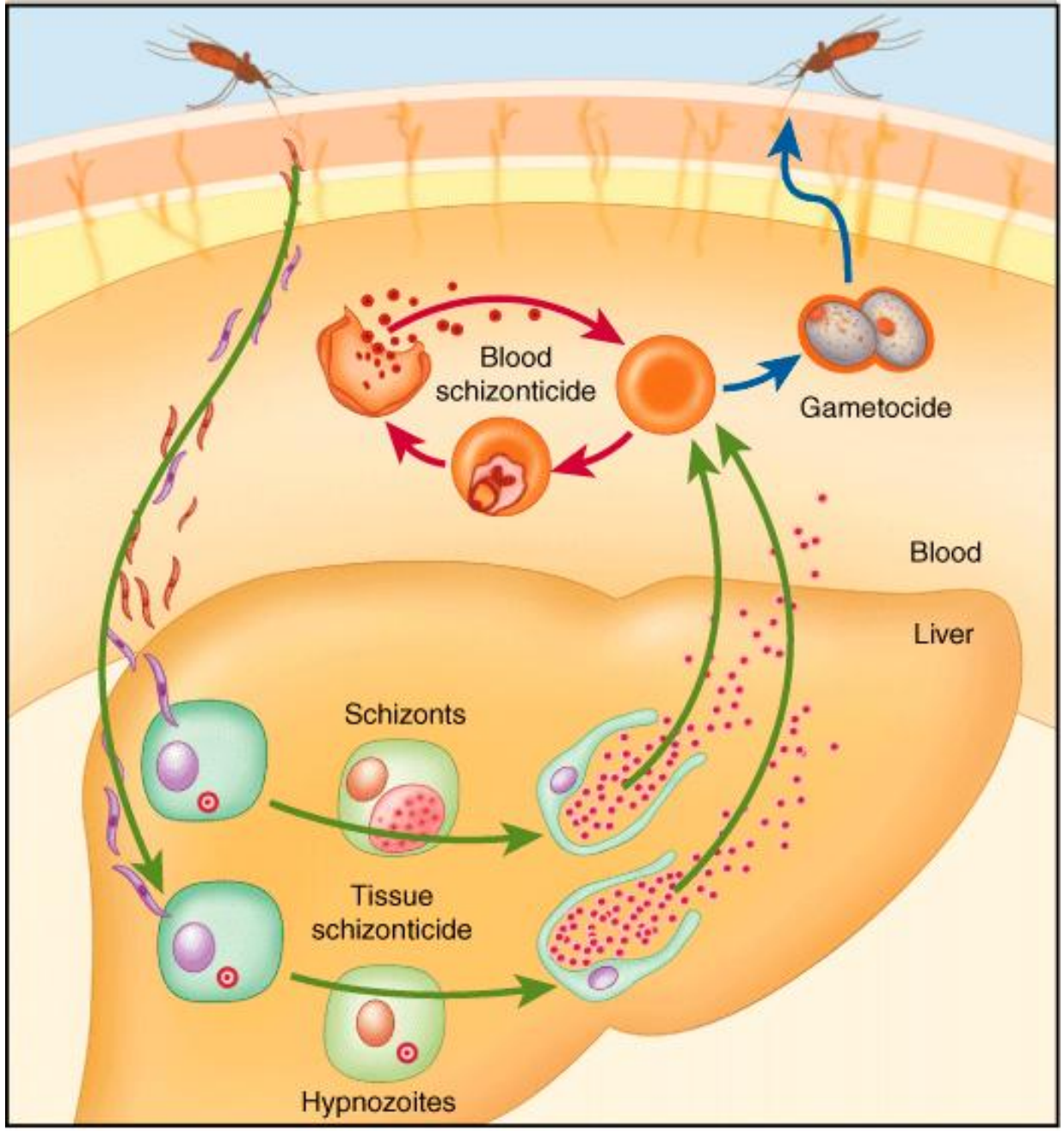
Drugs Used in Treatment of Malaria

Yacoub Irshaid, MD, PhD, ABCP

Department of Pharmacology



Life cycle of malaria parasites:

- **Only the asexual erythrocytic stage of infection causes clinical malaria.**
- **All effective antimalarial treatments are blood schizonticides that kill this stage.**

Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 11th Edition:* http://www.accessmedicine.com

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Drugs Used in Treatment of Malaria

Definition of terms:

