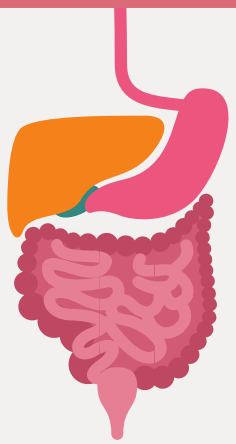
Anti-malarial drugs



Objectives:

- Classify the main antimalarial drugs depending on their goal of therapy.
- Detail the pharmacokinetics & dynamics of main drugs used to treat attack or prevent relapses.
- State the WHO therapeutic strategy for treatment.
- Hint on the CDC recommendations for prophylaxis in travelers to endemic areas.

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Drugs names | Doctors notes | Important | Extra

« **باذلًا وسعي** في استنقاذها من الهلاك والمرض، والألم والقلق »

Mind Map

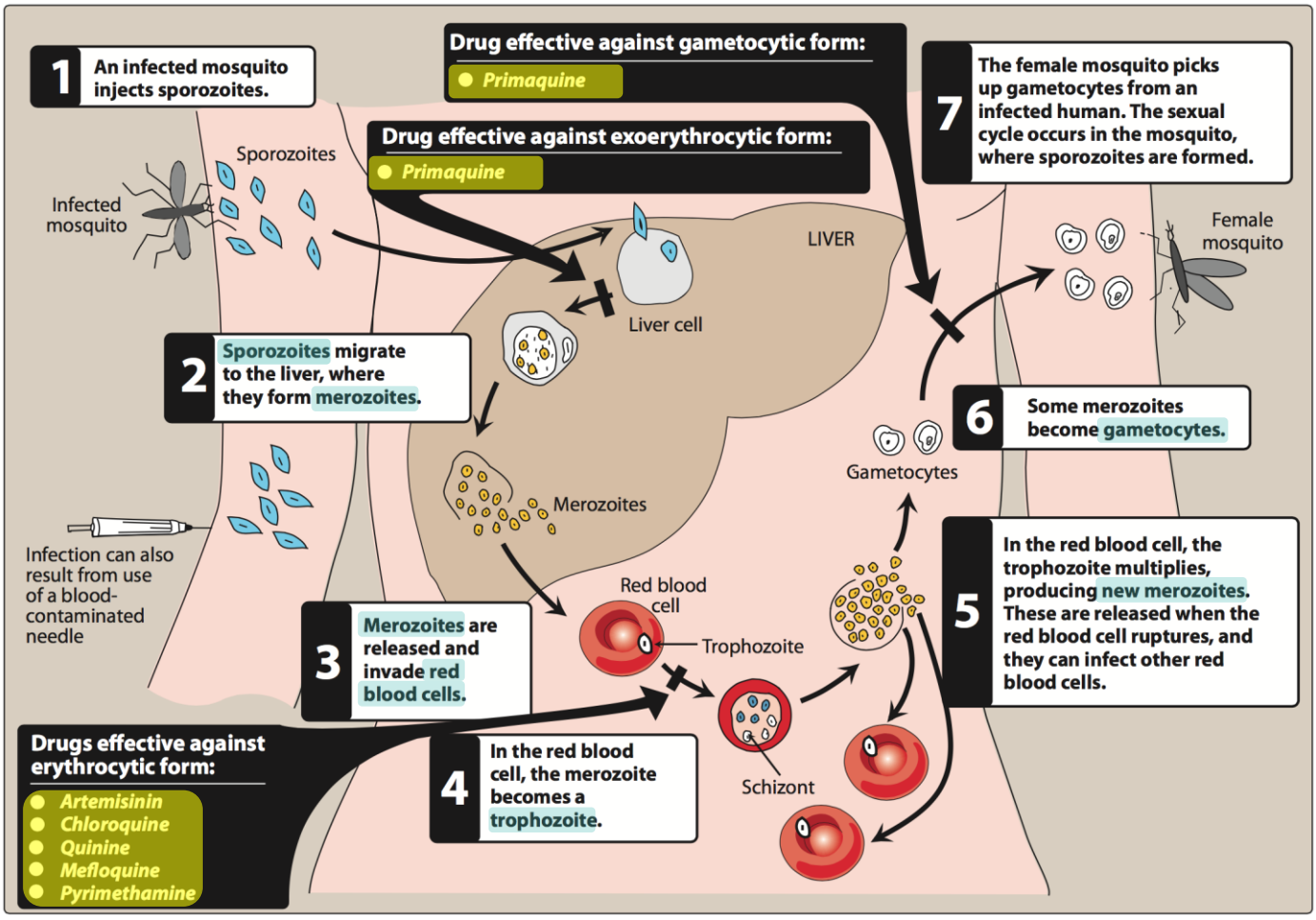
Therapeutic classification of Antimalarial drugs

