



Malaria Pathophysiology

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Learning Objectives



- Review microbiology of *Plasmodium* spp. parasites
- Survey pathology of severe malaria
- Review factors that govern malaria pathogenesis
 - Parasite – mainly *P. falciparum*
 - Human hosts

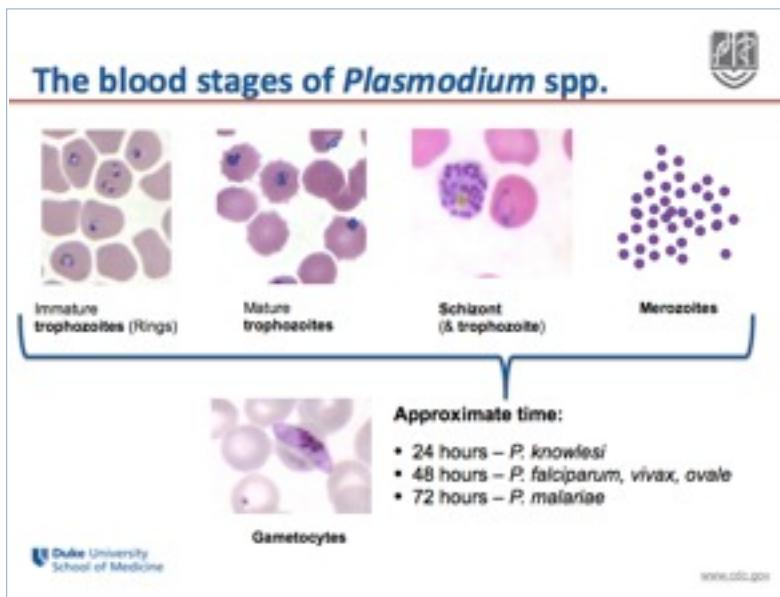
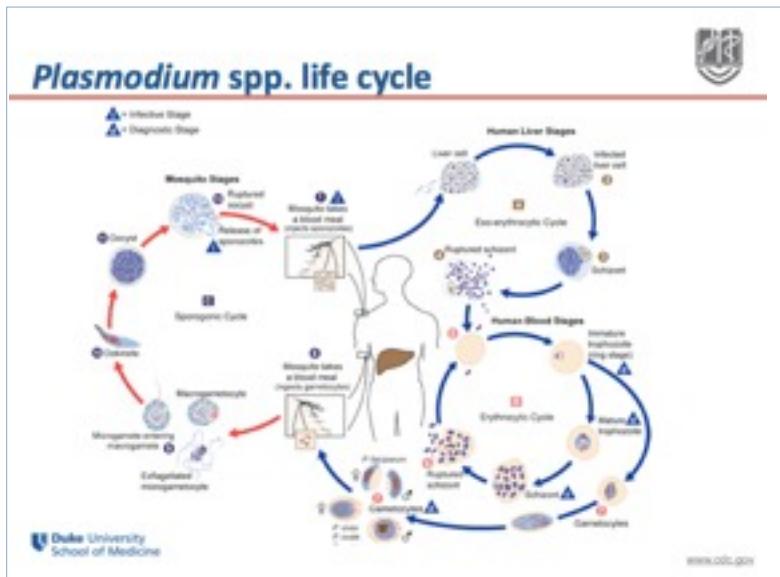


Plasmodium spp.



- Parasitic protozoa
 - More than 100 species
 - Infect humans, primates, birds, reptiles, rodents
- Host: vertebrate; Vector: mosquito
- Human *Plasmodium* spp.
 - *P. falciparum* – widespread, intense, deadly
 - *P. vivax* – debilitating, recurrent, S. Asia
 - *P. knowlesi* – newest human malaria, Malaysia
 - *P. malariae* & *P. ovale* – limited transmission

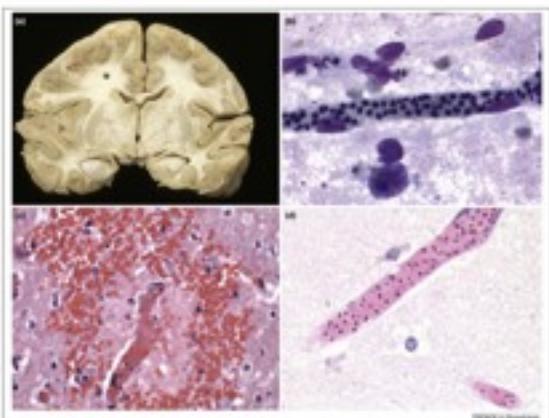




- ### Common signs & symptoms of malaria
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- Nonspecific symptoms
 - Fever, chills, rigors, headache, arthralgias, back pain
 - Red blood cell destruction
 - Anemia / pallor, splenomegaly, hepatomegaly
 - Severe malaria – primarily *P. falciparum*
 - Cerebral: obtundation, seizures
 - Severe malaria anemia
 - Multi-organ dysfunction: shock, respiratory distress, renal failure, lactic acidosis, coagulopathy
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Pathology of severe falciparum malaria

