Azi ngozi Stephanie 16/mhs07/008 Pharmacology



Lifecycle

The natural history of malaria involves cyclical infection of humans and female Anopheles mosquitoes. In humans, the parasites grow and multiply first in the liver cells and then in the red cells of the blood. In the blood, successive broods of parasites grow inside the red cells and destroy them, releasing daughter parasites ("merozoites") that continue the cycle by invading other red cells.

The blood stage parasites are those that cause the symptoms of malaria. When certain forms of blood stage parasites (gametocytes, which occur in male and female forms) are ingested during blood feeding by a female Anopheles mosquito, they mate in the gut of the mosquito and begin a cycle of growth and multiplication in the mosquito. After 10-18 days, a form of the parasite called a sporozoite migrates to the mosquito's salivary glands. When the Anopheles mosquito takes a blood meal on another human, anticoagulant saliva is injected together with the sporozoites, which migrate to the liver, thereby beginning a new cycle.

Thus the infected mosquito carries the disease from one human to another (acting as a "vector"), while infected humans transmit the parasite to the mosquito, In contrast to the human host, the mosquito vector does not suffer from the presence of the parasites.

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 (if untreated) 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 . 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 amebicidal drugs

1. Luminal amebicides

Acts on parasite in the lumen of bowel

Examples:

- 1. Diloxanide furoate
- 2. lodoquinol
- 3. Paromycin
- 2. Systemic amebicide

Against amebas in intestinal wall and liver Examples:

- 1. Tinidazole
- 2. Metronidazole
- 3. Chloroquine
- 4.Emetine
- 5. Dehydroemetine

Mixed amebicides

Against both the the Luminal and systemic form of disease

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.