

CHAPTER –III

ANTIMALARIAL, ANTIPROTOZOAL

AND ANTHELMINTIC

DRUGS

YEAR III Pharm.D
Dr. V. Chitra

Protozoal Infections

Parasitic protozoa: live in or on humans

- Malaria
- Leishmaniasis
- Amebiasis
- Giardiasis
- Trichomoniasis

Malaria

- Caused by *Plasmodium* protozoa – 4 different species
- Cause: the bite of an **infected** adult female anopheline mosquito
- Also transmitted by **infected individuals via blood transfusion, congenitally, or infected needles by drug abusers**

Malarial Parasite (*Plasmodium*)

Two interdependent life cycles

- Sexual cycle: occurs in the mosquito
- Asexual cycle: occurs in the human
- Knowledge of the life cycles is essential in understanding antimalarial drug treatment
- Drugs are effective only during the asexual cycle

Plasmodium Life Cycle

Asexual cycle: two phases

□ **Exoerythrocytic phase**

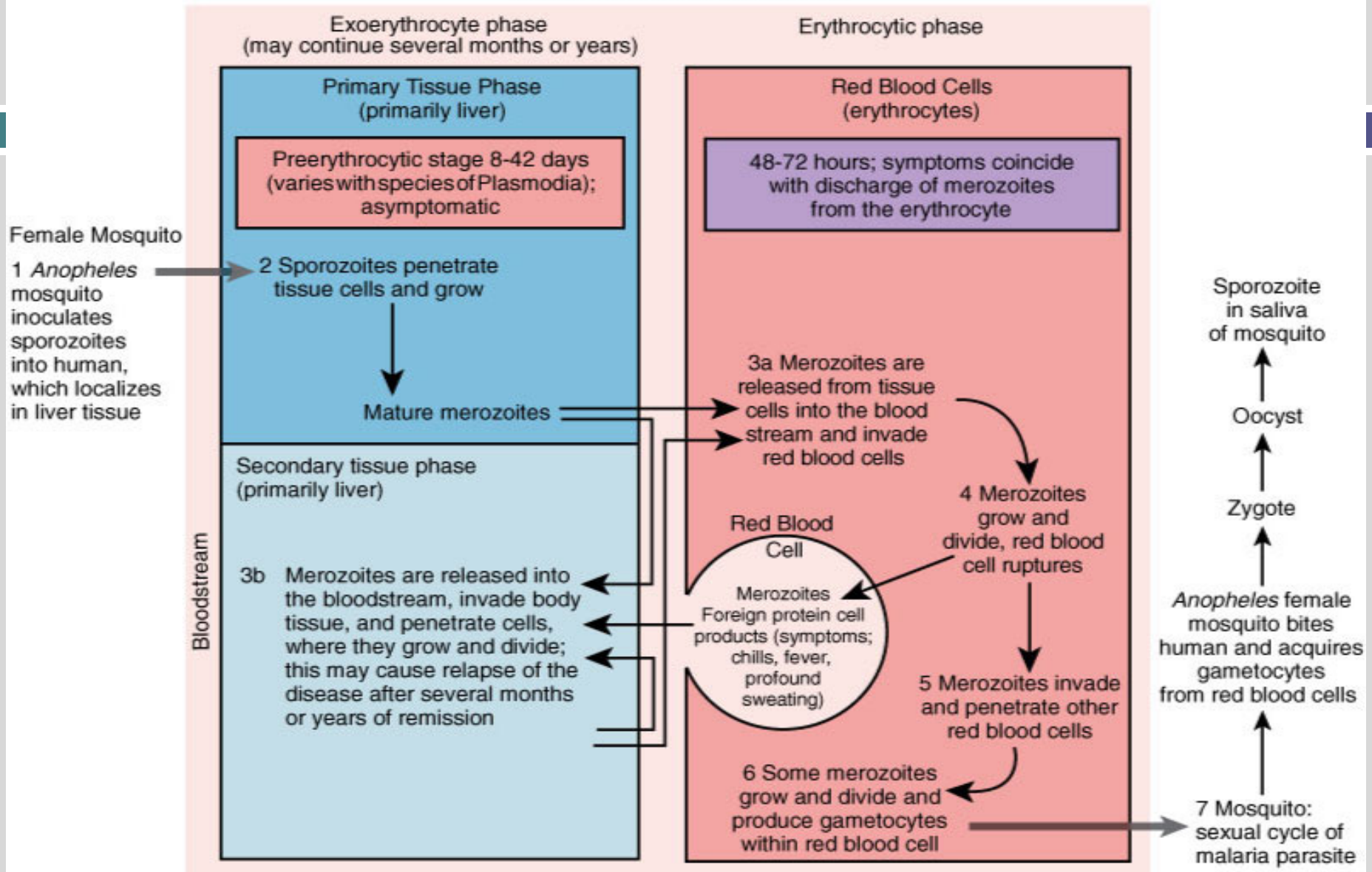
- ▣ Occurs “outside” the erythrocyte
- ▣ Also known as the tissue phase

□ **Erythrocytic phase**

- ▣ Occurs “inside” the erythrocyte
- ▣ Also known as the blood phase

Erythrocytes = RBCs

Human
Asexual cycle of malarial parasite



(From McKenry LM, Salerno E: Mosby's pharmacology in nursing—revised and updated, ed 21, St Louis, 2003, Mosby.)