1. **Causal prophylaxis**
   - destroy parasite in **liver** cell and **prevent invasion of Erythrocyte**.
   - **Primaquine**
2. **Suppressive prophylaxis**
   - Suppresses the **erythrocytic phase** & thus attack of malaria fever.
     - **Chloroquine.**
     - **mefloquine.**
     - **doxycycline.**
   - taken by people living in endemic areas but not recommended because of the side effects.
3. **Clinical cure (erythrocytic schizonicide)**
   - Used to terminate an episode of malarial fever.
   - Fast acting **high** efficacy:
     - **Chloroquine**.
     - **quinine**.
     - **mefloquine**.
     - **artemisinin**.
   - Slow acting **low** efficacy:
     - **Pyrimethamine**.
     - **Proguanil**.
     - **Sulfonamides**.
4. **Radical cure**
   - Eradicate all forms of vivax & ovale from the body.
     - **Suppressive drug**. (blood Schizontocidal)
     - **hypnozoitocidal**
5. **Gametocidal**
   - Destroys gametocytes & prevent transmission.
   - **Against vivax:**
     - **Chloroquine**.
     - **Quinine**
   - **Against all species:**
     - **Primaquine**
6. **Sporozoitocides**
   - Destroy sporozoites.
   - not very effective drugs
     - **Proguanil.**
     - **pyrimethamine.**

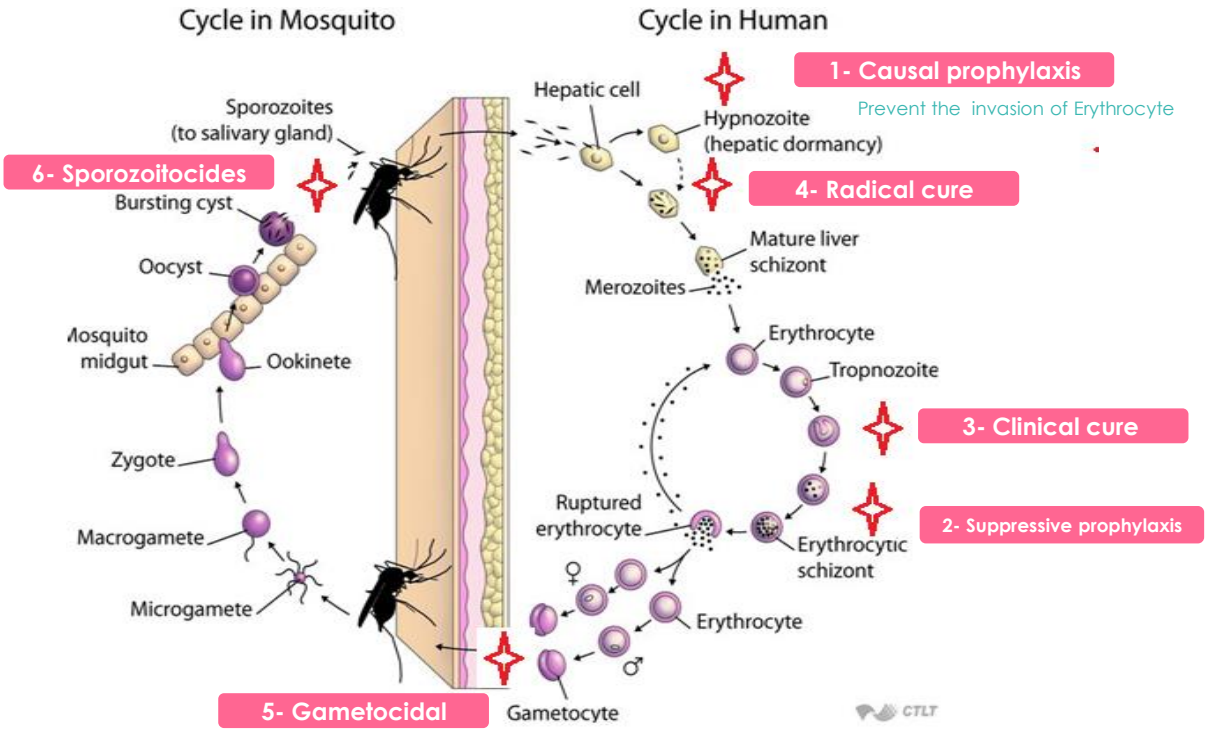
Do not forget to revise this mind map!

