Plasmodium Species

Disease Agent:

- *Plasmodium falciparum, P. vivax, P. malariae, P. ovale, P. knowlesi*

Disease Agent Characteristics:

- Protozoan, 2-4 µm (ring form)
- Order: Haemosporida
- Family: Plasmodiidae
- All are intraerythrocytic parasites with characteristic microscopic appearance, some with portion of life cycle in hepatic cells.
- Life cycle includes asexual and sexual stages.

Disease Name:

- Malaria

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Low in most nonendemic countries but high in hyperendemic countries. Risk and concern with regard to blood safety may be moderate to high in some nonendemic countries, based on donor demographics and travel patterns of the donor population.
- Public perception and/or regulatory concern regarding blood safety: Moderate; risk and concern with regard to blood safety may be moderate to high in some nonendemic countries, based on donor demographics and travel patterns of the donor population.
- Public concern regarding disease agent: Moderate

Background:

- Generally limited to tropical and subtropical regions where it remains stable despite continued efforts to eradicate the mosquito vector. Local epidemiology can change rapidly in response to local geophysical and sociological conditions.
- Remains major public health concern in endemic regions of the world, particularly for children less than 5 years of age
- Re-emergent in nonendemic areas because of immigration and travel
- Sporadic cases attributed to "airport malaria" and autochthonous transmission increasingly reported
- Role of global warming heavily debated
- Classically, there have been four *Plasmodium* species associated with human malaria. Recently, a fifth *Plasmodium* species that causes human malaria has been identified. *Plasmodium knowlesi*, whose natural hosts are forest-dwelling macaques (the long-tailed and pig-tailed macaque), has a rapid doubling time (once daily) and rapidly reaches high parasitemia levels in humans with rapid development of anemia, jaundice, renal failure, and fatal outcomes similar to severe *P. falciparum* malaria. Humans acquire monkey malarias when they share the same habitat. In Asia (Malaysia), four fatalities initially mistaken for *P. malariae* infections were subsequently attributed to *P. knowlesi*; all were hyperparasitemic and developed marked hepatorenal dysfunction. *P. knowlesi* was detected by PCR in 266 (27.7%) of 960 archived samples from patients with malaria in Malaysia and Malaysian Borneo.

Common Human Exposure Routes:

- Bite of an infected female anophelene mosquito

Likelihood of Secondary Transmission:

- Low
- Transmitted transplacentally, by parenteral inoculation including blood transfusion and organ transplantation

At-Risk Populations:

- Individuals at increased risk for exposure to infected mosquitoes because of travel to or residence in areas where *Plasmodium* species are endemic

Vector and Reservoir Involved:

- Female mosquitoes of the genus *Anopheles*

Blood Phase:

- Symptomatic patients: weeks to months before spontaneous clearance unless appropriately treated with antimalarial drugs
- Asymptomatic patients: persistence with periodic blood phase in semi-immune individuals for years (e.g., from 1 to greater than 50 years, depending on the species of malaria)

Survival/Persistence in Blood Products:

- Generally, 7-10 days, based on historic data, but information on RBCs stored in contemporary anticoagulants is not available

Transmission by Blood Transfusion:

- Multiple cases worldwide
  - Common in endemic countries
  - Only three cases in the US from 1998 through 2007
  - Overall, US case rate has dramatically decreased during the last 40 years.
- The large majority of transmissions are from RBCs, but platelet components have been implicated, probably because of presence of RBCs.
- Four of five species of *Plasmodium* transmitted, but a large majority of recent US cases have been a result of *P. falciparum* and, to a lesser extent, *P. vivax*.

Cases/Frequency in Population:

- In the US, approximately 1000-1500 cases of malaria are reported yearly; 75% attributable to *P. falciparum* and *P. vivax* infections.
- *Plasmodium* species infections are primarily found in tropical and subtropical regions, where current estimates suggest there are more than 500 million clinical cases of malaria and two million or more deaths annually. The frequency varies considerably by location, with highest rates in sub-Saharan Africa.

Incubation Period:

- Varies by infecting species, immune status of patient and number of parasites transmitted. For *P. falciparum* and *P. vivax*, incubation period may be 1 week to 1 month but may require several months for *P. malariae*.

Likelihood of Clinical Disease:

- Low/moderate in semi-immune residents of endemic areas, higher in nonimmune visitors.

Primary Disease Symptoms:

- Periodic fever and rigors, chills, headache, myalgias, arthralgias, splenomegaly, and hemolytic anemia
- In blood recipients, onset of symptoms may be delayed by months. The nonspecific nature of the symptoms, plus their delay in onset, makes recognition of clinical disease in blood recipients difficult.

Severity of Clinical Disease:

- Most severe forms of malaria are associated with *P. falciparum*. High levels of parasitemia observed, leading to microvascular obstruction and severe complications (e.g., cerebral malaria).

Mortality:

- 1.5-2.7 million deaths per year worldwide
- 11% of US transfusion cases are fatal, compared with 0.43% of vector-derived cases in the US

Chronic Carriage:

- Occurs classically for infections with *P. malariae*, less commonly with *P. ovale* and *P. vivax*. Chronic infections can also occur with *P. falciparum*, but are even less common.

Treatment Available/Efficacious

- Variety of drug treatments available worldwide (not all in the US): chloroquine, sulfadoxine-pyrimethamine, mefloquine, atovaquone-proguanil, quinine, doxycycline, and artemisinin derivatives
    - Widespread drug resistance has developed in many locations.
    - In cases with high parasitemia, exchange transfusion is recommended.

Agent-Specific Screening Question(s):

- Risk questions pertaining to residence in or travel to endemic areas or history of malaria are currently used in the US.

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists. Two testing strategies have been discussed—universal screening to allow consideration of modifying the current donor geographic-risk questions and the "testing-in" strategy for deferred donors. In the US, both strategies appear to be dependent on test kits containing antigens to the four main *Plasmodium* species infecting humans.
- IFA and EIA to detect IgG antibodies are used for "testing in" (i.e., shortened deferrals) by several European countries and in Australia (i.e., donors with a travel history that would otherwise lead to deferral are evaluated further by laboratory testing and allowed to donate sooner if their antibody test is negative; in Australia, plasma, but not RBCs from seropositive donors can be used during the deferral period).
- Options for laboratory testing include blood smear microscopy, IFA, EIA, antigen based rapid diagnostic tests, and NAT.

Currently Recommended Donor Deferral Period:

- 1 year for travel to endemic areas
- 3 years for those who have lived for 5 or more years in endemic areas
- 3 years for those who previously had malaria and are now asymptomatic

Impact on Blood Availability:

- Agent-specific screening question(s): Current questions result in the deferral of greater than 100,000 blood donors each year in the US, with very few likely infected or infectious.
    - The impact of self-deferrals is unknown but likely much greater.
- Laboratory test(s) available: Not applicable

Impact on Blood Safety:

- Agent-specific screening questions(s): Transfusion-transmitted cases continue to decline, with only three cases since 1998, suggesting that current geographic risk-factor questions are having a positive impact on blood safety; however, the impact of questions has not been evaluated empirically.
- Laboratory test(s) available: Not applicable

Leukoreduction Efficacy:

- Unlikely to be effective for this intraerythrocytic parasite

Pathogen Reduction Efficacy for Plasma Derivatives:

- No specific data are available but it is presumed that the agent should be sensitive to many measures used in the fractionation process.

Other Prevention Measures:

- Mosquito avoidance
- Antimalarial prophylaxis for visitors to endemic areas
- Feasibility of pathogen reduction demonstrated using several different compounds and approaches

Suggested Reading:

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