

5 | CRIMEAN-CONGO HEMORRHAGIC FEVER VIRUS

5.1 | Disease agent

- Crimean-Congo hemorrhagic fever virus (CCHFV)

5.2 | Disease agent characteristics

- Family: *Nairoviridae*; Genus: *Orthonairovirus*.
- Virion morphology and size: Enveloped, helical nucleocapsid symmetry, spherical to pleomorphic particles, 80–120 nm in diameter.
- Nucleic acid: Three single-stranded, circular, negative-sense RNA molecules, S, M, and L of about 2 kb, about 5 kb, and about 12 kb, respectively; 19.1 kb in length.
- Physicochemical properties: Susceptible to many disinfectants, UV light, low pH; inactivated by dry heat (56° C for 30 min) and solvent-detergent treatments.

5.3 | Disease name

- Crimean-Congo hemorrhagic fever (CCHF)

5.4 | Priority level

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical; there are reasonable scientific grounds to confirm or suggest that viremia is a feature of infection with these agents. However, asymptomatic viremia has been neither well-studied nor sought aggressively, so there are few or no data to make a critical assessment of risk.
- Public perception and/or regulatory concern regarding blood safety: Absent.
- Public concern regarding disease agent: Very low, but moderate in endemic areas.

5.5 | Background

- First recognized in Crimean Peninsula in the 1940s.
- Distribution of CCHFV covers the greatest geographic range of any tick-borne virus.
- Endemic in sub-Saharan Africa, Bulgaria, European Russia, former Soviet Union, the Arabian Peninsula, Iraq, Pakistan, former Yugoslavia, northern Greece, and northwest China

- In recent years, CCHFV has been recognized for the first time in several countries.
- Classified among the highest priority for bioterrorism agents by the CDC (Category A) and requires BSL-4 containment measures.

5.6 | Common human exposure routes

- Transmitted by the bite of infected ticks, especially from the genera *Hyalomma* (that also serves as a reservoir), *Dermacentor* and *Rhipicephalus*.
- Contact with infected ticks during their removal or direct contact with blood or tissues of viremic patients or infected livestock (sheep, goats, cattle) that generally do not appear ill.

5.7 | Likelihood of secondary transmission

- Nosocomial transmission is well described related to unprotected contact with blood and body fluid from infected patients.

5.8 | At-risk populations

- Healthy individuals residing in endemic areas who live or work in close contact with blood from livestock; for example, shepherds, ranchers, and abattoir workers.
- A threat as a bioterrorist weapon via the aerosol route for populations not previously considered being at risk; however, may be difficult to weaponize.

5.9 | Vector and reservoir involved

- Hard (*Ixodes* ticks, esp. *Hyalomma*) and soft (argasid) ticks serve as vectors and reservoirs.
- Amplifying vertebrate hosts include birds, humans, rodents, hares, shrews, ruminants, bats, ostriches, and hedgehogs.
- Documented transovarial and sexual transmission among ticks.

5.10 | Blood phase

- A human viremic phase exists but is poorly characterized. In wild and domestic animals without clinical signs, the viremic phase may range from 2 to 15 days.

5.11 | Survival/persistence in blood products

- Unknown, but CCHFV can survive for a short time in the environment, especially in some organic material. Infectious virus was found for up to 10 days, and occasionally longer, in blood kept at 4°C (39°F).

5.12 | Transmission by blood transfusion

- Never documented.
- 0.58%–1.16% of healthy blood donors in western Spain, a substantial proportion with recognized potential exposure risks, had serological evidence of past infection.
- Transmitted by contact with blood and body fluids from ill patients.
- Can be transmitted by IV inoculation in non-human primate model.
- Peripheral blood mononuclear cells, especially dendritic cells, can be infected.
- UVC and methylene blue have reduced the infectivity of experimentally inoculated platelets and plasma, respectively.