To Understand Better

Life cycle of the malarial parasite:



قبل بدئك بدراسة هذه المحاضرة، افهم هذه الصور جيدًا ☺



Antimalarial drugs

Drug

Artemisinin

General inf.

- It is the active principle of the plant Artemisia annua (qinghaosu).
- Fast acting blood schizonticide. (the fastest)
- Affect all forms including multi-drug resistant **P.falciparum** & chloroquine -resistant P.f
- **Short duration of action**. → disadvanatge → bc of that, it has **High recrudescence** (relapse) **rate**.
- Poorly soluble in water & oil, can only be used **orally**.
- → bc of these disadvantages, they made derivatives: Artesunate, Artemether.

MOA

They have **endoperoxide bridges** that are cleaved by **haem iron** to yield carbon-centered **free radicals**, that will: ➔

- Alkylate membranes of parasite's food vacuole and mitochondria ➔ no energy.
- Irreversibly bind & **inhibit** **sarco-endoplasmic reticulum Ca^{2+}-ATPase** of the parasite, thereby → inhibiting its growth.
- Inhibiting formation of transport vesicles ➔ no food vacuoles.

P.K

- Artemisinin, Artesunate, Artemether are **prodrugs**. They are rapidly **biotransformed** in liver into **Dihydroartemisinin** ➔ the **active metabolite**.
- Derivatives are rapidly absorbed orally.
- Widely distributed.
- T½: **Artemisinin** ➔ 4hrs, **Artesunate** ➔ 45min, **Artemether** ➔ 4-11hrs. → All have **short** plasma T1\2!
- **Artesunate** (water-soluble; oral, **IV**, IM, rectal administration) (the only drug can be given IV → can be used in **emergency or sever malaria**)
- **Artemether** (lipid-soluble; oral, IM, and rectal administration).
- **Dihydroartemisinin** (water-soluble; oral administration)
- They Induce its own CYP-mediated metabolism→ ↑ clearance 5 fold. → causing tolerance and decrease their efficacy if the drug used repeatedly)

ADRs

- **Transient heart block**.
- ↓ Neutrophil count.
- Brief episodes of **fever**.

* Resistance was **reported** recently in Cambodia-Thailand border.
→ The resistance will cause a great problem in treating malaria.

Clinical uses

Because artemisinin derivatives have **short T½:**

1. Monotherapy should be extended beyond disappearance of parasite to prevent recrudescence. (used repeatedly)
2. By **combining the drug with long-acting antimalarial drug**.

Preperation

- **Artesunate** (**IV** or IM preparations) for severe complicated cases as **cerebral malaria** (24h) **followed by** complete course of ACT.
- Artemisinin-Based Combination therapies (**ACTs**): → for 3 days
  - Artemether + lumefantrine.
  - Artemether + amodiaquine.
  - Artemether + mefloquine.
  - Artemether + sulfadoxine-pyrimethamine (its name: fansidar) not used now bc of the resistanne.

It is always recommended to give combinations to avoid development of resistance (similar to TB)

Drug

Chloroquine

The best drug to treat malaria, except for P.f

characteristic

- Potent blood Schizontocidal.
- Active against all forms of the **schizonts** (except chloroquine -resistant P.f. & P.v.)
- **Gametoside:** Against all species except *P. falciparum*
- **No activity** against tissue (liver) schizonts. (not used for causal prophylaxis)
- **Safe in pregnancy**.

MOA

- Malaria Parasite digest host cell's Hb to obtain amino acids.
- Heme is released → Toxic to the parasite, So parasite **detoxifies** it by **heme polymerase** → make it Hemozoin (NonToxic) & **traps it in food vacuole.**
- Prevent **polymerization of heme**, which will cause it to accumulate inside parasite and RBC leading to lysis of both of them. (see the figure below)

Mech. of resistance

- The resistance develop as a result of **mutation** of protein called plasmodium falciparum chloroquine resistance transporter (**PfCRT**), leading to **efflux** of chloroquine from **food vacuole of plasmodium**.

P.K

- Given orally → Rapidly & completely absorbed from the GIT (has high bioavailability)
- Has **high volume of distribution**.(100-1000l/kg) (hypothetical volume not true volume)
- Concentrated into parasitized **RBCs**.
- Released slowly from tissues. (that's why it has long duration of action)
- 30% is metabolized in the liver.
- Excreted in the urine 70% unchanged.
- Initial T½ = 2-3 days & terminal T½ = 1- 2 months.

Bc of the increased T1\2 we have to administer a loading dose then a maintenance dose, Bc if we administer the loading dose as one single dose → this will cause very toxic effect! Why? Bc all of the loading dose will be concentrated in the 1st compartment. That's why we have to **divide the doses.**

- Initial t½ : for distribution of drug from central compartment to the peripheral compartment.
- Terminal t½: for elimination of drug from central and peripheral compartments.

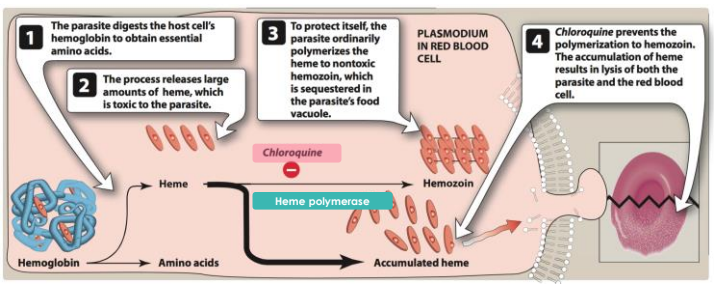
Why does it have 2 plasma T1\2?
Bc of the distribution of the drug into tissues .1st T1\2 → for **distribution** to the tissues (2-3days) , 2nd T1\2 → for **elimination**. The drug has to distributed from the 1st compartment to the 2nd compartment, then it has to be eliminated from the 2nd compartment. كلام الدكتور نفسه يشرح المكتوب بالذهبي (الإكسترا) بطريقة أخرى

Indications

- Eradicate blood schizonts of Plasmodium.
- Hepatic amoebiasis.
- Rheumatoid arthritis → it acts as anti-inflammatory drug.

ADRs

- **For short period:** (2-3 days)
  - Mild headache & visual disturbances.
  - Gastro-intestinal upsets; Nausea,
  - Vomiting.
  - **Pruritus, urticaria**.
- **For prolonged periods:** (2 years, as in case of Rheumatoid arthritis)
  - Ocular toxicity (Loss of accommodation, lenticular opacity, retinopathy) (bc it has affinity to **melanin**)
  - Ototoxicity.
  - Weight loss.
  - If given IV (Bolus injection): may cause hypotension & dysrhythmias.



Drug	Quinine
characteristic	○ It is quinidine (anti-arrhythmic drug) isomer, both extracted from cinchona bark **so it has some side effects of quinidine** as depression of myocardium, reduce excitability & conductivity. → quinidine is also considered as anti-malarial drug. ○ Potent **blood schizonticide** of **all malarial parasites** & weak **gametocide** for vivax & ovale. ○ It has other effects like: Mild analgesic, **antipyretic**, **stimulation of uterine smooth muscle** (mild), curaremimetic effect (neuromuscular blocking effect). ○ **Safe in pregnancy.**
MOA & Mech. of Resistance	○ **Same as chloroquine:** • **MOA:** Prevent polymerization of heme. • **Mech. of resistance:** by mutation of **chloroquine resistance transporter**, also **increased expression of P-glycoprotein transporter.**
P.K	○ Rapidly & completely absorbed from the GIT. ○ Peaks Plasma concentration 1-3 hrs. ○ Metabolized in the liver & excreted in urine (5-20% excreted in the urine unchanged) ○ T½ = 10 h but **longer** in case of **sever falciparum infection** (18h) Bc it binds to a-glycoprotein ○ Administered: **orally** for 7 day course or by slow **IV** for severe *P. falciparum* infection. (7 days course for both oral and I.V)
Uses	○ **I.V (parenteral)** treatment of severe falciparum malaria (e.g. cerebral malaria) ○ **Oral** treatment of mild and moderate falciparum malaria. ○ Nocturnal leg cramps. Till now they don't know how does it work.
ADRs	○ **Therapeutic dose**: no adverse drug reactions but it has a very bitter taste, so the patient stops taking it (poor compliance). ○ **Higher doses** : • **Cinchonism syndrome**: (tinnitus, deafness, headaches, nausea & visual disturbances). • Abdominal pain & diarrhea. • Hypotension, arrhythmias & hypoglycemia. • Rashes, fever, hypersensitivity reactions. • **Blood dyscarasis** : anemia, thrombocytopenic purpura & hypoprothrombinemia. • **Blackwater fever** (rare, but it's the **most serious side effect**), a fatal condition in which acute hemolytic anemia is associated with renal failure. • If given **I.V** will cause neurotoxicity → stimulation causing **tremor of the lips** and limbs, delirium, fits → followed by depression of respiration & coma.
C.I	○ **Prolonged QT Interval** (because the drug it self prolongs the QT interval). ○ **G6PD Deficiency** → hemolysis (but the effect is mild compared to Primaquine). ○ Hypersensitivity, **Optic Neuritis** and **auditory problems** (bc it is ototoxic). ○ Myasthenia Gravis (it has a neuromuscular blocking effect). ○ Dose should be reduced in renal insufficiency.
Interactions	○ **Antacids**: Antacids containing **aluminum** &/or **magnesium** may delay or decrease absorption of quinine. ○ **Mefloquine** (because it prolongs QT interval). → 1 month interval between the drugs ○ **Quinine** can raise plasma levels of **warfarin** and **digoxin**.

