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**COURSE: PHA 312**

ASSIGNMENT

1. Draw and explain the life cycle of the malaria parasite.
2. Mention two major classification of antiamoebic drugs
3. Highlight the name of the drugs used under each group and give appropriate examples.
4. Explain vividly the mechanism of action of Metronidazole
5. The malaria parasite life cycle involves two hosts. During a blood meal, a malaria-infected female Anopheles mosquito inoculates sporozoites into the human host

Sporozoites infect liver cells and mature into schizonts, which rupture

and release merozoites . (Of note, in P. vivax and P. ovale a dormant stage [hypnozoites] can persist in the liver and cause relapses by invading the bloodstream weeks, or even years later.) After this initial replication in the liver (exo-erythrocytic schizogony ), the parasites undergo asexual multiplication in the erythrocytes (erythrocytic schizogony ). Merozoites infect red blood cells. The ring stage trophozoites mature into schizonts, which rupture releasing merozoites . Some parasites differentiate into sexual erythrocytic stages (gametocytes). Blood stage parasites are responsible for the clinical manifestations of the disease.The gametocytes, male (microgametocytes) and female (macrogametocytes), are ingested by an Anopheles mosquito during a blood meal. The parasites’ multiplication in the mosquito is known as the sporogonic cycle C. While in the mosquito's stomach, the microgametes penetrate the macrogametes generating zygotes . The zygotes in turn become motile and elongated (ookinetes)  which invade the midgut wall of the mosquito where they develop into oocysts. The oocysts grow, rupture, and release sporozoites, which make their way to the mosquito's salivary glands. Inoculation of the sporozoites into a new human host perpetuates the malaria life cycle.



**Classification of antiamoebic drugs**

* Nitroimidazole derivative
* Dichloroacetamide derivatives

**- Nitroimidazole derivatives**

* [Metronidazole,](http://howmed.net/pharmacology/metronidazole/) eg. Flagyl
* Tinidazole, eg Fasigen & Tindamax
* Secnidazole eg Solosec

Benznidazole, eg Rochagan, Radanil

* Ornidazole, eg Albitrol, Alor, Bitazol, Entamizole plus.
* Nimorazole eg Naxogin
* **Dichloroacetamide derivatives**
* Diloxanide furoate eg Amicline, Furamide (also used with [metronidazole](http://howmed.net/pharmacology/metronidazole/) called entomazale)
* Clefamide, eg Mebinol
* Teclozan, eg Falmonax. Falmonaz 500
* Etofamide eg Kitnos Forte

1. MECHANISM OF ACTION OF METRONIDAZOLE

Metronidazole diffuses into the organism, inhibits protein synthesis by interacting with DNA and causing a loss of helical DNA structure and strand breakage. Therefore, it causes cell death in susceptible organisms.

The mechanism of action of metronidazole occurs through a four-step process. Step one is the entry into the organism by diffusion across the cell membranes of anaerobic and aerobic pathogens. However, antimicrobial effects are limited to anaerobes.Step two involves reductive activation by intracellular transport proteins by altering the chemical structure of pyruvate-ferredoxin oxidoreductase. The reduction of metronidazole creates a concentration gradient in the cell that drives uptake of more drug and promotes free radical formation that is cytotoxic. Step three, interactions with intracellular targets, is achieved by cytotoxic particles interacting with host cell DNA resulting in DNA strand breakage and fatal destabilization of the DNA helix. Step four is the breakdown of cytotoxic products. Metronidazole is also cytotoxic to facultatively anaerobic bacteria like*Helicobacter pylori* and *Gardnerella vaginalis*, but the mechanism of action to these pathogens is not well understood.