Drugs Used in Treatment of Malaria

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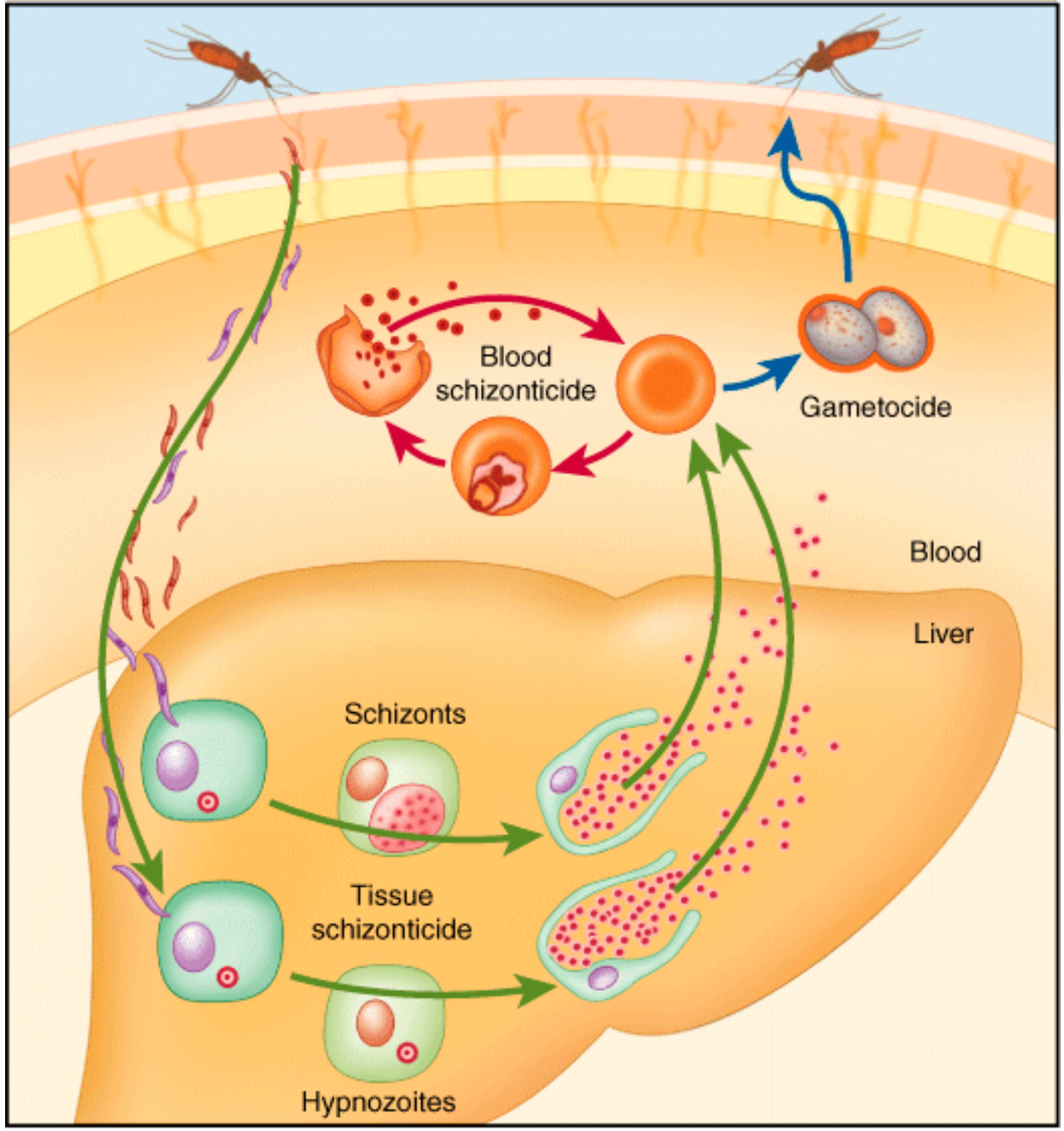

Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 11th Edition:* http://www.accessmedicine.com

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.

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

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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 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:

- **Controversial.**
- **It diffuses into, and concentrates in the food vacuole of the parasite and inhibits hem polymerase which converts hem into hemozoin.**
- **Hem is toxic to the parasite.**

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 (2-3 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 plasmaodia, and thus, prevents transmission of disease.**
- **Mechanism of action is unknown.**
- **Well absorbed after PO, widely distributed and rapidly metabolized.**
- **t½ ~ 3-8 hours.**

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.**