5.13 | Cases/frequency in population

- No cases in the United States.
- CCHF is found in Bulgaria, Yugoslavia, the former Soviet Union, China, Iraq, United Arab Emirates, Pakistan, and sub-Saharan Africa.

5.14 | Incubation period

- Incubation period following tick bite is commonly 3–7 days (range 1–14 days).

5.15 | Likelihood of clinical disease

- High

5.16 | Primary disease symptoms

- Sudden onset with development of fever, myalgia, dizziness, neck pain and stiffness, backache, headache, and photophobia; nausea, vomiting, and sore throat are present early on and may be accompanied by diarrhea. Other signs include tachycardia,

lymphadenopathy, and a petechial rash on trunk and limbs.

- Hemorrhagic phenomena include melena, hematuria, epistaxis and bleeding from gums, vagina, and other mucosal surfaces or needle puncture sites about 5 days after onset of symptoms.
- In early infection, sharp mood swings may occur accompanied by confusion and aggressive behavior.
- After 2–4 days, agitation may be replaced by sleepiness and depression associated with abdominal pain in the right upper quadrant with detectable hepatomegaly as a result of hepatitis.

5.17 | Severity of clinical disease

- High morbidity and mortality

5.18 | Mortality

- Mortality rates of those with overt disease average 30% and range from 5% to 80%, usually occurring 5–14 days after onset of illness.

5.19 | Chronic carriage

- Not recognized

5.20 | Treatment available/efficacious

- In observational studies, both oral and parenteral ribavirin have been used and seem to be effective.

5.21 | Agent-specific screening question(s)

- No specific question is in use; however, current geographic deferrals for malaria would exclude at-risk populations from co-endemic sub-Saharan Africa and parts of South Asia if an asymptomatic viremia exists.
- Not indicated because transfusion transmission has not been definitively demonstrated.
- No sensitive or specific question is feasible. In endemic areas, a question on exposure to tick bites is ineffective due to a lack of sensitivity and specificity.
- Under circumstances of a bioterrorism threat, the need for, and potential effectiveness of, specific donor screening questions would need to be addressed.

5.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test exists.
- Virus isolation in newborn mice or cell culture (e.g., Vero, BHK-21) is rarely used for diagnosis because the agent is a BSL-4 pathogen.
- Laboratory tests used to diagnose CCHFV infection include EIA detecting antibodies and PCR in blood or in tissues; in survivors, antibodies can be diagnostic.
- Immunohistochemical staining can also show evidence of viral antigen in formalin-fixed tissues.

5.23 | Currently recommended donor deferral period

- No FDA Guidance or AABB Standard exists.
- There are insufficient data to make recommendations regarding an indefinite deferral period.
- The deferral interval applied to geographic risk for malaria is expected to be longer than what might be recommended for donors from CCHF co-endemic areas who have clinically recovered from their disease. A prudent minimum deferral period would be until complete recovery has been determined.

5.24 | Impact on blood availability

- Agent-specific screening question(s): Not applicable; in response to a bioterrorism threat, impact of a local deferral could be significant.
- Laboratory test(s) available: Not applicable.

5.25 | Impact on blood safety

- Agent-specific screening question(s): Not applicable; unknown impact in response to a bioterrorism threat
- Laboratory test(s) available: Not applicable

5.26 | Leukoreduction efficacy

- Probably ineffective because high viral titers are detectable in serum specimens from infected individuals.

5.27 | Pathogen reduction efficacy for plasma derivatives

- Multiple pathogen reduction steps used in fractionation process have been shown to be robust in the removal of enveloped viruses.

5.28 | Other prevention measures

- No safe and effective vaccine is available, although an inactivated, mouse-brain derived vaccine has been developed and used in Eastern Europe. DNA vaccines have shown promise in macaque models.
- Tick control with acaricides and standard personal protective measures in animal husbandry and health care settings.
- Barrier nursing procedures should be implemented, and standard precautions should be maintained when caring for infected patients.

5.29 | Other comments

- BSL-4 biocontainment level required for working with this pathogen.

SUGGESTED READING

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