Drug

Primaquine

Characteristics

- Hypnozotiocides → against **liver hypnozoites** and **gametocytocidal**
- Radical cure of **P. Ovale** and **P. Vivax** → the **only agent** that can lead to radical cures for P.o, P.v, which may remain in the liver in the exoerythrocytic form after the erythrocytic form of the disease is eliminated.
- Prevents spread of **all forms**.
- RESISTANCE: is **rare,** especially when combined with **chloroquine.**
- Primaquine is **not effective against the erythrocytic stage** of malaria and, therefore, is often used in conjunction with a **blood schizonticide**, such as chloroquine, quinine, mefloquine, or pyrimethamine.

MOA

- Not well understood. It may be acting by:-
  - Generating **ROS** → can **damage** lipids, proteins & nucleic acids
  - Interfering with the **electron transport** in the parasite → **no energy**
  - Inhibiting formation of **transport vesicles** → **no** food vacuoles.

P.K

- Well absorbed orally.
- Rapidly metabolized to etaquine & tafenoquine → **more active**.
- T1/2 is 3-6 hours

Indications

- Radical cure of relapsing malaria, 15mg/day for 14 days.
- In ***falciparum malaria***: a single dose (45mg) to kill gametes & cut down transmission. → prevent the transmission of malaria.
- G6PD Normal → 15 mg \day for 14dys.
- G6PD deficiency (mild African form) → 45mg \week for 8 wks.
- G6PD deficiency (more sever Mediterranean variety) → 30mg\week for 30 wks.

ADRs

- At regular doses:
  - G6PD deficient patients → hemolytic anemia → Click here to see the mechanism
    - Oxidation of primaqune produces free radicals → cause oxidative damage of RBCs → Affecting glutathione system (e.g. H_2O_2 oxidized GSH –the reduced form) → Hemolysis.
- At larger doses:
  - Epigastric distress, Abdominal Cramps
  - Mild Anemia, cyanosis, methemoglobinemia (mild) (When the red cell is exposed to oxidants, haemoglobin is converted to methaemoglobin and denatured)
  - Severe Methemoglobinemia → in patients with deficiency of **NADH methemoglobin reductase** (rare)
  - Granulocytopenia, agranulocytosis (rare)

C.I

- **Pregnancy** → the fetus is relatively **G6PD-deficient** → at risk of hemolysis.
- G6PD deficiency.

Notes

- إيش بتسوي إذا عندك وحدة حامل وتبي تتخلص من الملاريا نهائيًا؟ وما فيه إلا Primaquine يسوي هذا الأكشن. أستخدمه للحامل يعني؟ طبعًا لا!!!! لأنه خطير على الجنين، فأيش تسوي للملاريا اللي في الكبد؟ الإجابة **chloroquine** طول فترة الحمل عشان أول ما تطلع من الكبد إلى الدم يكون موجود يتصدى لها لين ما تولد وتخلص الرضاعة، بعدها تعطيها primaquine عشان تنظف الكبد. الزبدة لو كان سؤال خيارات تختار **chloroquine**
- طيب بالنسبة لG6PD deficiency أعطيهم هذا الدرق إذا أبي أتخلص من الملاريا نهائيا؟ إيه، بس أعطيه بالdoses المكتوبة في indications ، وخلال هذي الفترة we monitor the blood for hemolysis

WHO treatment guidelines

	Sensitive to Chloroquine	Resistant to Chloroquine
In *P. Vivax*	• Chloroquine (3 days) • Followed by Primaquine (14 days)	• ACT (3 days) • Followed by Primaquine (14 days)
In *P. Falciparum* (all show resistance to Chloroquine)	**Uncomplicated**	**Complicated**
	• ACT	• Artesunate (IV for 24 hours) followed by:- ▪ ACT ▪ Or: Artemether + [Clindamycin / doxycyline] ▪ Or: Quinine + [Clindamycin / doxycyline]

