* Anti-malarial drugs

Pharmacology

HLS

Sheet No. 3

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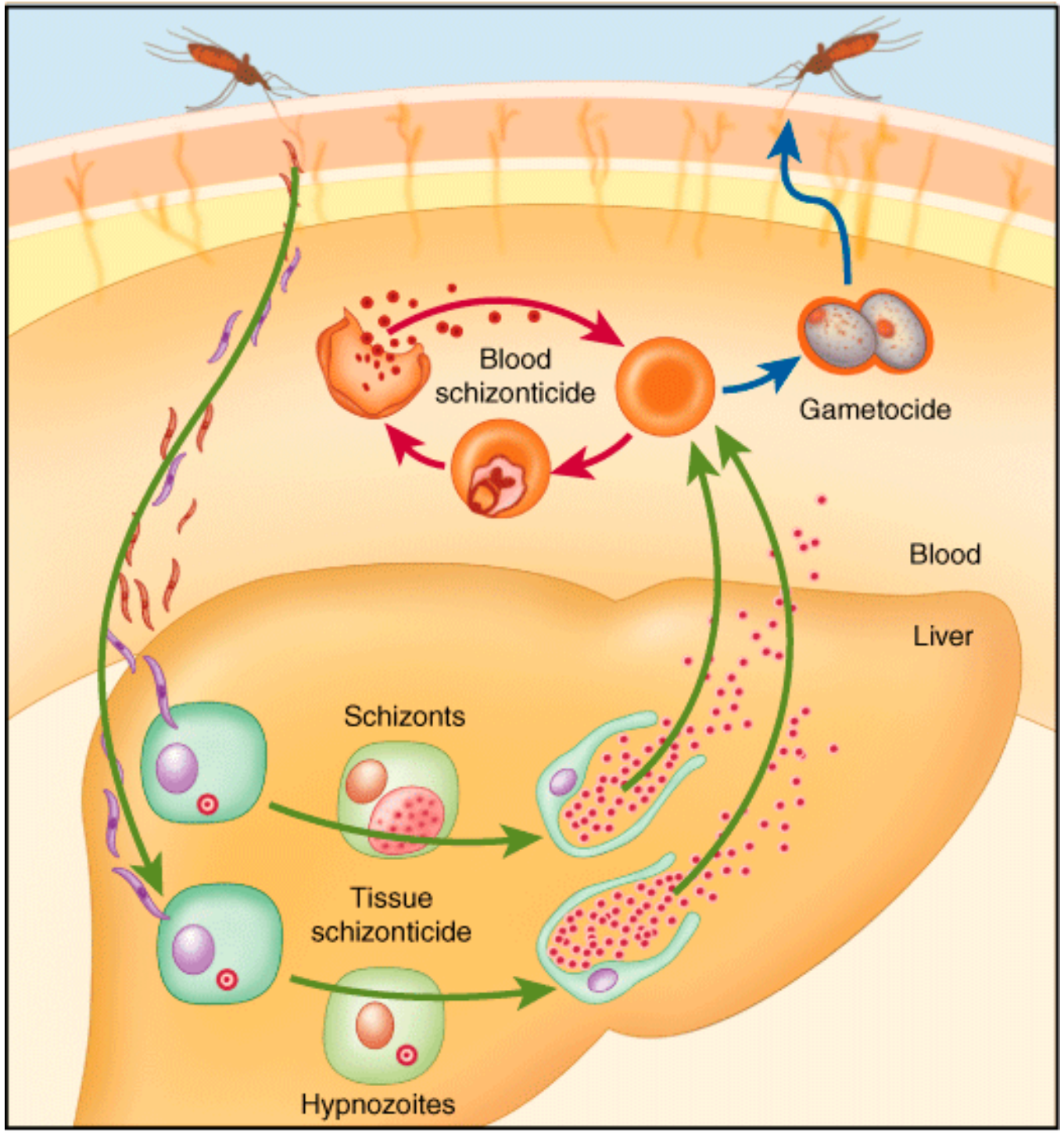

Life cycle of malaria parasites. Only the asexual erythrocytic stage of infection causes clinical malaria. All effective antimalarial treatments are blood schizonticides that kill this stage.

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

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*.**

when we eliminate (er) stage the mosquito can't get the infection from you so other people are safe (prophylactic for others)

we can't give drugs to stop hepatic and erythrocytic stages at the same time because it's toxic. so we first stop erythrocytic (the cause of symptoms) then the hepatic

Drugs Used in Treatment of Malaria

1. **Drugs that treat acute attacks (clinical cure): Blood Schizonticides.** (drugs that Kill schizonts in the blood)

   Chloroquine

   Quinine, quinidine, Artemisinin derivatives, Pyrimethamine, Halofantrine, Atovaquone, Proguanil, Sulfones, Tetracyclines

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

   Primaquine

↳ by first using Chloroquine (clinical cure) the Primaquine (tissue) ⇒ so you eleminate 2 stages

Drugs Used in Treatment of Malaria

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

   even when we have dormant stage and the reinfection

   Chloroquine

   Mefloquine, Malarone, Proguanil, Pyrimethamine, Dapsone, Doxycycline

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

   when someone travels to country where malaria is endemic he take Chloroquine with him

   Chloroquine V.I.P * provided that this country isn't resistant to Chloroquine

   Quinine, Artemisinin derivatives

Drugs Used in Treatment of Malaria

Drugs for malaria during pregnancy (?): most are not safe

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.** effective only on erythrocytic stage
- **It has NO effect on sporozoites or hypnozoites.**
- **Moderately effective gametocide for all species except *P. falciparum*.**

no effect on " gamets

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

treament with chloroquine takes 3 days only

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.** efflux mechanism become more

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

Other Actions:

removes (arrist) the disease process

1. **Disease-modifying anti-rheumatic effect.** (hydroxy chloroquine)
2. **Anti-amebic action.**

used in hepatic-amebic abscess not responding to usual treatment (metronedazol)

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** (nueroligical)
7. **Ototoxicity and hearing impairment**
8. **Hemolysis in patients with G6PD deficiency**
9. **Agranulocytosis** => cause septicemia (without symptoms some time)
10. **Exfoliative dermatitis** (fatal) تقشر الجلد
11. **Alopecia, bleaching of hair**

تساقط شعر

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.**

* not active against erythrocytic stage

- **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.** if the fetus has G6PD deficiency