNA repair.

- Most important protozoa are those which cause malaria (plasmodium) and amoeba that is very common in developing countries especially among restaurants' workers, usually restaurants' workers are the ones who transmit amoeba to others, of course it can be transmitted in households within a family or in schools and nursery schools but restaurants' workers are the most important.

Metronidazole (flagyl) >> trade name

Spectrum of Activity: (wide spectrum of activity)

E. histolytica

G. lamblia

T. vaginalis

Blastocystis hominis

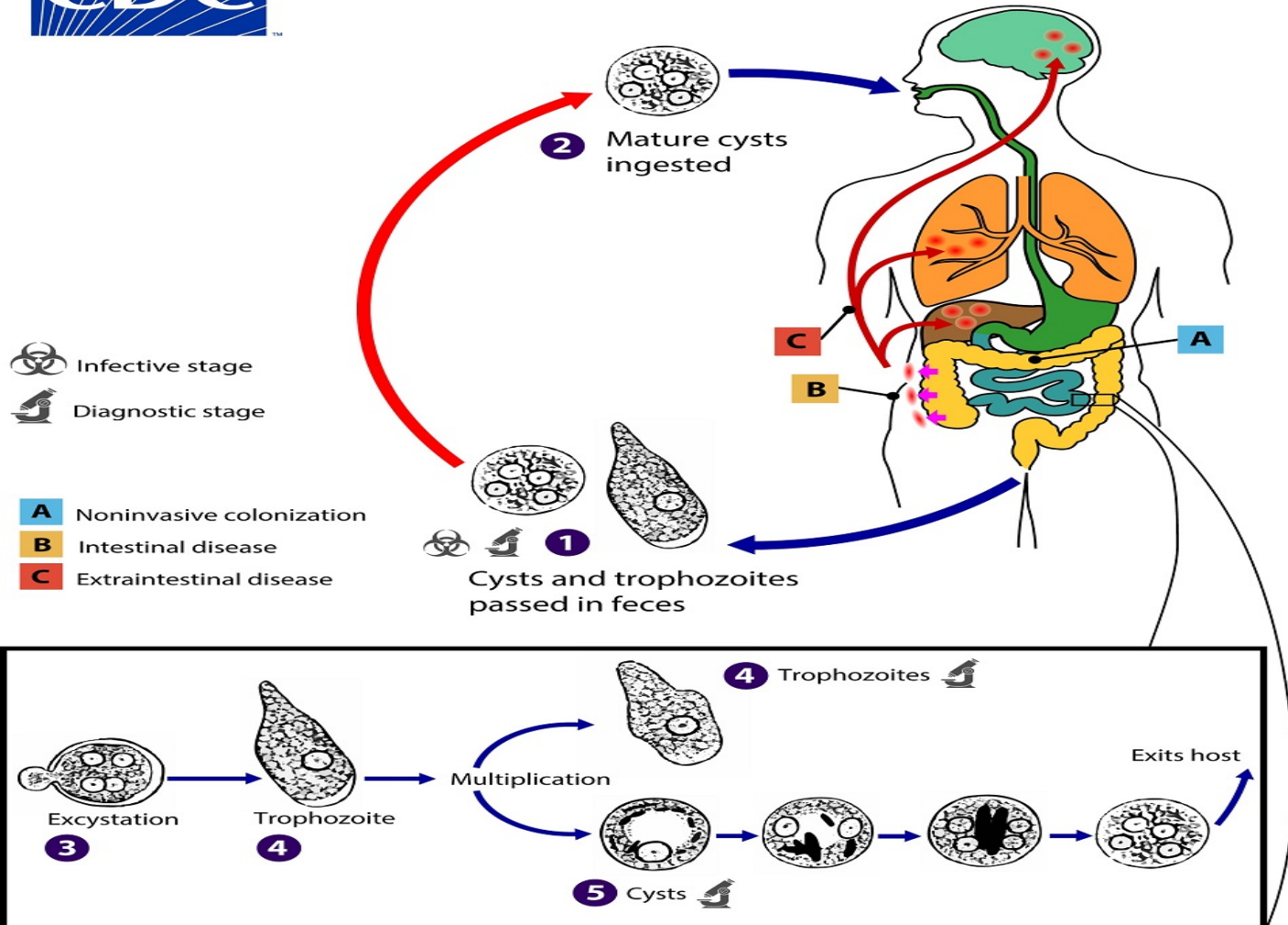
B. coli

Dracunculus medinensis

Also, anaerobic G+ve and G-ve bacteria

Resistance is rare.

Metronidazole is an old drug but still used until now, typically it's an anti-protozoal drug but nowadays it was proved to be very effective against anaerobic gram positive and gram negative bacteria, especially in the oral cavity, dentists for example prescribe amoxicillin and metronidazole as a second drug of choice.



