

## 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 meningoencephaloradiculitis.
- 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:**

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6. Saksida A, Duh D, Lortic-Furlan S, Strle F, Petrovec M, Avsic-Zupanc T. The importance of tick-borne encephalitis virus RNA detection for early differential diagnosis of tick-borne encephalitis. *J Clin Virol* 2005; 33:331-5.
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8. Wahlberg P, Saikku P, Brummer-Korvenkontio M. Tick-borne viral encephalitis in Finland. The clinical features of Kumlinge disease during 1959-1987. *J Intern Med* 1989;225:173-7.