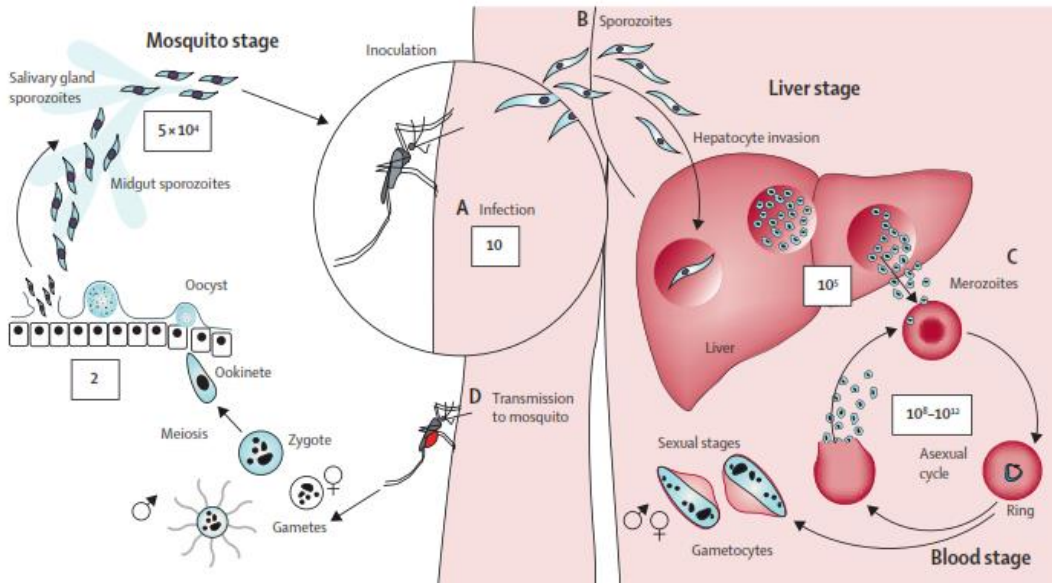
Plasmodium species

2014 tutorial : John Hunter Hospital advanced trainees in Infectious Diseases & Microbiology session

Plasmodium parasites belong to the *Apicomplexa* group of protozoa (this group also includes *Babesia, Toxoplasma, Cryptosporidium* sepcies.)



Female anopheles mosquito takes a blood feed → Innoculates motile sporozoites → Invading into hepatocytes → Multiply to produce daughter merozoites in 5.5 to 8 days → Hepatic schizont bursts → Liberated merozoites invade RBCs → Asexual cycle in bloodstream (falciparum/ vivax/ ovale 48 hrs; malariae 72 hrs; knowlesi 24 hrs) → Intraerythrocytic parasite consumes the RBCs and changes RBC membrane → Parasite population expands in blood reaching 50/uL in 8 days after exiting from liver. So, incubation is 12 to 14 days from infected bite.

P vivax and ovale have intrahepatic forms remaining dormant as hypnozoites for 2 wks to >1 yr, and can cause relapses. For vivax in trop areas, relapses can occur q3-4wks (or 6-8 wks after Rx); in temperate areas, latent for 8-10months.

Bloodstage infection can persist for months or years (or decades in P. malariae) when untreated. Also, waves of parasitemia or gametocytemia result from antigen variation or antigen switching, ie escaping the antibody response produced against previous waves. This increases with age.

Genetics

HbSS homozygote gets sickle cell disease. HbS heterozygote is protected against malaria ie balanced polymorphism.

Protective mechanisms: decreased parasite growth at low O2 tensions (HbA), reduced invasion (ovalocytosis), reduced cytoadherence (HbAC, HbCC, HbAS), reduced parasite densities (G6PD deficiency), and reduced multiplication at high densities (HbAE).

Protective against malaria also seen in: mutations associated with thalassemiaa, blood group O (reduced resetting in type O RBCs), people from west Africa carrying Duffy negative FyFy phenotype (resistant to P vivax).

Clinical features

First symptoms: non-specific, headache, fatique, headache, m aches, abdo discomfort, irregular fever. Fever occurs when schizont releases parasites and host cellular material into blood, activating monocytes and macrophages and inducing release of proinflammatory cytokines). Other symptoms may be nausea, vomiting, orthostatic hyptotension. More common to have enlarged liver in children, but jaundice in adults. In endemic areas, young children get recurrent infection with chronic anemia, and splenomegaly.

Uncomplicated malaria: fevers, mild anemia,+/- palpable spleen (after several days). Severe malaria: decreased LOC, jaundice, oliguria, severe anemia, hypoglycaemia, parasitemia >100,000/mm3 (2% of RBC), vomiting, acidosis.

Treatment

For severe malaria, assume to be chloroquine resistant falciparum. Rx Artesunate IV (first 24 hrs). Second line Rx is quinine hydrochloride IV. After that, PO artemether+lumefantrine. For Ped, can give artemther oil based IM or rectally.

For uncomplicated falciparum, Aust ETG: 1. Artemether+lumefantrine PO for 60 hrs, 2. Atovaquone + proguanil (not if used as prophylaxis)(cost issue and propensity for high grade resistance in endemic areas), 3. Quinine + Doxy/clindamycin. International literature: Artemisin component (rapid, effective, curative in 90%) for 3 days then a slowly eliminated partner drug (eg mefloquine SE vomiting dizziness neuropsych reactions in up to 1/200, CI in epilepsy and cardiac conduction defects) which can provide prophylaxis for 4-6 wks. Reinfection can occur 1 month after Artemether treatment. Primaquine can be added as a single gametocytocidal dose for falciparum (except infants and pregnancy).

Vivax outside Indonesia, Timor,Pac Islands, and ovale and malariae → chloroquine. Vivax from R areas → artemether+lumefantrine or mefloquine. Knowles → treat as for severe malaria. Vivax and ovale → Add Primaquine to eliminate liver forms.

Diagnosis

Thick and thin film still the gold standard. They should be prepared and read immediately by experienced staff. Thick film: parasitemia % can be calculated. Thin smear Giemsa stained can detect species (five species infecting humans)

Rapid tests are simple sensitive and specific. Some are fingerprick tests. Some are pan-malaria or some are species specific. Cannot quantity parasitemia.

1. PfHRP2 (histidine rich protein 2)- based tests can be positive weeks after acute infection. Not useful in high transmission areas. Good in Dx falciparum.
2. Newer generation tests detect plasmodium lactate dehydrogenase. Effective or Dx of both falciparum and vivax. But sens is low at vivax densities <200/uL.
3. Adolase-bases test are less sensitive, esp for non falciparum.

Prevention Latest vaccine development is the RTS,S subunit vaccine. It targets the circumsporozoite protein of falciparum. Trial of monthly doses for 3 mons shows good safety but efficacy is moderate (30%). Vector control: WHO emphasises integrated vector management. Pyrethroid insectide treated nets reduced all cause mortality by 20% in <5yo in Africa. Newer long-lasting nets are available. Other methods: Residual indoor spraying with DDT, personal insect repellents. ?Prophylaxis for children and pregnant women in Africa.