### Risk factors for anaemia

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

-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
- Anaemia or decreased haemoglobin
- Impaired red blood cell production

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

### Red blood cell loss

- Low haptoglobin & haemopexin
- High LDH & α-HBDH [71]

### Anaemia or decreased haemoglobin

- Nuclear abnormalities of erythroblasts more frequent in children with chronic infection [66,68,69]
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### Impaired red blood cell production

- 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-harbouiring 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]