Risk factors for anaemia

In *P. falciparum*-infected subjects: young age, splenomegaly, chronic infection, recrudescence [70,71]

Anaemia or decreased haemoglobin

In *P. vivax*-infected subjects: young age, splenomegaly, chronic infection, repeated attacks [27,72]

Key data on major processes

In *P. falciparum* malaria: 8 uninfected RBC lost for 1 infected RBC in peripheral blood [67,70]

Red blood cell loss

In *P. vivax* malaria: 34 uninfected RBC lost for 1 infected RBC in peripheral blood [73]

In *P. falciparum* malaria: reticulocytes not high enough for level of anaemia [71]

Impaired red blood cell production

In *P. vivax* malaria: reticulocytes low during the first 10 days then appropriately increased during 3–6 weeks [60,61]

Markers of processes

Intravascular haemolysis RBC breaks in the bloodstream before being phagocytosed	**Extravascular haemolysis** RBC phagocytosed as intact cell	**Dyserythropoiesis** Progenitors proliferate but do not exit from the bone marrow	**Bone marrow insufficiency** Progenitors do not proliferate enough
↓	↓	↓	↓
Low haptoglobin & haemopexin High LDH & α-HBDH [71]	High annexin V & neopterin Low CD35 & CD55 [71] *In vitro* phagocytosis of uninfected RBC [71] Accumulation & phagocytosis of infected & uninfected RBC in the spleen [74] & bone marrow [66] Phagocytosis of infected & uninfected RBC in the spleen [75] & bone marrow [76]	Nuclear abnormalities of erythroblasts more frequent in children with chronic infection [66,68,69] 0.23-15.1% of erythroblasts with marked nuclear abnormalities in 6 of 9 adults with acute infection [76] Phagocytosis of erythroblasts (also in falciparum malaria) [69]	Decreased cellularity at acute stage in 3/11 adults [77] Rare observations of parasitized erythroblasts [78,79]. Not seen in 9 adults [76] No data in children or in severe anaemia. Proportion of erythroblasts normal or increased in 8 of 9 adults with acute infection [76]
↓	↓	↓	↓

Identified or suspected cellular mechanisms

Rupture of sequestered schizonts [80] Rupture of circulating schizonts including parasite-harbouring reticulocytes [63,64]. Intravascular haemolysis due to rupture of schizonts lower in *P. vivax* than in *P. falciparum* as parasitaemia is lower in P. vivax [9] Rupture of uninfected RBC (increased fragility) [81]	Mechanical retention of uninfected RBC in the spleen due to decreased deformability [82,83] Mechanical retention of rings in the spleen due to decreased deformability [84-87] Phagocytosis & opsonization of uninfected RBC decorated with RSP-2/RAP-2 [88], complement [89-91], immunoglobulins [92] or low levels of CD55 [104] Oxidative stress on uninfected RBC & infected RBC [93] (also in falciparum malaria) [94,95] Increased osmotic fragility & Heinz body formation of uninfected RBC [72]	Macrophage activation by cytokines or parasite products enhancing phagocytosis of progenitors (including erythroblasts) [69] although cytokine levels are generally lower in severe malarial anaemia than in cerebral or uncomplicated attacks [96,97] Toxic effect of parasite products (eg haemozoin) on progenitors (including erythroblasts) (also in falciparum malaria) [69] RAP-2 on the surface of erythroblasts & phagocytosis in vitro [98] Impaired iron utilization (also in falciparum malaria) [99]	Inappropriate bone marrow response to appropriate EPO levels in children [100,101] though possibly not in adults [102,103]