1. **Radical cure: elimination of both hepatic and erythrocytic stages of the malaria parasite. No one drug can do this.**
2. **Causal prophylaxis: prevention of erythrocytic infection. Can be done by prophylactic agents.**
3. **Terminal prophylaxis: eradication of dormant hepatic stages of *Plasmodium vivax* and *P. ovale.***

Drugs Used in Treatment of Malaria

1. **Drugs that treat acute attacks (clinical cure): Blood Schizonticides.**

   Chloroquine, Quinine, Quinidine, Artemisinin derivatives, Pyrimethamine, Halofantrine, Atovaquone, Proguanil, Sulfones, Tetracyclines

2. **Drugs that effect radical cure: Tissue (hepatic) schizonticides.**

   Primaquine

Drugs Used in Treatment of Malaria

3. **Drugs for chemoprophylaxis: Kill the parasites when they emerge from the liver.**

   Chloroquine, Mefloquine, Malarone, Proguanil, Pyrimethamine, Dapsone, Doxycycline

4. **Self Treatment by Travellers: (recommendations may change).**

   Chloroquine, Quinine, Artemisinin derivatives

Drugs Used in Treatment of Malaria

Drugs for malaria during pregnancy (?):

A. **May be used:**

Chloroquine, Proguanil, Quinine

B. **Not recommended:**

Mefloquine, Malarone, Fansidar, Artemisinin.

C. **Contraindicated:**

Doxycycline, Primaquine, Clindamycin, Malarone, Halofantrine.

Chloroquine

- **It is a very effective blood schizonticide for all plasmodial species.**
- **It has NO effect on sporozoites or hypnozoites.**
- **Moderately effective gametocide for all species except *P. falciparum*.**

Chloroquine

Mechanism of action:

- **It diffuses into and concentrates in the food vacuole of the parasite and inhibits hem polymerase which converts the toxic hem into the harmless hemozoin.**
- **Raising the pH of acidic cellular compartments directly disrupts parasite survival while suppressing dangerous, hyper-inflammatory host immune responses.**

Chloroquine

Mechanism of resistance:

- ***P. falciparum*** **resistance is widely spread all over the world, and is due to enhanced efflux of the drug from the parasite due to increased expression of a transporter.**

  P. vivax **resistance to chloroquine is increasing.**

Other Actions:

1. **Disease-modifying anti-rheumatic effect.**
2. **Anti-amebic action.**

Chloroquine

Pharmacokinetics:

- **Given orally.**
- **Kaolin, and Calcium- and magnesium containing antacids interfere with absorption.**
- **Can be given IM or by slow IV infusion.**
- **Vd ~ 100-1000L/kg**
- **Eliminated slowly by renal excretion (70%) and hepatic metabolism.**
- **Half-life of elimination ~ 1-2 months.**

Chloroquine

Clinical uses:

1. Acute attacks of non-falciparum and falciparum-sensitive malaria (~3 days)
2. Chemoprophylaxis in areas without resistance
3. Amebic liver abscess that fails initial treatment with metronidazole

Chloroquine

Adverse effects:

1. **Nausea, vomiting, abdominal pain and anorexia**
2. **QRS and T wave abnormalities**
3. **Respiratory and cardiac arrest – arrhythmias**
4. **Visual field abnormalities, retinopathy, blurring of vision.**
5. **Peripheral neuropathy and myopathy**

Chloroquine

6. Psychosis and seizures
7. Ototoxicity and hearing impairment
8. Hemolysis in patients with G6PD deficiency
9. Agranulocytosis
10. Exfoliative dermatitis
11. Alopecia, bleaching of hair

Primaquine

- **Active against hypnozoites of all plasmodia → effects radical cure and causal prophylaxis.**
- **Has gametocidal action in all plasmodia, and thus, prevents transmission of disease.**

Mechanism of action:

- **It acts through a two-step biochemical relay that induces localized oxidative stress and hydrogen peroxide (H_2O_2) accumulation in infected tissues.**

Primaquine

- **Well absorbed after PO, widely distributed and rapidly metabolized.**
- **t½ ~ 3-8 hours.**
- **Duration of use 14 days after treatment with a blood schizonticide.**

Primaquine

Adverse Effects:

1. **Hypotension if used parenterally.**
2. **Nausea, abdominal pain.**
3. **Headache.**
4. **Hemolysis in G6PD deficient individuals.**
5. **Methemoglobinemia**
6. **Leukopenia, agranulocytosis**
7. **Cardiac arrhythmias.**
8. **Should NOT be given during pregnancy because it may cause hemolysis in the fetus.**