CRIMEAN-CONGO HEMORRHAGIC FEVER STANDARD OPERATING PROCEDURES:

1. OVERVIEW OF ETIOLOGY AND ECOLOGY

FAD PReP

Foreign Animal Disease Preparedness & Response Plan

United States Department of Agriculture

United States Department of Agriculture • Animal and Plant Health Inspection Service • Veterinary Services

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The Foreign Animal Disease Preparedness and Response Plan (FAD PReP) Standard Operating Procedures (SOPs) provide operational guidance for responding to an animal health emergency in the United States.

These draft SOPs are under ongoing review. This document was last updated in **January 2017**. Please send questions or comments to:

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Disease

Crimean-Congo hemorrhagic fever, Central Asian hemorrhagic fever, Congo fever, Congo virus disease, Crimean hemorrhagic fever, Hungribta (blood taking), Karakhalak (black death), Khunymuny (nose bleeding), and viral tick-borne hemorrhagic fever disease.

Mortality and Morbidity

Small vertebraetes (excluding birds) and livestock may become viremic but do not experience signs. Human mortality varies from 5–80 percent, but rates are often around 30 percent.

Susceptible Species

Small vertebrates, livestock, ostriches, and humans.

Zoonotic Potential (yes/no)?

Yes.

Transmission

The primary modes of CCHF transmission to humans are through tick bites (primarily of the genus *Hyalomma)*, exposure to blood or tissues of infected livestock, and direct contact with blood or body fluids of other infected persons.

Persistence in the Environment

Virus stable in blood up to 10 days at 40°C, in wet conditions for 7 hours at 37°C, 11 days at 20°C, and 15 days at 4°C, and in dry conditions for 90 minutes to 24 hours.

1.1 Introduction

Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne zoonotic viral disease that can be severe in humans but does not produce clinical signs in domestic and wild ruminants (cattle, sheep, and goats), insectivores, small lagomorphs, and rodents. Humans are very susceptible to CCHF, which, after a 3–7 day incubation period, causes fever, myalgia, headaches, and gastrointestinal symptoms.[1] Though CCHF is endemic in many parts of Africa, Asia, Eastern Europe, and the Middle East, it does not currently exist in the United States.[2,3]

1.1.1 Goals

As a preparedness goal, the Animal and Plant Health Inspection Service (APHIS) will provide etiology and ecology summaries for CCHF and update these summaries at regular intervals.

As a response goal, the Unified Command and stakeholders will have a common set of etiology and ecology definitions and descriptions, to ensure proper understanding of CCHF when establishing or revising goals, objectives, strategies, and procedures.

1.2 Purpose

The purpose of this document is to provide responders and stakeholders with a common understanding of the disease agent.

1.3 Etiology

1.3.1 Name

CCHF is also referred to as Central Asian hemorrhagic fever, Congo fever, Congo virus disease, Crimean hemorrhagic fever, Hungribta (blood taking), Karakhalak (black death), Khunymuny (nose bleeding), and viral tick-borne hemorrhagic fever disease.[4]

1.3.2 Virus Characteristics

This disease has the following characteristics:[5]

- Family: *Bunyaviridae*
- Genus: *Nairovirus*
- Species: Crimean-Congo hemorrhagic fever virus.

[1] Center for Agriculture and Biosciences International. (2015). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cabi.org/isc/datasheet/87383.
[2] Appannanavar, S.B. and B. Mishra. (2011). An Update on Crimean-Congo Hemorrhagic Fever. *Journal of Global Infectious Diseases*, *3*(30), 285–292.
[3] CABI. (2015). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cabi.org/isc/datasheet/87383.
[4] Center for Food Security and Public Health (CFSPH), Iowa State University. (2007). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cfsph.iastate.edu/Factsheets/pdfs/crimean_congo_hemorrhagic_fever.pdf.
[5] International Committee on Taxonomy of Viruses. (2016). Retrieved from http://www.ictvonline.org/virusTaxonomy.asp.