Ameoba affects mainly the GI tract, it might cause severe acute inflammation and severe acute amoebiasis with diarrhea, fever and other manifestations but it might also go through portal circulation to the liver and cause hepatic amoebiasis and from the liver it might go to the lungs or the brain. Infected person would shed cysts and trophozoites and these are the infective sources for other people.

Metronidazole

Kinetics:

Good absorption and distribution,

$t_{1/2}$ 8h.

An advantage of metronidazole is that its half life not short and not too long so it can be given twice or three times daily

Metabolized by oxidation and glucucuronide formation.

It doesn't interfere with enzyme CYP450 function

Metronidazole

Clinical Uses:

All forms of amebiasis, except for the cyst passers (**Diloxanide Furoate, Paromomycin or diiodohydroxyquin**).
Giardiasis.

- **Trichomoniasis.** (Very common among women)
Anaerobic bacterial infection(in dentistry).
***D. medinensis* (guinea worm).**

*Cyst passers are asymptomatic patients who shed cysts and can transmit amoeba to other people, metronidazole can not kill cysts so we use the other mentioned drugs for them

Larvae undergoes two molts in the copepod and becomes a L3 larvae. **6**

Human drinks unfiltered water containing copepods with L3 larvae. **1**

Dog eats infected fish

Larvae are released when copepods die. Larvae penetrate the host's stomach and intestinal wall. They mature and reproduce.

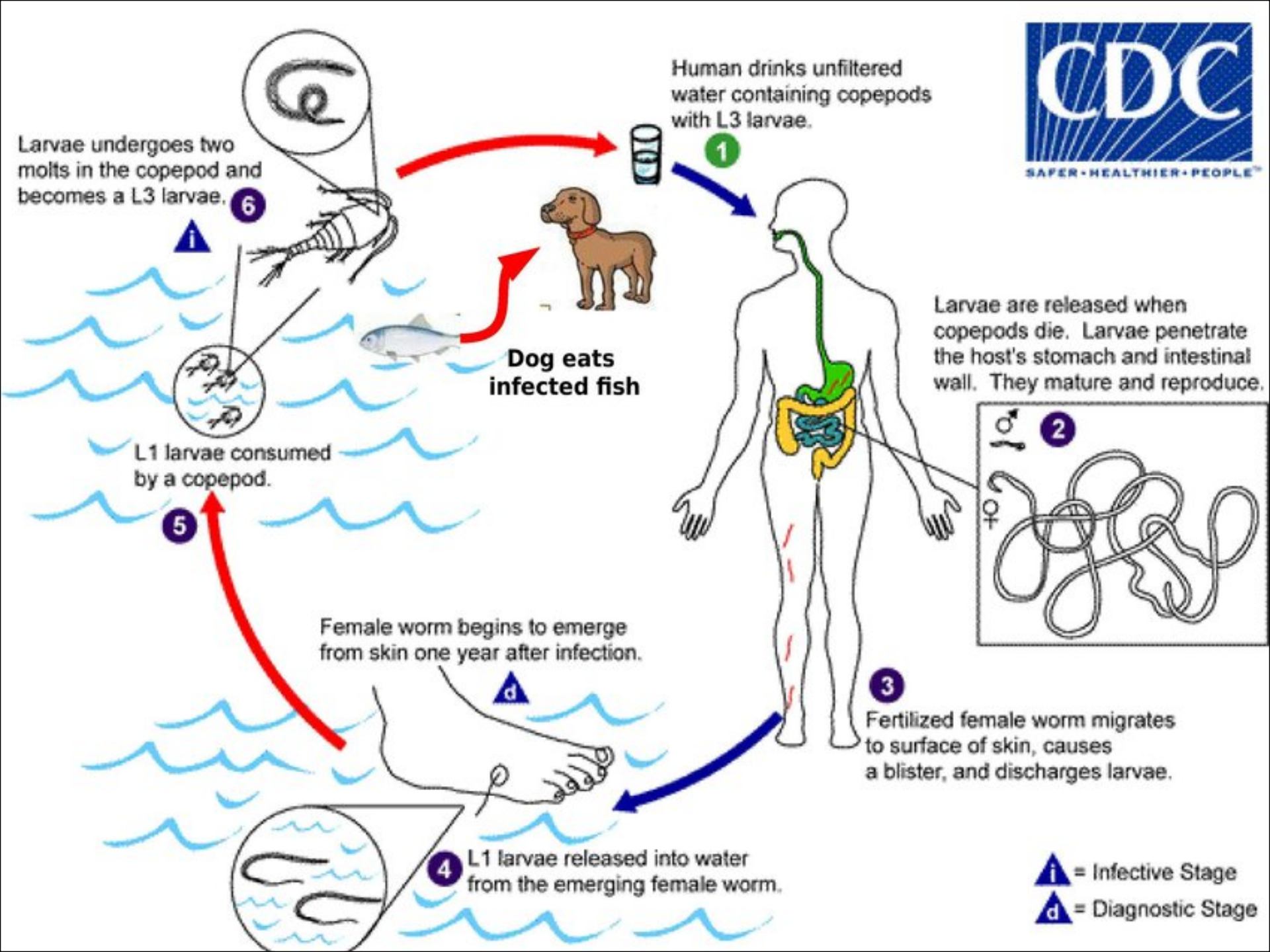
L1 larvae consumed by a copepod. **5**

Female worm begins to emerge from skin one year after infection. **d**

Fertilized female worm migrates to surface of skin, causes a blister, and discharges larvae. **3**

L1 larvae released into water from the emerging female worm. **4**

i = Infective Stage
d = Diagnostic Stage



Metronidazole

Adverse Reactions:

Nausea, headache, dry mouth and *metallic taste*.

