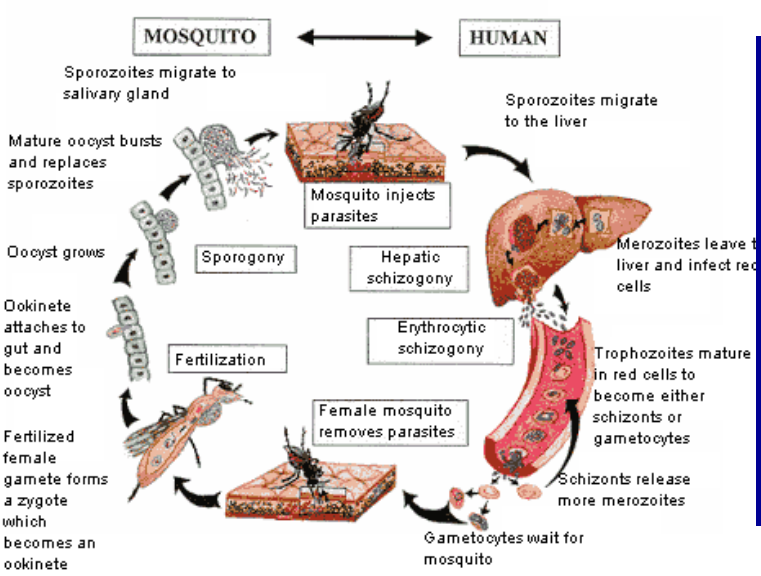
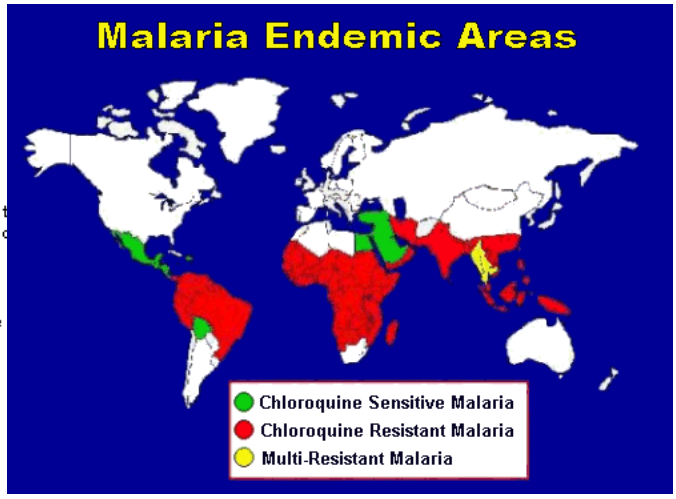
Malaria

Notifiable protozoan disease transmitted by female anopheles mosquito often endemic in developing nations and usually seen in developed countries secondary to travel exposure.

Life-cycle



Distribution



Epidemiology

- Tropics and subtropics <2000m in altitude.
  - Locally PNG, Solomon Islands, Vanuatu, SE Asia (P. vivax and P. falciparum)
- 40% world population at risk esp sub-Saharan Africa
- 500 million cases & 3 million deaths per year World-wide

Risk factors

- The poor, young children and infants, pregnant women (especially primigravidae), elderly people, non-immune people (e.g. travellers, foreign workers)
- In endemic areas:
  - High humidity and ambient temperature (20-30°C), altitude<2000m above sea level
  - Travel at times of high seasonal rainfall
  - Visits to rural locations
  - Staying in cheap backpacker accommodation
  - Being outdoors between dusk and dawn
  - Longer durations of travel
- Rare cases from blood transfusions, IVDU or "airport malaria" in airport workers or travellers to non-malarial areas.

Presentation

There are no specific symptoms of malaria - so need low index of suspicion.
Take exposure history (travel, prophylaxis compliance)

Symptoms:

- Fever (recurring)
- Chills or rigors
- Headache
- Cough
- Myalgia
- GI upset

Signs:

- Fever
- Splenomegaly
- Hepatomegaly
- Jaundice
- +/- Abdominal tenderness

Signs of severe disease (usually P. falciparum):