- **Special Risk Groups:**
  - Quinine + Clindamycin **(7 days):**
    - ✓ (**pregnancy 1st** trimester)

      Why don't we use **Artemisinin**? Bc they found that it is an embryotoxic in rats & rabbit, but no evidence in human, so until now be in the safe side & don't use it in the 1st trimester
  - ACT:
    - ✓ (Pregnancy **2nd**, **3rd** trimesters, lactating women, infants, and young children)

Prophylaxis in travellers

Cdc recomendations

Chloroquine	Areas **without resistant** P. Falciparum	Begin 1-2 weeks before departure (except doxycycline 2 days prior) continue for 4 weeks after leaving **endemic** area
Mefloquine & Malarone	Areas with **chloroquine-resistant P. Falciparum**.	
Doxycycline	Areas with **multidrug-resistant P. Falciparum**.	

Summary

Antimalarial drugs

Causal prophylaxis	Suppressive prophylaxis
Clinical cure (erythrocytic schizonicide)	Radical cure
Gametocidal	Sporozoitocides

Drug: Artemisinin

Gen. info

Artemisinin is the active principle of the plant Artemisia annua (qinghaosu).Fast acting blood schizonticide. Affect all forms including multi-drug resistant **P.falciparum.** Short duration of action. High recrudescence rate. Poorly soluble in water & oil, can only be used orally.

MOA

They have endoperoxide bridges that are cleaved by haem iron to yield carbon- centered free radicals, that will:

- Alkylate membranes of parasite's food vacuole and mitochondria → no energy.
- Irreversibly bind & inhibit sarco-endoplasmic reticulum Ca2+-ATPase of the parasite, thereby inhibiting its growth.
- Inhibiting formation of transport vesicles →no food vacuoles.

P.K

- Rapidly biotransformed in liver into Dihydroartemisinin →active metabolite.
- Artemisinin, Artesunate, Artemether are prodrugs.
- Derivatives are rapidly absorbed orally.
- Widely distributed.
- t½: Artemisinin → 4hrs, Artesunate → 45min, Artemether → 4-11hrs.
- Artesunate (water-soluble; oral, IV, IM, rectal administration).
- Artemether (lipid-soluble; oral, IM, and rectal administration).
- Dihydroartemisinin (water-soluble; oral administration).

ADRs

- Transient heart block.
- ↓ Neutrophil count.
- Brief episodes of fever.

*Resistance was reported recently in Cambodia-Thailand border.

Clinical uses

Because artemisinin derivatives have short t½:

1. monotherapy should be extended beyond disappearance of parasite to prevent recrudescence.
2. Or by combining the drug with long- acting antimalarial drug.

Preperation

- Artesunate (IV or IM preparations) for severe complicated cases as cerebral malaria (24h) followed by complete course of ACT.
- Artemisinin-based combination therapies (ACTs):
  - Artemether + lumefantrine.
  - Artemether + amodiaquine.
  - Artemether + mefloquine.
  - Artemether + sulfadoxine-pyrimethamine.

Drug: chloroquine

characteristic

Potent blood Schizontocidal. Active against all forms of the **schizonts** .(except chloroquine -resistant P.f. & P.v.) Effect against all **Gametocide** species except falciparum. No activity against liver schizonts. Safe in pregnancy.

MOA

Prevent polymerization of heme , which will cause it to accumulate inside parasite and RBC leading to lysis of both of them.

resistance

The resistance develop as a result of **mutation** of protein called plasmodium falciparum chloroquine resistance transporter (PfCRT) ,leading to **efflux** of chloroquine from food vacuole of plasmodium.

P.K

Given orally. Rapidly & completely absorbed from the GIT. Has high volume of distribution.(100-1000l/kg) Concentrated into parasitized RBCs. Released slowly from tissues. Metabolized in the liver. Excreted in the urine 70% unchanged. Initial t½ =2-3 days & terminal t ½=1- 2 months.

Indications

eradicate blood schizonts of Plasmodium. Hepatic amoebiasis. Rheumatoid arthritis.

ADRs

For short period:
Mild headache and visual disturbances.Gastro-intestinal upsets; Nausea, Vomiting. Pruritus, urticaria.

For prolonged periods:
Ocular toxicity. Ototoxicity. Weight loss.
if given IV : may cause hypotension & dysrhythmias.

