

Anti-malarial drugs

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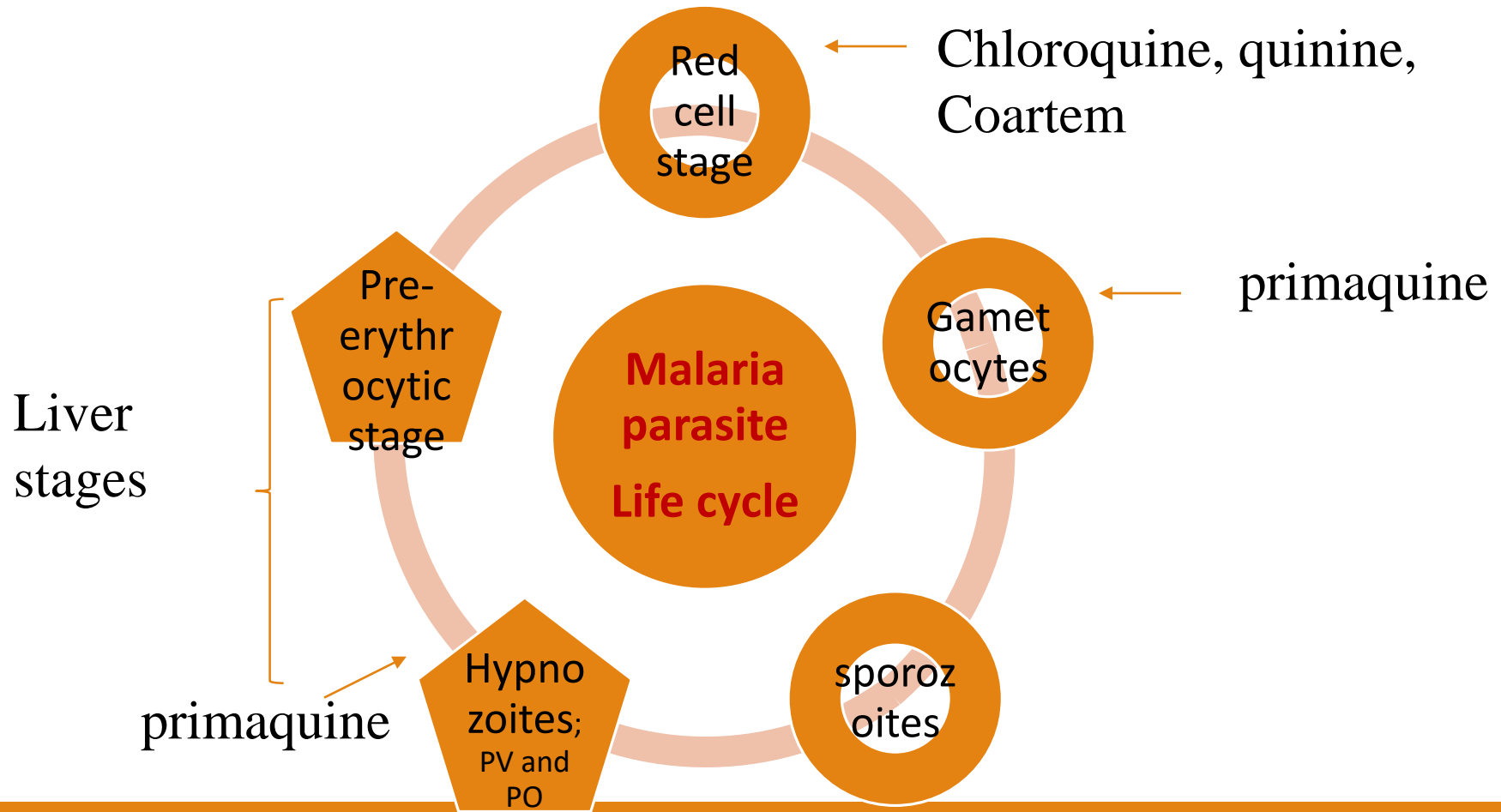
Objectives

- Introduction
- Pharmacology of different anti-malarial drugs
- Principles of drug usage

Anti-malarial drugs

- Drugs used to treat and prevent malaria
 - chloroquine
 - quinine, mefloquine
 - primaquine
 - halofantrine, lumefantrine
 - artesunate, artemether
 - Coartem (artemeter + lumifantrine)
 - proguanil, pyrimethamine, sulfadoxine, dapsone
 - tetracycline, doxycycline
- But usage restricted to prevent development of drug resistant strains

Anti malarial drugs; site of action



Chloroquine

- Safe, cheap, rapid acting drug but drug resistance has developed esp. for *Plasmodium falciparum*
- MOA – inhibit production of non-toxic haem-compound and parasite die of toxic haem
- Well absorbed at GIT
- Act on all blood stages of all the species and all gametocytes except *P falciparum*.
- ADR- very mild e.g.. Pruritus
- Safe in pregnancy

Chloroquine cont.