Fig. 42-1. Life cycle of the malarial parasite.

Antimalarial Drugs

- Attack the parasite during the asexual phase, when it is vulnerable
 - Erythrocytic phase drugs: chloroquine, hydroxychloroquine, quinine, mefloquine
 - Primaquine: kills parasite in both phases
- May be used together for synergistic or additive killing power

Antimalarials:

Mechanism of Action

4-Aminoquinoline derivatives: chloroquine and hydroxychloroquine

- Bind to parasite nucleoproteins and interfere with protein synthesis; also alter pH within the parasite
- Interfere with parasite's ability to metabolize and use erythrocyte hemoglobin
- Effective only during the erythrocytic phase

Antimalarials:

Mechanism of Action

4-Aminoquinoline derivatives: quinine and Mefloquine (Lariam)

- Alter pH within the parasite
- Interfere with parasite's ability to metabolize and use erythrocyte hemoglobin
- Effective only during the erythrocytic phase

Antimalarials:

Mechanism of Action

Diaminopyrimidines (pyrimethamine (Daraprim) & trimethoprim)

- Inhibit protein synthesis essential for growth and survival
- Only effective during the erythrocytic phase
- These drugs may be used with sulfadoxine or dapsone or synergistic effects

Antimalarials:

Mechanism of Action

□ Primaquine

- ▣ Only exoerythrocytic drug (works in both phases)
- ▣ Binds and alters parasitic DNA

□ Sulfonamides, tetracyclines, clindamycin

- ▣ Used in combination with antimalarials to increase protozoacidal effects

Antimalarials

Drug Effects

- Kill parasitic organisms
- Chloroquine and hydroxychloroquine also have antiinflammatory effects

Indications

- Kills *Plasmodium* organisms, the parasites that cause malaria
- The drugs have varying effectiveness on the different malaria organisms
- Some drugs are used for prophylaxis against malaria
 - 2 weeks prior and 8 weeks after return
- Chloroquine is also used for rheumatoid arthritis and systemic lupus erythematosus

Antimalarials

Adverse Effects

- **Many adverse effects** for the various drugs
- **Primarily gastrointestinal**: nausea, vomiting, diarrhea, anorexia, and abdominal pain

Protozoal Infections

- **Patients with compromised immune systems are at risk for acquiring these infections**
 - ▣ Taking immunosuppressive drugs after a transplant
 - ▣ Leukemia
 - ▣ AIDS

- **Protozoal infections are often fatal in these cases**

Protozoal Infections

- ☐ Amebiasis
- ☐ Giardiasis
- ☐ Pneumocystosis
- ☐ Toxoplasmosis
- ☐ Trichomoniasis

Transmission

- ☐ Person to person
- ☐ Ingestion of contaminated water or food
- ☐ Direct contact with the parasite
- ☐ Insect bite (mosquito)

Antiprotozoals

- atovaquone (Mepron)- *Pneumocystis jirovecii* pneumonia
- metronidazole (Flagyl) – anti-bacterial / anaerobes
- pentamidine (Pentam-300) – *P. jirovecii* pneumonia
- iodoquinol (Yodoxin)- intestinal amebiasis; *Giardia*; *Trichomonas vaginalis*
- paromomycin (Humatin) – acute & chronic intestinal amebiasis; hepatic coma

Antiprotozoals:

Mechanism of Action and Indications

atovaquone (Mepron)

- Protozoal energy comes from the mitochondria
- atovaquone: selective inhibition of mitochondrial electron transport
- Result: no energy, leading to cellular death
 - ▣ Used to treat mild to moderate *Pneumocystis jiroveci*

Adverse Effects: atovaquone (Mepron)

- Nausea, vomiting, diarrhea, anorexia, altered liver function, many others

Antiprotozoals

Mechanism of Action and Indications

Metronidazole (Flagyl)

- ❑ Disruption of DNA synthesis as well as nucleic acid synthesis
- ❑ Bactericidal, amebicidal, trichomonacidal
- ❑ Used for treatment of trichomoniasis, amebiasis, giardiasis, and antibiotic-associated pseudomembranous colitis
- ❑ Also has anthelmintic activity

Adverse Effects: Metronidazole (Flagyl)

