Crimean-Congo Hemorrhagic Fever Virus

Disease Agent:

- Crimean-Congo hemorrhagic fever virus (CCHFV)

Disease Agent Characteristics:

- Family: *Bunyaviridae*; Genus: *Nairovirus*
- Virion morphology and size: Enveloped, helical nucleocapsid symmetry, spherical to pleomorphic particles, 80-120 nm in diameter
- Nucleic acid: Circular, segmented, negative-sense and ambisense, single-stranded RNA, 17.1-22.8 kb in length
- Physicochemical properties: Inactivated by dry heat (56°C for 30 min) and solvent-detergent treatments

Disease Name:

- Crimean-Congo hemorrhagic fever

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. 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

Background:

- First recognized in Crimean peninsula in the 1940s
- Endemic in sub-Saharan Africa, Bulgaria, European Russia, former Soviet Union, the Arabian Peninsula, Iraq, Pakistan, former Yugoslavia, northern Greece, and northwest China
- Appears stable in the population
- Distribution of CCHFV covers the greatest geographic range of any tick-borne virus.
- Classified among the highest priority for bioterrorism agents by the CDC (Category A)

Common Human Exposure Routes:

- Transmitted by the bite of infected ixodid ticks, especially from the genera *Hyalomma* (also serves as a reservoir), *Dermacentor*, and *Rhipicephalus*.
- Contact with infected ticks during their removal or contact with blood or tissues of infected livestock (sheep, goats, cattle, or ostriches)

Likelihood of Secondary Transmission:

- Significant with blood and body fluid contact
- Documented nosocomial transmission

At-Risk Populations:

- Healthy individuals residing in endemic areas who live or work in close contact with blood from livestock
- Shepherds, ranchers, and abbatoir 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

Vector and Reservoir Involved:

- Transmitted by ixodid ticks, especially from the genus *Hyalomma* that can also serve as a reservoir
- Documented transovarial transmission among ticks
- Vertebrate hosts include livestock (e.g., sheep, goats, cattle, ostriches), large wild herbivores, hares, and hedgehogs.

Blood Phase:

- Viremic phase exists, but the length is unknown.
- In animals, viremia develops 1-9 days after infection.

Survival/Persistence in Blood Products:

- Unknown

Transmission by Blood Transfusion:

- Never documented
- Virus has been transmitted by contact with body fluids from ill patients.

Cases/Frequency in Population:

- No cases in the US
- Has not been carefully quantified in endemic areas

Incubation Period:

- Incubation period following tick bite is commonly 3-7 days, with a documented maximum limit of 13 days.

Likelihood of Clinical Disease:

- High

Primary Disease Symptoms:

- Sudden onset with development of fever, myalgia, dizziness, neck pain and stiffness, backache, headache, and photophobia; nausea, vomiting, and sore throat present early on and may be accompanied by diarrhea.
- Over the next few days, 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.
- Other signs are tachycardia, lymphadenopathy, and a petechial rash on trunk and limbs.
- Other 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.

Severity of Clinical Disease:

- High morbidity and mortality

Mortality:

- Mortality rates range from 10 to 50%, usually occurring 5-14 days after onset of illness.

Chronic Carriage:

- Not observed

Treatment Available/Efficacious:

- Ribavirin, with encouraging results

Agent-Specific Screening Question(s):

- No specific question is in use; however, current geographic deferrals for malaria and group O HIV would exclude at-risk populations from endemic sub-Saharan Africa if an asymptomatic viremic interval 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 has been shown to be ineffective in distinguishing Babesia infected from uninfected donors. This question probably also lacks sensitivity and specificity for this agent.
- Under circumstances of a bioterrorism threat, the need for, and potential effectiveness of, specific donor screening questions would need to be addressed.

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)
- EIA for IgG and IgM antibodies (detectable after 1 week)
  - Fatal cases rarely show antibody development.
- Virus detection by RT-PCR
  - Virus and antigen are usually detectable up to 1-2 weeks after onset of illness.

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 because of geographic risk for malaria and group O HIV is expected to be longer than what might be recommended for donors from Crimean-Congo endemic areas who have clinically recovered from their disease.

Impact on Blood Availability:

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

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

Leukoreduction Efficacy:

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

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.

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.
- Tick control with acaricides and personal protective avoidance measures
- Barrier nursing procedures and universal precautions should be implemented when caring for infected patients.

Other Comments:

- BSL-4 biocontainment level

Suggested Reading:

1. Flick R, Whitehouse CA. Crimean-Congo hemorrhagic fever virus. Curr Mol Med 2005;5:753-60.
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4. World Health Organization Crimean-Congo haemorrhagic fever. 2001. [cited 2009 May]. Available from: http://www.who.int/mediacentre/factsheets/fs208/en/print.html
5. Yapar M, Aydogan H, Pahsa A, Besirbellioglu BA, Bodur H, Basustaoglu AC, Guney C, Avci IY, Sener K, Setteh MH, Kubar A. Rapid and quantitative detection of Crimean-Congo hemorrhagic fever virus by one-step real-time reverse transcriptase-PCR. Jpn J Infect Dis 2005;58:358-62.