Japanese Encephalitis Virus

Disease Agent:
- Japanese encephalitis virus (JEV)

Disease Agent Characteristics:
- Family: Flaviviridae; Genus: Flavivirus
- Virion morphology and size: Enveloped, icosahedral nucleocapsid symmetry, spherical particles, 40 to 60 nm in diameter
- Nucleic acid: Linear, positive-sense, single-stranded RNA genome, ~11.0 kb in length
- Physicochemical properties: Infectivity inactivated and destroyed by heating for 10 minutes at >56°C; half life of 7 hours at 37°C; sensitive to treatment with lipid solvents, detergents, ether, trypsin, chloroform, formaldehyde, heat and β-propiolactone; infectivity reduced after exposure to irradiation and inactivated at pH 1-3

Disease Name:
- Japanese encephalitis

Priority Level:
- Scientific/Epidemiologic evidence regarding blood safety: Theoretical; because of the similarity to WNV, transfusion risk during JEV outbreaks may occur.
- Public perception and/or regulatory concern regarding blood safety: Absent
- Public concern regarding disease agent: Absent

Background:
- Recognized in horses and humans in 1871; severe epidemic occurred in Japan in 1924; isolated from human brain in 1935
- Increasing in India, Nepal, and South East Asia while declining in Japan, S. Korea, Taiwan, and China since 1970 because of widespread vaccination programs and other preventive measures
- Most recently detected in Australia
- Over 50,000 cases and 10,000 deaths occur annually in Asia, but the disease is greatly underreported.

Common Human Exposure Routes:
- Vector-borne (mosquitoes)

Likelihood of Secondary Transmission:
- Absent

At-Risk Populations:
- Widely distributed in Asia
- Affects all ages, but especially children and the elderly

Vector and Reservoir Involved:
- Main epidemic vector is mosquitoes of the Culex species, especially C. tritaeniorhynchus.
- In temperate regions, pigs and birds (principally ardeid species, such as egrets and black-crowned night herons, and possibly ducks) are effective amplifying hosts.

Blood Phase:
- Virus can be isolated from the blood infrequently after the appearance of symptoms. It is unknown whether a biologically relevant viremic phase occurs during asymptomatic infections.

Survival/Persistence in Blood Products:
- Unknown

Transmission by Blood Transfusion:
- No cases documented; however, because of similarity to WNV (i.e., mosquito-borne flavivirus that results in community epidemics), transfusion transmission might be expected to occur during JEV outbreaks.

Cases/Frequency in Population:
- Widely distributed in Asia; infection rates may exceed 1% during periods of peak transmission
- Where vaccination programs are not in place, nearly all persons in endemic areas have been infected (antibody-positive) by young adulthood.
- Not endemic in the US but imported by travelers from endemic areas

Incubation Period:
- 6-16 days from exposure to onset of symptoms

Likelihood of Clinical Disease:
- Inapparent-to-apparent infection rate ranges from 200-300 to 1

Primary Disease Symptoms:
- Febrile headache syndrome
- Aseptic meningitis
- Encephalitis characterized by rapid onset with a 2- to 4-day prodrome of headache, fever, chills, nausea, vomiting, dizziness, and drowsiness followed by nuchal rigidity, photophobia, altered states of consciousness, hyperexcitability, and neurologic signs of CNS involvement.

Severity of Clinical Disease:
- Severe manifestations of the disease can occur with accompanying mortality.
- Neuropsychiatric sequelae are frequent (45%-70% of survivors) and include Parkinsonism, convulsive dis-
orders, paralysis, mental retardation, and psychiatric disorders.

**Mortality:**
- Children and elderly are at highest risk for mortality which ranges from 5%-40% with the highest frequency usually associated with poor medical care and the most severe cases (2%-11% in US military personnel)

**Chronic Carriage:**
- Evidence for persistent/latent infection in humans based on recovery of JEV from PBMC of asymptomatic children 9 months after acute JEV as well as in children developing recurrent disease. JEV was also recovered from CSF 4 months after onset of symptoms. The relevance of these data remains to be elucidated.

**Treatment Available/Efficacious:**
- Supportive treatment

**Agent-specific Screening Question(s):**
- No specific question is in use.
- No sensitive or specific question is feasible.

**Laboratory Test(s) Available:**
- No FDA-licensed blood donor screening test exists.
- Virus can occasionally be isolated in cell culture from the blood of symptomatic cases. Isolation possibilities are better from the CSF (up to one-third of cases).
- Serology on paired serum samples showing fourfold rise in titer by neutralization, CF or HI is diagnostic.
- An IgM-capture EIA test is helpful in diagnosing JEV by detection of serum and intrathecal antibody.

**Currently Recommended Donor Deferral Period:**
- No FDA Guidance or AABB Standard exists.
- Prudent practice would be to defer for 1 year after resolution of symptoms based on limited data regarding persistence in PBMC.

**Impact on Blood Availability:**
- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

**Impact on Blood Safety:**
- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

**Leukoreduction Efficacy:**
- Unknown, but PBMC isolation study mentioned previously suggests that leukoreduction might lower a theoretical risk

**Pathogen Reduction Efficacy for Plasma Derivatives:**
- Multiple pathogen reduction steps used in the fractionation process have been shown to be robust in removal of enveloped viruses.

**Other Prevention Measures:**
- Formalin-inactivated vaccines for humans have an efficacy of 91%; a live attenuated vaccine is in use in China yielding seroconversion in 95% after one dose. Genetically engineered vaccines are in development.
- Mosquito control

**Suggested Reading:**