- Preparations – oral or slow IV
 - Never give IM or rapid injections (reduce BP)
- Dose 1500mg within 48hrs (25mg/Kg over 3d)
- Indications
 - Now used only for uncomplicated pv malaria
 - Previously used for malaria prophylaxis when drug resistance level was less

Quinine

- Very effective
- Against blood schizonts
- Was the choice of drug in severe falciparum malaria pre-Coartem era
- Inhibit parasitic protein synthesis
- Well absorbed in GIT
- Metabolized by liver
- Excreted by kidney

Quinine

- **ADR** - a lot ...
 - Cinchonism - tinnitus, diminished auditory acuity, headache, blurred vision, nausea and diarrhea
 - Hypoglycaemia
 - AV conduction disturbances
 - Idiosyncratic reactions – pruritus, urticaria and rashes
- **Dosage**
 - Loading dose 20mg/Kg →
 - Then 10 mg/kg, 8-12hrly, slow iv infusion over 4-6hrs in dextrose
or
 - Oral 600mg 8hrly
 - for 7dys (1tab = 200mg)

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Primaquine

- Act on and kill –
 - gametocytes of all species
 - hypnozoites (only drug acting on these)
- Affect mitochondrial function of plasmodium
- **Dose –**
 - *P. vivax* / *ovale* hypnozoites – 15mg/day x 14 d
 - *p. falciparum* – single dose 45mg on day3 or prior to discharge

Primaquine

■ ADR-

- Intravascular hemorrhages in G6PD, but unlikely with single dose

■ Contraindicated in

- pregnancy
- <1 year olds
- G6PD deficient patients

Artemisinin based combination therapies (ACT)

- Fast acting blood schizonticides
- For *pv* and *pf* malaria
- No effect on hypnozoites
- Rapidly absorbed and converted into active metabolites in liver
- Preparations
 - Artesunate and artemether are derivatives of artemisinin
 - Artemether – lipid soluble, $t_{1/2}$ 4-11hrs
 - Used in combination with lumifantrine, which has a long $t_{1/2}$ to kill residual parasites
 - Currently used ACT in Sri Lanka is **Coartem**.
 - Coartem = 20mg artemether + 120mg lumifantrine

Artemisinin based combination therapies (ACT)

- Well absorbed with a fatty meal
- Weight appropriate doses given for 3d
- Not recommended for children with body mass less than 5kg
- ADR –few;
Transient heat blocks, neutropaenia, fever
- Always use the combination therapy to prevent emergence of resistance

Treatment principles

- Treat according to country's anti-malarial campaign guidelines
- Restricted drug use

P. vivax, uncomplicated disease

Chloroquine

Followed by Primaquine for 14dys

P. falciparum, uncomplicated disease

Coartem x3d

Followed by single dose primaquine

P. falciparum, complicated disease

IV/IM artesunate - 1st line

if not available, IV quinine

- At least for 24hrs and then full course of Coartem

Followed by single dose primaquine

Mixed infections

Treated as *P. falciparum* malaria with ACT

Except; Primaquine given for **14 days**

Pregnancy

- Use chloroquine or quinine only in T1
- Do not give primaquine
- Coartem used in treatment of complicated malaria or mixed infections in T2 and T3

Chemoprophylaxis for malaria

- Differs with parasite resistance patterns in different parts of the world.
- No need for prophylaxis to visit Sri Lanka
- E.g..
 - Chloroquine: 300 mg once weekly (start one week before travel)
 - Proguanil: 200mg once daily (start one week before travel)
 - Mefloquine: 250mg once weekly (start 1wk, preferably 2-3wks before travel)
 - Doxycycline: 100mg once daily (start 1-2dys before travel)