**Tick-Borne Encephalitis Virus Complex**

**Disease Agent:**
- Tick-borne encephalitis (TBE) virus complex

**Disease Agent Characteristics:**
- **Family:** Flaviviridae; **Genus:** Flavivirus; **Subtypes:** European, Far Eastern, and Siberian
- **Virion morphology and size:** Enveloped, polyhedral nucleocapsid symmetry, spherical particles, 40-60 nm in diameter
- **Nucleic acid:** Linear, positive-sense, single-stranded RNA, ~11.0 kb in length
- **Physicochemical properties:** Nonionic detergents solubilize the entire envelope; infectivity sensitive to acid pH and high temperatures (total inactivation at 56°C for 30 min); virus stable at low temperatures, especially at ~60°C or below; aerosol hazard noted; virus inactivated by UV light, gamma-irradiation and disinfectants (relatively more resistant than mosquito-borne agents)

**Disease Name:**
- Tick-borne encephalitis (TBE)

**Priority Level:**
- **Scientific/Epidemiologic evidence regarding blood safety:** Very low
- **Public perception and/or regulatory concern regarding blood safety:** Absent
- **Public concern regarding disease agent:** Absent

**Background:**
- Clinically described in 1931 and virus isolated in 1937
- Natural distribution throughout north central Eurasia

**Common Human Exposure Routes:**
- Bite of infected ticks
- Consumption of unpasteurized goat, sheep, or cow milk or cheese from virus-infected livestock
- Aerosol hazard in laboratory

**Likelihood of Secondary Transmission:**
- Unlikely

**At-Risk Populations:**
- Forestry workers, farmers, military, outdoor enthusiasts

**Vector and Reservoir Involved:**
- *Ixodes ricinus* (Western Europe); *I. persulcatus* (eastern Eurasia); *I. ovatus* (China and Japan)
- *Dermacentor* species and *Haemaphysalis* species also implicated vectors in Ixodes-free areas
- Maintained in nature in small wild vertebrate hosts (rodents and insectivores); large mammals, such as goats, sheep, and cattle are a less important source of infection.

**Blood Phase:**
- Viremia can occur prior to the onset of symptoms (based on a single example of transfusion-transmitted TBE) and likely persists for some days after onset of symptoms. Duration of viremia not well documented.
- Transient viremia is probable in subclinical infections.

**Survival/Persistence in Blood Products:**
- Unknown

**Transmission by Blood Transfusion:**
- Two recipients in Finland developed symptoms after receiving components from a donor who became symptomatic (febrile) hours after donating blood. A serological diagnosis of TBE was made in the donor and both recipients, and no other risk factors were identified in the recipients.

**Cases/Frequency in the Population:**
- No cases in the US
- ~3000 cases in Europe; ~11,000 cases in Russia and former Soviet Union
- Seroprevalence studies, primarily in Europe (endemic areas), show rates ranging from 3 to 23%

**Incubation Period:**
- 2-28 days to onset of symptoms, but usually between 7 and 14 days

**Likelihood of Clinical Disease:**
- Clinical symptoms may develop in ~1 out of 60 persons infected but may approach 25% in some endemic areas

**Primary Disease Symptoms:**
- The European subtype typically shows a biphasic course. The first phase is flu-like including fever, headache, and myalgia; the second phase involves the CNS including aseptic meningitis, meningoencephalitis, meningoencephalomyelitis, and meningoencephaloradicalulitis.
- Onset of illness with the Siberian and Far Eastern subtypes of TBE is more insidious with a febrile prodrome that includes headache, anorexia, nausea, vomiting, and photophobia followed by stiff neck, sensorial changes, visual disturbances, and neurologic manifestations that include paresis, paralysis, sensory loss, and convulsions.
Severity of Disease:
- Infections with the Far Eastern and Siberian subtypes are generally more severe than with the European subtype; infections with the Far Eastern subtypes are more severe in children than in adults.

Mortality:
- Case-fatality rate for the European subtype of TBE is 1-2%.
- Case-fatality rate for the Far Eastern and Siberian subtypes is ~20%, but this is possibly biased by not including mild cases in the calculation.

Chronic Carriage:
- Evidence for persistent infection in neuronal tissue has been observed but not evidence for persistent viremia.

Treatment Available/Efficacious:
- Supportive

Agent-Specific Screening Question(s):
- No specific question is in use.
- Not indicated because transfusion transmission is limited to a single report.
- No sensitive or specific question is feasible. In endemic areas, a question on exposure to tick bites has been shown to be ineffective in distinguishing Babesia-infected from Babesia-uninfected donors. This question probably also lacks sensitivity and specificity for this agent.

Laboratory Test(s) Available:
- No FDA-licensed blood donor screening test exists.
- Diagnosis is made serologically by detection of IgM antibodies (EIA) and/or virus isolation from blood in cell culture or experimental animals, but sensitivity of the latter is ~10%.
- Protocols are available for NAT.

Currently Recommended Donor Deferral Period:
- No FDA Guidance or AABB Standard exists.
- At a minimum, donors should be recovered and free of signs and symptoms, but there are insufficient data (i.e., unknown duration of viremia) to make recommendations regarding a deferral period.

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:
- Unlikely to have an impact

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:
- Effective vaccines are available in endemic areas.
- Specific TBE immunoglobulin is available for pre- and postexposure prophylaxis
- Avoidance of tick bites in tick-infected forested areas during spring and summer by using insect repellants (e.g., DEET) and using protective clothing in addition to inspecting body and clothing for ticks; avoiding unpasteurized dairy products
- Education

Suggested Reading: