4 | COLORADO TICK FEVER VIRUS

4.1 | Disease agent
- Colorado tick fever virus (CTFV)

4.2 | Disease agent characteristics
- Family: Reoviridae; Genus: Coltivirus within Spinareovirinae subfamily.
- Nonenveloped, icosahedral nucleocapsid structure, 80 nm in diameter.
- Twelve double-stranded RNA gene segments encoded within two capsids that are, ~29 kb in length.
- Stable at −70°C, 4°C, and room temperature, but loss of infectivity is accelerated at higher temperatures; may be inactivated by 70% ethanol; sodium hypochlorite (1000 mg/L) is highly effective after brief exposure; sensitive to UV light.

4.3 | Disease name
- Colorado tick fever

4.4 | 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 but very low in endemic areas

4.5 | Background
- Recognized as a distinct entity in the United States in 1930.
- Etiologic agent isolated from blood in 1943.
- Disease range corresponds to distribution of wood tick, Dermacentor andersoni, in the United States and Canadian Rocky Mountains, Sierra Nevada Range, and Black Hills at elevations 4000–10,000 feet. Type-specific CTFV has also been found in China and Europe.
- Transmission season is usually March-October with an April-July peak.
- Up to 400 cases are reported in the United States each year making it the second most common arboviral disease in the United States.

4.6 | Common human exposure routes
- Tick exposure has been reported in more than 90% of cases but only 48% have documented tick attachment. Transmission can occur following a brief tick attachment.

4.7 | Likelihood of secondary transmission
- None

4.8 | At-risk populations
- Predominantly persons hiking, fishing, or camping in enzootic locations
- 2.5 times more common in males than females with highest incidence in the 50–70-year age group

4.9 | Vector and reservoir involved
- Adult wood ticks of the species Dermacentor andersoni; other tick species may carry the virus, but their roles in transmission are uncertain.
- Major enzootic hosts include squirrels, chipmunks, mice, rats, porcupines, and rabbits.

4.10 | Blood phase
- The virus infects erythroblasts and prolonged intraerythrocytic viremia lasts up to several months and parallels survival of RBCs.

4.11 | Survival/persistence in blood products
- At least 8 days as documented in the single posttransfusion case
- 18 months in refrigerated blood clots

4.12 | Transmission by blood transfusion
- One documented case transmitted by transfusion
4.13 | Cases/frequency in population

- Endemic in mountainous regions that are within the distribution of the vector.
- A CTFV-like agent (Eyach virus) in France, Germany, Netherlands, and former Czech Republic and CTFV variants found in California in black-tailed jackrabbits have been associated with human disease.
- US disease surveillance reports document decreasing annual case numbers, from 80/year 1987–1994 to 5/year 2002–2012, likely due to changes in required reporting. Cases are thought to be greatly underreported.
- There are no good serologic survey data.

4.14 | Incubation period

- Mean incubation period is 3–5 days following a tick bite (range: <1–14 days).

4.15 | Likelihood of clinical disease

- Unknown

4.16 | Primary disease symptoms/signs

- Abrupt onset of fever (biphasic course in 50% of cases), chills, myalgia, headache, retroorbital pain, photophobia, malaise.
- GI symptoms in ~20% of cases (abdominal pain, nausea, vomiting).
- A maculopapular or petechial rash is seen in 5%–15% of patients.
- Leukopenia common.

4.17 | Severity of clinical disease

- Approximately 20% of CTFV patients are hospitalized.
- Protracted convalescence for several weeks or months (fatigue, asthenia) is more likely to be seen in adults (70%) than in children.
- Severe CNS and hemorrhagic forms have been described but occur at low frequency (CNS complications reported primarily in children with 15%–20% of all cases associated with stiff neck/meningeal irritation).

4.18 | Mortality

- Rare; three deaths reported in children, one in an octogenarian.

4.19 | Chronic carriage

- There is no evidence of a persistent carrier state, but prolonged viremia can occur after clinical disease.

4.20 | Treatment available/efficacious

- Ribavirin possibly effective in animal models; no data in humans.

4.21 | Agent-specific screening question(s)

- No specific question is in use.
- Not indicated because transfusion transmission is limited to a single reported case.
- 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 uninfected donors. This question probably also lacks sensitivity and specificity for this agent.

4.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test exists.
- Virus isolation from blood or stored refrigerated clots (up to 1.5 years) for diagnosis of acute infection.
- Direct fluorescent antibody assay to detect infected cells in clinical samples; indirect fluorescent antibody (IFA) assay to detect patient antibodies using infected cell cultures.
- Presumptive diagnosis with IgM EIA single sample or IgG EIA followed by plaque neutralizing antibody testing to detect a four-fold antibody titer rise between acute and convalescent samples; may require 14–21 days for antibody to become positive
- NAT often used to detect viral RNA in whole blood early in disease course.

4.23 | Currently recommended donor deferral period

- No FDA Guidance or AABB Standard exists.
- Given the prolonged viremia in some patients, a deferral of 6 months after resolution of symptoms is prudent and recommended by the US CDC.
4.24 | Impact on blood availability

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

4.25 | Impact on blood safety

- Agent-specific screening question(s): Not applicable
- Laboratory test(s): Not applicable

4.26 | Leukoreduction efficacy

- This would not be effective given that the replication site of the virus is the RBC.

4.27 | Pathogen reduction efficacy for plasma derivatives

- Theoretically, highly susceptible to inactivation because other viruses in the same family (e.g., bluetongue virus) are inactivated by pathogen reduction steps used in the fractionation.

4.28 | Other prevention measures

- Tick-avoidance measures (e.g., long pants, long sleeves, repellants)

SUGGESTED READING