– Brain

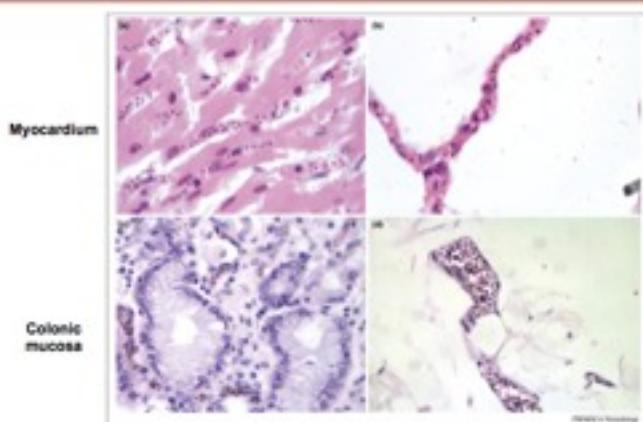


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Miner D et al. Trends Parasitol 2008

Pathology of severe falciparum malaria

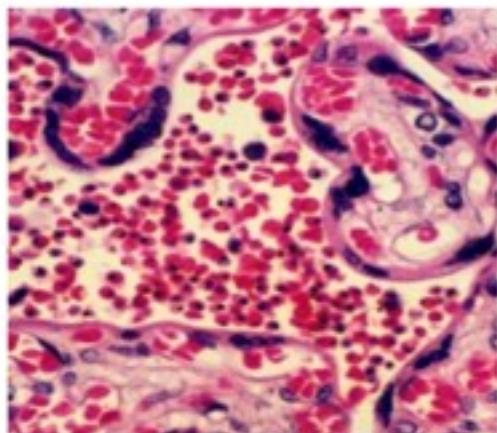
– Other Organs



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Pathology of placental falciparum malaria



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www.cdc.gov

Parasite factors



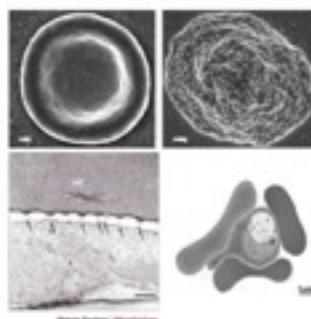
- Anemia
 - Red blood cell destruction, dyserythropoiesis
 - Cytokine activation
 - Initiated by hemozoin, parasite antigens
 - Parasite density
 - *P. falciparum* infects all RBCs; *P. vivax* only reticulocytes
 - Sequestration
 - Adherence to microvascular endothelium
 - Rosetting
 - Adherence to uninfected erythrocytes
- } Only *P. falciparum*

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Sequestration & rosetting



- Primarily mediated by *P. falciparum* erythrocyte membrane protein 1 (PfEMP1)
 - RBC "sticky knobs"
 - Bind to ICAM-1, CD36, CSA, CR1
- PfEMP1 also a major immunogen



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Painhuai PM et al. Nature 2009
Mayer AJ et al. Nat Rev Microbiol 2009
<http://tinyurl.com/DuKEEMP1>

Host factors



- Innate immune response
 - Comprises TNF, IFN- γ , NO, HO-1
 - Activated by hemozoin, PfEMP1, endothelium
- Acquired immune responses
 - IgG recognition of PfEMP1
 - Immunologic memory
- Innate resistance
 - *P. falciparum*: Hemoglobin S (sickle trait), hemoglobin C, G6PD deficiency, type O blood, ovalocytosis
 - *P. vivax*: G6PD-Mahidol, G6PD-Mediterranean, ovalocytosis

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Summary points



- Parasitic protozoa
 - Human & mosquito stages
 - Five species in humans
 - Blood stages of *Plasmodium* spp. malaria
 - Host-parasite dialogue pathogenesis
 - Parasite: RBC destruction, activation of innate responses, sequestration (*P. falciparum*)
 - Host: innate & adaptive responses, innate resistance

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