Drug	QUININE
characteristic	•It is quinidine isomer, both extracted from cinchona bark **so it has some side effects of quinidine** as depression of myocardium, reduce excitability & conductivity. • It has other effects like : Mild analgesic, antipyretic, stimulation of uterine smooth muscle, curaremimetic effect (neuromuscular blocking effect). •Safe in pregnancy.
MOA, Resistance	**Mechanism of action :** Prevent polymerization of heme. **Mechanism of resistance :** Mutation of chloroquine resistance transporter & Also it increase expression of P-glycoprotein transporter
P.K	•Rapidly & completely absorbed from the GIT. •Peaks Plasma concentration 1-3 hrs. •5-20% excreted in the urine unchanged. •t½ = 10 hrs but longer in case of sever falciparum infection(18hrs). •Metabolized in the liver & excreted in urine. •Administered: orally for 7 day course or by slow IV for severe P. falciparum infection.
Indications	•**I.V** treatment of severe falciparum malaria. •**Oral** treatment of mild and moderate falciparum malaria.
ADRs	**Therapeutic dose** : no adverse drug reactions but it has a very bitter taste , so the patient stops taking it(poor compliance). **Higher doses** : ● **Cinchonism syndrome** : (tinnitus, deafness, headaches, nausea & visual disturbances). ● Abdominal pain & diarrhea. ● Hypotension & arrhythmias. ● Rashes, fever, hypersensitivity reactions. ● **Blood dyscarasis** : anemia, thrombocytopenic purpura & hypoprothrombinemia. ● **Blackwater fever** (rare , but it's the most serious side effect) , a fatal condition in which acute hemolytic anemia is associated with renal failure. ● if given **I.V** will cause neurotoxicity →stimulation causing tremor of the lips and limbs, delirium, fits →followed by depression of respiration & coma.
C.I	•Prolonged QT Interval •Hypersensitivity. •Glucose-6-Phosphate Dehydrogenase Deficiency . •Optic Neuritis and auditory problems. •Myasthenia Gravis •Dose should be reduced in renal insufficiency.
Drug interactions	Antacids: Antacids containing aluminum &/or magnesium may delay or decrease absorption of quinine. Mefloquine Quinine can raise plasma levels of warfarin and digoxin.
Drug	PRIMAQUINE
Characteristics	**-Hypnozotiocides → against liver hypnozoites and gametocytocidal** **-Radical cure of P. Ovale and P. Vivax** **-Prevents spread of all forms** **-RESISTANCE: is rare when combined with chloroquine**
MOA	Not well understood. It may be acting by:- - Generating ROS → can damage lipids, proteins & nucleic acids - Interfering with the electron transport in the parasite → no energy - Inhibiting formation of transport vesicles → no food vacuoles
P.K	-Well absorbed orally -t1/2 is 3-6 hours
Indications	- Radical cure of relapsing malaria, 15mg/day for 14 days - In falciparum malaria: a single dose (45mg) to kill gametes & cut down transmission
ADRs	At regular doses: -G6PD deficient patients → hemolytic anemia At larger doses: - Epigastric distress, Abdominal Cramps - Mild Anemia, cyanosis, methemoglobinemia - Severe Methemoglobinemia >> patients with deficiency of NADH methemoglobin reductase (rare) - Granulocytopenia, agranulocytosis (rare)
C.I	pregnancy ,G6PD deficiency

Treatment and prevention of malaria:

All Plasmodium species except chloroquine-resistant P. falciparum

Chloroquine

Chloroquine-resistant P. falciparum

Quinine* plus: *Pyrimethamine-sulfadoxine* or *doxycycline* or *clindamycin

Alternate: *Mefloquine*

Prevention of relapses: P. vivax and P. ovale only

Primaquine

Prevention of malaria

Chloroquine-sensitive geographic areas

Chloroquine

Chloroquine-resistant geographic areas

Mefloquine

In pregnancy

Chloroquine* or *mefloquine

Antimalarial drugs

- **Chloroquine** is a blood schizonticide that is concentrated in the parasite and inhibits the haem polymerase. Orally active; half-life 50 h. Unwanted effects: gastrointestinal disturbances, dizziness and urticaria. Bolus intravenous injections can cause dysrhythmias. Resistance is now common.
- **Quinine** is a blood schizonticide. It may be given orally or intravenously; half-life 10 h. Unwanted effects: gastrointestinal tract disturbances, tinnitus, blurred vision and, in large doses, dysrhythmias and central nervous system disturbances. It is usually given in combination therapy with:
  - **pyrimethamine**, a folate antagonist that acts as a slow blood schizonticide (orally active; half-life 4 days), and either
  - **dapsone**, a sulfone (orally active; half-life 24–48 h), or
  - **sulfadoxine**, a long-acting sulfonamide (orally active; half-life 7–9 days).
- **Proguanil**, a folate antagonist, is a slow blood schizonticide with some action on the primary liver forms of *P. vivax*. Orally active; half-life 16 h.
- **Mefloquine** is a blood schizonticidal agent active against *P. falciparum* and *P. vivax*, and acts by inhibiting the parasite haem polymerase. Orally active; half-life 30 days. The onset of action is slow. Unwanted effects: gastrointestinal disturbances, neurotoxicity and psychiatric problems.
- **Primaquine** is effective against the liver hypnozoites and is also active against gametocytes. Orally active; half-life 36 h. Unwanted effects: gastrointestinal tract disturbances and, with large doses, methaemoglobinaemia. Erythrocyte haemolysis in individuals with genetic deficiency of glucose 6-phosphate dehydrogenase.
- **Artemisinin** derivatives are now widely used particularly in combination with other drugs such as **lumefantrine**. They are fast-acting blood schizonticidal agents that are effective against both *P. falciparum* and *P. vivax*.
- **Artesunate** is water soluble and can be given orally or by intravenous, intramuscular or rectal administration. Side effects are rare. Resistance is so far uncommon.
- **Atavoquone** (in combination with proguanil) is used for prevention, and for the treatment of, acute uncomplicated *P. falciparum* malaria. The drug combination is effective orally. It is given at regular intervals over 3 to 4 days. Unwanted effects: diarrhoea, nausea and vomiting. Resistance to atavoquone develops rapidly if it is given alone.

MCQs

1- Which antimalarial drug causes transient heart block?
A- Artemisinin
B- Quinine
C- Chloroquine
D- Primaquine

2- Which one of the following drugs is used as causal prophylaxis?
A- Chloroquine
B- Quinine
C- Primaquine
D- Artemisnin

3- If Chloroquine is used for a short time (2-3 days) which of the following side effects could happen:
A- Ocular toxicity
B- Ototoxicity
C- Hypotension
D- Mild headache

4- Quinine and Mefloquine can't be used together, because both of them cause:
A- Prolongation of QT interval
B- Hypersensitivity
C- Optic neuritis
D- G6PD deficiency

5- In case of sensitive plasmodium vivax you should treat with:
A- Chloroquine for 3days then primaquine for 14 days
B- ACT followed with primaquine
C- ACT ONLY
D- Artesunate ONLY

6- Primaquine is contraindicated in case of:
A- pregnancy
B- Mild Anemia
C- G6PD deficiency
D- A & C

7- Erythrocytic schizontocide antimalarial drugs are used as:
A- Suppressive prophylactic
B- Clinical curative
C- Radical curative for P.vivax
D- A & B

Answers: 1-A 2-C 3-D 4-A 5-A 6-D 7-D

MCQs

8- An adult male living in nonmalarious area has to visit an area where chloroquine resistant P . falciparum is prevalent. He is intolerant to mefloquine and his G- 6PD status is unknown. Select the drug that you will prescribe for prophylaxis of malaria:

A- Primaquine
B- Doxycycline
C- Amodiaquine
D- Quinine

9- Recrudescence of malaria in use of Artemisinin refers to recurrence of malarial fever due to:

A- Reinfection of the patient by mosquito bite
B- Reinfectionofbloodbyexoerythrocytichyp-
nozoites
C- Incomplete clearance of schizonts from
blood
D- Any of the above

10- Chloroquine resistant P. falciparum malaria can be cured by the following drugs except:

A- Quinine
B- Pyrimethamine + sulfadoxine
C- Primaquine
D- Artesunate

11- Select the correct statement about primaquine:

A- It has no role in falciparum malaria
B- It is used as a gametocidal drug in falciparum malaria
C- It is combined with chloroquine to treat resistant P. falciparum infection
D- It is used to prevent recrudescence of falciparum malaria

12- In addition to malarial parasite, chloroquine is active against:

A- Microfilariae
B- Trichomonas vaginalis
C- Entamoeba histolytica
D- Dermatophytes

Answers: 8-B 9-C 10-C 11-B 12-C

Thank you for checking our team!

Pharmacology 435

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Sources:

1. 435's slides.
2. Pharmacology (Lippincotts Illustrated Reviews Series), chapter 36, 5th edition.
3. Basic & Clinical Pharmacology by Katzung, chapter 52, 12th edition.
4. Rang & Dale's pharmacology, chapter 53, 7th edition.