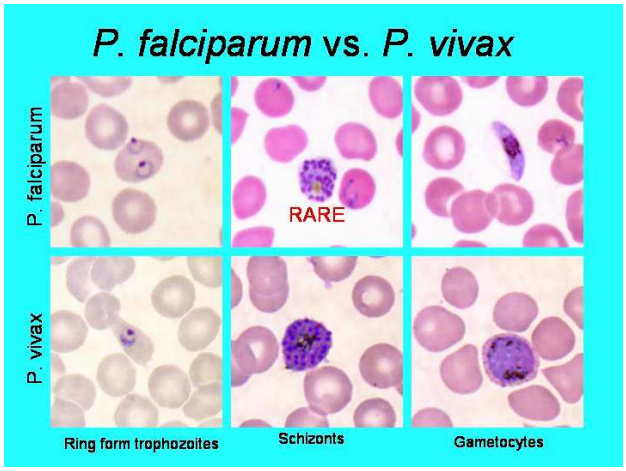
- Impaired LOC
- Shortness of breath
- Bleeding
- Fits
- Hypovolaemia
- Hypoglycaemia
- Renal failure
- Nephrotic syndrome
- ARDS (during treatment)

Plasmodium species differentiation

Species	Clinical features
P. falciparum	Responsible for severe disease and malaria related deaths. Incubation 7-14 days (up to 1 year if semi-immune), most travellers present within 2mo. Classical tertian & subtertian (3d & 1-2d intervals) rare, daily (quotidian) or irregular more common
P. vivax	Causes benign tertian malaria - fever every third day. Incubation period of 12-17 days. But may present several months later. Relapse due to dormant parasites in the liver.
P. ovale	Relapsing course as with P.vivax. Incubation period of 15-18 days. But may present several months later.
P. malariae	Causes benign quartan malaria - fever every 4th day- but this is frequently not observed. Long incubation period (18-40 days). Parasites can remain dormant in the blood. 5-10% present over a year after infection. With chronic infection, can cause nephrotic syndrome.

Differential diagnosis

Other traveller infections: Typhoid, hepatitis, dengue fever, avian influenza, SARS, HIV.
Also meningitis/encephalitis, viral hemorrhagic fevers



Investigations

Urine: U/A for Hb – 'black water fever'
Blood: FBC (normocytic anaemia, haemolysis, mildly ↓WCC & ↓plt), ESR, thick & thin blood film + Giemsa stain, UEC (↓Na, ↑Cr), BSL (↓), LFT, G6PD
Other: Rapid antigen tests, PCR, VDRL falsely +ve
DDx: Blood, urine and stool culture, coags, LP, CXR

Management

Non-falciparum malaria

- **Chloroquine** 620mg PO (child 10mg/kg) stat then 310mg (5mg/kg) @ 6hr, 24hr and 48hr.
  - If resistance suspected treat as for uncomplicated *Falciparum* malaria
- If not G6PD def: **primaquine** 30mg (child 0.5mg/kg)[*vivax*] or 15mg (0.25mg/kg)[*ovale*] od PO for 2wks.
- Discharge with LMO follow up.

Uncomplicated Falciparum malaria

- **Artemether+lumefantrine** 20/120mg: 4 tabs (child 5-14kg: 1 tab; 15-24kg: 2 tabs; 25-34kg: 3 tabs) PO with fatty food stat and @ 8, 24, 36, 48 & 60hrs **OR**
- **Quinine sulphate** 600mg (child 10mg/kg) q8h PO x 7d plus **doxycycline** 200mg PO OD (or **clindamycin** 300mg (child<8y 5mg/kg) PO q8h for pregnant women) x 7d **OR**
- **Atovaquone-proguanil** 250/100mg (Malarone®): 4 tabs (child 11-20kg: 1 tab; 21-30kg: 2 tabs; 31-40kg: 3 tabs) PO with fatty food OD x 3d **OR**
- **Mefloquine** (if not vomiting) 750mg (child: 15 mg/kg) PO stat, then 500mg (child: 10mg/kg) 6-8hrs later

Last 2 options should not be used if patients took these drugs as prophylaxis

Severe or complicated Falciparum malaria

Defined as:

- Altered LOC, jaundice, oliguria, severe anaemia or hypoglycaemia
- Parasite count above 100 000/mm3 (>2% of red blood cells parasitised)
- Patient is vomiting or clinically acidotic.

Treatment options – use artesunate if possible (not licenced but may be available in Australia)

- **Artesunate** 2.4 mg/kg IV stat q12h x 3 doses, then OD until oral therapy is possible with **artemether+lumefantrine**, as for *Uncomplicated Falciparum malaria*. **OR**
- **Quinine dihydrochloride** 20 mg/kg loading dose IV over 4hrs, then 10mg/kg q8h IV x 2d. ECG monitoring is required. Then **quinine sulphate** 600mg PO q8h PO when patient is well enough to complete a 7d course. A second oral drug should accompany PO quinine. See *Uncomplicated Falciparum malaria*.

Spread of drug resistance to *P. falciparum*

- Resistance to antimalarial drugs has spread rapidly over the past few decades.
- Currently no effective alternatives to artemisinins for resistant *P. falciparum* malaria.
- Artemisinin-based combination therapies (ACTs) are life-saving in high resistance areas.
- To preserve the efficacy of artemisinins, WHO supports a ban on PO monotherapy use.