- ❑ Metallic taste, nausea, vomiting, diarrhea, abdominal cramps, many others

Antiprotzoals

Mechanism of Action and Indications

Pentamidine

- ❑ Inhibits DNA and RNA
- ❑ Binds to and aggregates ribosomes
- ❑ Directly lethal to *Pneumocystis jiroveci*
- ❑ Mainly used to prevent & treat *P. jiroveci* pneumonia
- ❑ Used for other protozoal infections

Adverse Effects: pentamidine

- ❑ Bronchospasms, leukopenia, thrombocytopenia, acute pancreatitis, acute renal failure, increased liver function studies, hypotension, many others

Antiprotozoals

Mechanism of Action and Indications

iodoquinol (Yodoxin)

- Acts primarily in the intestinal lumen of the infected host
- Directly kills the protozoa
- Used to treat intestinal amebiasis

Adverse Effects: iodoquinol (Yodoxin)

- Nausea, vomiting, diarrhea, anorexia, agranulocytosis, many others

Antiprotozoals:

Mechanism of Action and Indications

paromomycin (Humatin)

- Kills by inhibiting protein synthesis
- Used to treat amebiasis and intestinal protozoal infections, and also adjunct therapy in management of hepatic coma

Adverse Effects: paromomycin (Humatin)

- Nausea, vomiting, diarrhea, stomach cramps, hearing loss, dizziness, tinnitus

Anthelmintics

- Drugs used to treat parasitic worm infections: helminthic infections
- Unlike protozoa, helminths are large and have complex cellular structures
- Drug treatment is very specific to the organism

Anthelmintics

- ❑ albendazole (Albenza)
- ❑ diethylcarbamazine (Hetrazan)
- ❑ ivermectin (Stromectol)
- ❑ mebendazole (Vermox)
- ❑ praziquantel (Biltricide)
- ❑ pyrantel (Antiminth)
- ❑ thiabendazole (Mintezol)

- ❑ **It is VERY IMPORTANT to identify the causative worm**
 - Done by finding the parasite ova or larvae in feces, urine, blood, sputum, or tissue
 - **Cestodes (tapeworms)**
 - **Nematodes (roundworms)**
 - Trematodes (flukes)
 - Platyhelminthes (flatworm)

Anthelmintics:

Mechanism of Action and Indications

diethylcarbamazine (Hetrazan)

- Inhibits rate of embryogenesis of nematodes

thiabendazole (Mintezol)

- Inhibits the helminth-specific enzyme, fumarate reductase
- Both used for nematodes
(tissue and some **roundworms**)

pyrantel (Antiminth)

- Blocks acetylcholine at the neuromuscular junction, resulting in paralysis of the worms, which are then expelled through the GI tract
- **roundworm infections**, ascariasis, enterobiasis, nematodes (giant worm and pinworm), other helminthic infections

Anthelmintics:

Mechanism of Action and Indications

mebendazole (Vermox)

- ❑ Inhibits uptake of glucose and other nutrients, leading to autolysis and death of the parasitic worm
- ❑ Used to treat cestodes and nematodes (hookworm, pinworm, roundworm, whipworm, tapeworm)

oxamniquine (Vansil) and praziquantel (Biltricide)

- ❑ Paralyze worms' musculature and immobilize their suckers
- ❑ Cause worms to dislodge from mesenteric veins to the liver, then killed by host tissue reactions
- ❑ Used to treat trematodes; praziquantel is used to treat cestodes also

Anthelmintics

Adverse Effects

Effects will vary with each drug

□ Common adverse effects:

- ▣ Nausea, vomiting, diarrhea, dizziness, headache

- ▣ mebendazole

- May cause myelosuppression

Antimalarial, Antiprotozoal, and Anthelmintic Drugs: Nursing Implications

- ❑ Before therapy, thorough health history, medication history,
- ❑ Assess for allergies
- ❑ Collect specimens before beginning drug therapy
- ❑ Check baseline VS
- ❑ Check for contraindications and interactions
- ❑ Some drugs may cause the urine to have an asparagus-like odor, or cause an unusual skin odor, or a metallic taste; be sure to warn the patient ahead of time
- ❑ Administer *all* drugs as ordered and for the prescribed length of time
- ❑ Most drugs should be taken with food to reduce GI upset

Antimalarial Drugs

Nursing Implications

- ❑ Assess for presence of malarial symptoms
- ❑ When used for prophylaxis, these drugs should be started 1 to 2 weeks before potential exposure to malaria, and for 4 weeks after leaving the area
- ❑ Medications are taken with 8 ounces of water
- ❑ Instruct patient to notify physician immediately if ringing in the ears, hearing decrease, visual difficulties, nausea, vomiting, profuse diarrhea, or abdominal pain occurs
- ❑ Alert patients to the possible recurrence of the symptoms of malaria so that they will know to seek immediate treatment

Monitor for adverse effects

- ❑ Ensure that patients know the adverse effects that should be reported
- ❑ Monitor for therapeutic effects and adverse effects with long-term therapy