

# CHAPTER –III

# ANTIMALARIAL, ANTIprotozoal

# AND ANTHELMINTIC

# DRUGS

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# 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

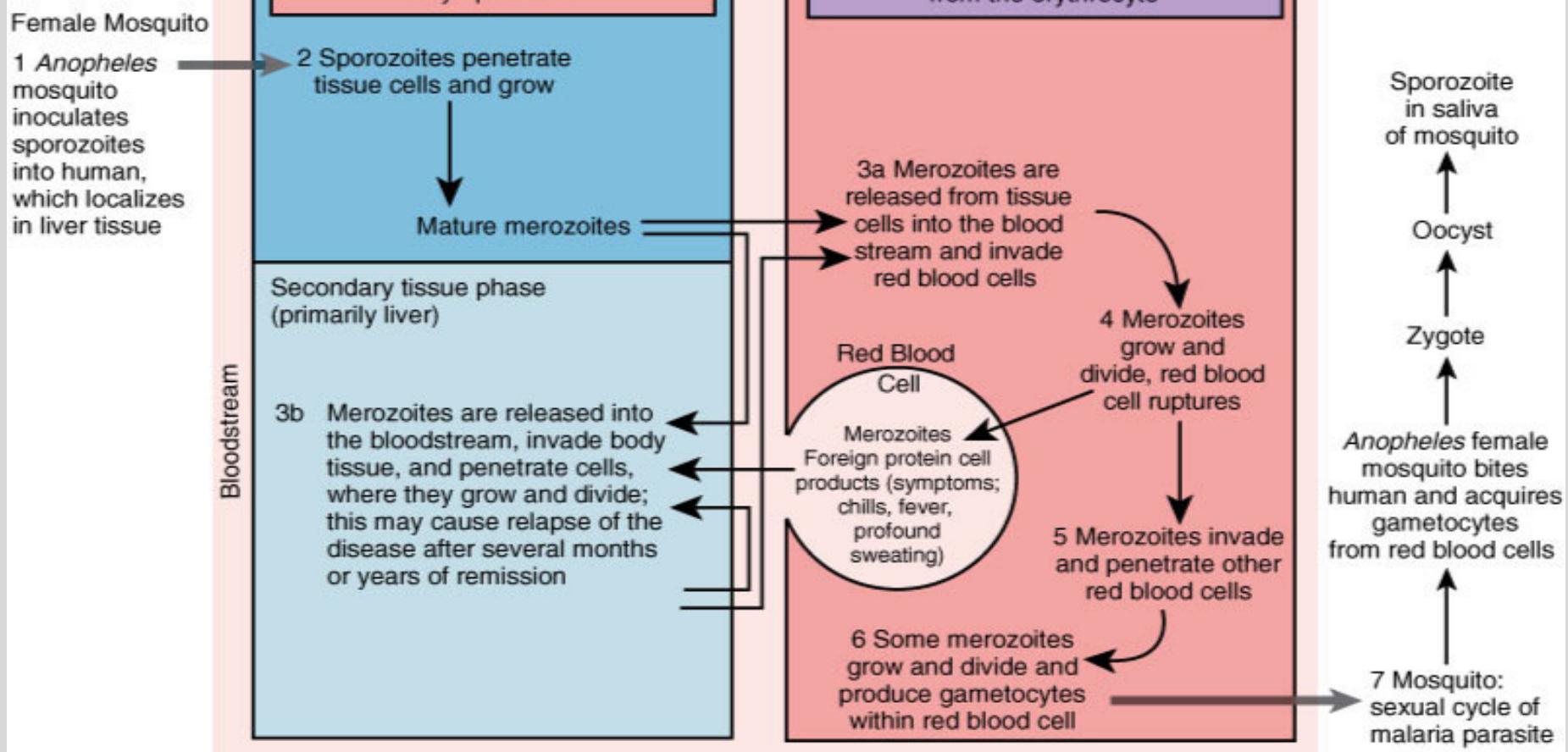
Human  
Asexual cycle of malarial parasite

Female Mosquito

1 Anopheles mosquito inoculates sporozoites into human, which localizes in liver tissue

Bloodstream

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



Sporozoite in saliva of mosquito

Oocyst

Zygote

Anopheles female mosquito bites human and acquires gametocytes from red blood cells

7 Mosquito: sexual cycle of malaria parasite

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

# 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. jiroveci* 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

# Antiprotozoals

## 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