Complications

Complications are almost always associated with *P. falciparum* infection and include:

- Impaired consciousness or seizures (cerebral malaria)
- Renal impairment
- Acidosis
- Hypoglycaemia
- Pulmonary oedema or acute respiratory distress syndrome
- Anaemia
- Splenic rupture
- Spontaneous bleeding or DIC
- Chronic malaria (*vivax*, *ovale*)
- Shock secondary to complicating bacteraemia/septicaemia (algid malaria)
- Haemoglobinuria ('black water fever')
- Multiple organ failure
- Death

Prognosis

If untreated or delayed Rx, malaria may be fatal. Cerebral malaria has a mortality of 20-50%.

Prevention

- **A**wareness of the risk of malaria – avoid endemic areas, esp if asplenic or pregnant
- **B**ites - reducing likelihood of bites from anopheline mosquitoes
    - Avoiding outdoor activity after sunset.
    - Wearing light-coloured long sleeved shirts, and trousers.
    - Avoid aftershave/perfumes.
    - Using insecticide-treated bed nets (ITNs)
    - Using insect repellent (50% DEET), on skin, clothing, and re-treating netting.
- **C**hemoprophylaxis (see below)
- **D**iagnosis and prompt treatment to prevent complications
- (Vaccine under development)

Malaria Chemoprophylaxis

Chemoprophylaxis

- Prophylaxis is not absolute, need other precautions and infection can still occur.
- Consider risks of drugs versus benefits based on risk assessment.
- Wide variation in recommendations, tailor to local risk.

Chloroquine sensitive area (increasingly rare):

- **Chloroquine** 310mg (child 5mg/kg) weekly, from 1wk before to 4wks after travel.
    - It remains effective against most P. vivax, all P. ovale and virtually all P. malariae.
    - It will however not prevent dormant liver stages of vivax and ovale.

Chloroquine resistant area (incl. Pacific Islands, SE Asia, India, China, Africa and S.America):

- **Atovaquone-proguanil** (Malarone®): 250/100mg 1 tab (child use 62.5/25mg tablets: 11-20kg: 1 tab; 21-30kg: 2 tabs; 31-40kg: 3 tabs) PO with fatty food OD from 1-2d before to 7d after travel **OR**
    - >90% effectiveness against falciparum
    - Only licensed for up to 28 days.
    - Few **SE**, mainly gastrointestinal and headaches.
    - Avoid in renal impairment.
    - Lack of safety data in pregnancy.
- **Doxycycline** 100 mg (child >8 years: 2.5 mg/kg up to 100 mg) PO OD from 2d before to 4wks after travel OR
    - >90% effectiveness against falciparum
    - Main **SE**: diarrhoea, photosensitive dermatitis and vaginal thrush.
    - CI: children under 12, pregnancy or lactation, liver impairment.
    - Used with caution in patients with liver impairment, myasthenia gravis and SLE
- **Mefloquine** 250mg tablet (child 5-9kg: 1/8 tab; 10-19kg: 1/4 tab; 20-29kg: ½ tab; 30-44kg: 3/4 tab) PO weekly from 2-3wks before to 4wks after travel.
    - 90% efficacy in Africa, but resistance is high in other areas (e.g. parts of SE Asia)
    - Major **SE** (convulsions, coma and psychotic disturbances) rare - 1 in 10,000 users.
    - CI: epilepsy, cardiac conduction defect, liver impairment or psychiatric disorder.
    - May not be safe in 1st trimester
- **Chloroquine** (as above)+**Proguanil** 200mg (child <2yr: 50mg; 2-6yr: 100mg; 7-10yr: 150mg) PO OD, from 1wk before to 4wks after travel. Certain parts of Africa only.

Mefloquine resistant area (incl. parts of SE Asia, Africa and S.America):

- Malarone® or doxycycline as above

Special situations

- Asplenia and severe splenic dysfunction: high risk of severe malaria..
- Pregnancy:
    - Pregnant women are twice as likely to be bitten by anopheline mosquitoes, the malaria is more severe, and the disease can cause miscarriage.
    - If must travel, give chloroquine and proguanil in areas where falciparum sensitive.
    - If proguanil is used, prescribe **folic acid** 5mg PO OD.
- Lactation:
    - Chloroquine, proguanil, and mefloquine are suitable. Doxycycline is contraindicated.
    - Lack of safety data re Malarone but may be considered if no suitable alternative.
    - Prophylaxis is required in breast-fed infants, as the amount in BM unpredictable.