NAME: SHEHU SAFIYA AHMAD

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ASSIGNMENT

QUESTIONS;

1. Draw and explain the life cycle of malaria parasite.
2. Mention two major classification of antiamoebic drugs.
3. Highlighting the names of drugs under each group and give appropriate examples.
4. Explain vividly the mechanism of action of metronidazole.

ANSWERS;

1. The infection is initiated by the bite of a female anopheles mosquito, which introduce the parasite(sporozoites) into the blood. From the blood the sporozoite migrate to the liver cell and mature into schizonts. The schizonts develops and eventually rupture and release merozoites (some may enter further into liver cells and become resting form of parasite hypnozoites which cause relapses by invading the blood stream weeks or even years after if not treated). The merozoites enters the red blood cells and form motile trophozoites. The ring stage trophozoites mature into schizonts, which rupture releasing merozoites. Some parasites differentiate into sexual erythrocytic stages (gametocytes). The blood stage parasites are responsible for the clinical manifestation of the disease.



Life cycle of malaria parasite

1. Tissue amoebicides and luminal amoebicides
2. Tissue amoebicides;
	1. For both intestinal and extra intestinal amoebiasis:
		1. Nitroimidazole; e.g metronidazole, tinidazole, secnidazole, ornidazole and santranidazole.
		2. Alkaloids; e.g emitine and dehydroemitine.
	2. For extra intestinal amoebiasis only; chloroquine.

Luminal amoebicides;

1. Amides; e.g diloxanide furoate and nitazoxanide
2. 8’hydroxylquinolines; e.g diiodohydroxyquin and iodochlorhydroxyquin
3. Antibiotics; e.g tetracycline, oxytetracycline, erythromycin and paromomycin.
4. Mechanism of action of metronidazole:

Metronidazole is a prodrug that is activated by reduction of the nitro group by susceptible organisms. It has broad spectrum cidal activity against many anaerobic protozoans and microaerophilic pathogens such as Trichomonas vaginalis, Entamoeba histolytica, and Giardia lamblia and anaerobic bacteria. Anaerobic microbes contain electron transport components that have a sufficiently negative redox potential to donate electrons to metronidazole. Electron transfer forms a highly reactive nitro radical anion that kills susceptible organisms by radical-mediated mechanisms that target DNA. Metronidazole is catalytically recycled; loss of the active metabolite’s electron regenerates the parent compound. Increasing levels of oxygen inhibit metronidazole-induced cytotoxicity because oxygen competes with metronidazole for electrons generated by energy metabolism. Thus, oxygen can both decrease reductive activation of metronidazole and increase recycling of activated drug. In susceptible organisms, pyruvate decarboxylation, catalyzed by pyruvate:ferredoxin oxidoreductase (PFOR), produces electrons that reduce ferredoxin, which then catalytically donates electrons to biological electron acceptors or to metronidazole.