

## 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  $-70^{\circ}\text{C}$ ,  $4^{\circ}\text{C}$ , 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

1. Centers for Disease Control. Transmission of Colorado tick fever virus by blood transfusion—Montana. *Morb Mortal Wkly Rep MMWR*. 1975;24:422–7.
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8. Yendell SJ, Fischer M, Staples JE. Colorado tick fever in the United States, 2002–2012. *Vector Borne Zoonotic Dis*. 2015;15:311–6.