Urine discoloration (very dark color that resembles jaundice).

Vertigo, unsteadiness, ataxia, paresthesia, neuropathy, encephalopathy.

Neutropenia.

Disulfiram-like reaction.

- **Tinidazole is better tolerated.** (It's more expensive than flagyl)

Disulfiram is a drug used as a support treatment of alcoholism, when the patient consumes alcohol it will cause very unpleasant reaction, this reaction is caused by disulfiram not by alcohol but the patient would think that consuming alcohol is the reason behind this reaction so he/she would stay away from alcohols and **metronidazole** can cause a similar reaction if alcohols were consumed during the course of treatment and that's what we mean by **disulfiram-like reaction**.

Diloxanide Furoate

- Effective luminal amebicide (luminal cyst).
- Mechanism unknown.
- Drug of choice for asymptomatic cyst passers.
- Flatulence, nausea, cramps, rashes.

Antibiotics

Erythromycin

Tetracycline

Alter bacterial flora and prevent secondary infection.

- Lesions of amoeba often surrounded by bacterial infection (non specific bacterial lesion) so you have to treat this bacterial lesion and reduce the bacterial load with these antibiotics

Paromomycin:

Aminoglycoside.

- Aminoglycosides are usually given intravenously or intramuscularly but paromomycin is given **orally** to treat intestinal bacteria

Direct action on ameba in the lumen.

Anthelmintic and for visceral leishmaniasis.

Anthelmintic Drugs

Albendazole:

Broad spectrum, which inhibits microtubule synthesis.

- Hydatid disease. (*Echinococcus granulosus*)
- Cysticercosis: usually given with corticosteroids to decrease inflammation caused by dying organisms.
- Pinworm.
- Hookworm. (*Ancylostoma*)
 - it's one of the causes of severe anemia (iron deficiency anemia)
- Ascariasis. (Very common)
- Trichuriasis.
- Strongyloidiasis.
- Others

Anthelmintics

Ivermectin:

Strongyloidosis:

Paralyzes nematodes and arthropods by intensifying GABA mediated transmission of signals in peripheral nerves.

- Onchocerciasis:

Blocks the release of microfilaria for some months after therapy.

Also effective in controlling scabies (الجرب), lice (القمل), and cutaneous larva migrans.

Inhibitory ~~neuro transmitter~~ neuron



Ivermectin

Mazotti Reaction:

Occurs in 5-30% of patients, usually mild.

Due to killing of microfilaria.

Fever, headache, dizziness, somnolence, weakness, rash, pruritus, diarrhea, joint and muscle pains, hypotension, tachycardia

Anthelmintics

Mebendazole:

- **Wide spectrum.**
- **Inhibits microtubule synthesis.**
- **Ascariasis.**
- **Trichuriasis.**
- **Hookworm.**
- **Pinworm. (ENTEROBIUS VERMICULARIS)**
- **Tablets chewed before swallowing.**
- **Safe drug.**

Anthelmintics

Niclosamide:

Second-line drug for most tapeworm (taenia) infections.

- **Kills adult worms, but not the ova.**
- **Works by inhibition of oxidative phosphorylation.**
- **2 gm single dose on an empty stomach, chewed and swallowed.**

Purgative needed. To expel the worm out from the body

Anthelmintics

Piperazine: (old drug)

- Ascariasis.
- Causes paralysis by blocking acetylcholine, worms expelled by normal peristalsis.

70 mg/day for 2-8 days.
Or, repeat after 2 weeks.

Anthelmintics

Praziquantel:

- **Schistosomes, all species, drug of choice.**
- **Trematodes: Clonorchiasis, Opisthorchiasis and Paragonimiasis**
- **Cestodes including cysticercosis.**
- **Increases permeability of the worm to calcium, resulting in paralysis, dislodgment and death.**
- **Mild and transient adverse effects, except for neurocysticercosis.**

Anthelmintics

Pyrantel Pamoate:

Broad spectrum:

Pinworm.

Ascaris.

Trichostrongylus orientalis.

Hookworms.

***But not for taenia**

Effective within the intestinal tract, not in the tissues or against the ova.

Works as a neuromuscular blocker.

11 mg/kg, single dose

***doses are not required**