1.3.3 Morphology

Crimean-Congo hemorrhagic fever virus (CCHFV) is a spherical enveloped ribonucleic acid virus with a diameter of approximately 100 nm. The virus can be differentiated from other members in the *Bunyaviridae* family under electron microscopy.[6]

1.4 Ecology

1.4.1 General Overview

There are 7 CCHFV genotypes—Asia-1, Asia-2, Euro-1, Euro-2, Africa-1, Africa-2, and Africa-3—recognized by the region in which they originated and still circulate. More than one genotype, however, can be found throughout multiple countries.[7]

CCHF was first described in the Crimean Peninsula in 1944 and later in the Democratic Republic of the Congo in 1956. Currently CCHF is widely reported in Africa, but in recent years, outbreaks in Asia and the Middle East have become more common.[8] Significantly, as no previous sporadic cases or outbreaks had ever been reported there, clinical cases of CCHF were observed in Turkey for the first time in the early 2000s, affecting people who handled livestock or were exposed to infected patients.[9]

1.4.2 Susceptible Species

A wide variety of domestic and wild vertebrates, including birds, may experience subclinical infection. Host preference of ticks carrying CCHF vary by life stage, with larvae and nymphs preferring small mammals and ground birds whereas adults may more likely be found on large mammals, such as livestock.[10,11]

1.4.3 Reservoirs

Reservoirs of CCHF include various domestic and wild animals. Common examples include livestock (cattle, sheep, and goats), hares, hedgehogs, and other small vertebrates.[12] CCHFV remains in livestock for up to a week. All animals appear to show no clinical signs.[13]

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[6] Appannanavar, S.B. and B. Mishra. (2011). An Update on Crimean-Congo Hemorrhagic Fever. *Journal of Global Infectious Diseases, 3*(30), 285–292.

[7] Alam M.M., et al. (2013). Crimean-Congo Hemorrhagic Fever Asia-2 Genotype, Pakistan. *Emerging Infectious Diseases, 19*(6). Retrieved from http://dx.doi.org/10.3201/eid1906.120771.

[8] CABI. (2015). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cabi.org/isc/datasheet/87383.

[9] Karti S.S., et al. (2004). Crimean-Congo hemorrhagic fever in Turkey. *Emerging Infectious Diseases, 10*(8). Retrieved from http://wwwnc.cdc.gov/eid/article/10/8/03-0928.

[10] CABI. (2015). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cabi.org/isc/datasheet/87383.

[11] World Health Organization. (2013). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.who.int/mediacentre/factsheets/fs208/en/.

[12] Appannanavar, S.B. and B. Mishra. (2011). An Update on Crimean-Congo Hemorrhagic Fever. *Journal of Global Infectious Diseases, 3*(30), 285–292.

[13] CFSPH, Iowa State University. (2007). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cfsph.iastate.edu/Factsheets/pdfs/crimean_congo_hemorrhagic_fever.pdf.

1.4.4 Transmission and Vectors

CCHF is a tick-borne disease. The major vectors are ticks of the genus *Hyalomma*. Other viable tick vectors include, but are not limited to: *Amblyomma*, *Rhipicephalus*, and *Dermacentor* species.[14] The primary modes of CCHF transmission to humans are through tick bites, exposure to blood or tissue of infected livestock, and direct contact with blood or body fluids of other infected persons.[15]

The virus is transmitted within tick populations through:

- transstadial transmission: larvae to nymphs to adults,
- vertical transmission: adult females to their eggs,
- venereal transmission: male ticks to female ticks during reproduction, and
- non-viremic transmission: infected to uninfected ticks feeding on the same host.[16,17]

1.4.4.1 Mechanical Vectors

Although most birds (excluding ostriches) seem to be resistant to CCHF infection, they have the potential to serve as mechanical vectors. Migratory birds, along with ungulates and livestock, can carry attached ticks great distances into new, previously unpopulated areas.[18] Furthermore, livestock have the potential to carry large numbers of ticks; for example, the presence of 100 *Hyalomma marginatum* individuals on a single animal is not considered unusual.[19,20]

1.4.4.2 Amplifying Hosts

Other wild vertebrate hosts, such as hares and hedgehogs, are considered amplifying hosts.[21] In one study, sheep inoculated with CCHF infected ticks became viremic and consequently infected newly attached, uninfected ticks 3–6 days post-inoculation. This experiment demonstrated that sheep have the potential to replicate the virus and pass it to uninfected tick vectors.[22]

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[14] CABI. (2015). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cabi.org/isc/datasheet/87383.
[15] Mardani, M. and B. Pourkaveh. (2012). Crimean-Congo Hemorrhagic Fever. *Iranian Journal of Clinical Infectious Diseases*, *7*(1), 36–42.
[16] CABI. (2015). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cabi.org/isc/datasheet/87383.
[17] Mardani, M. and B. Pourkaveh. (2012). Crimean-Congo Hemorrhagic Fever. *Iranian Journal of Clinical Infectious Diseases*, *7*(1), 36–42.
[18] CFSPH, Iowa State University. (2007). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cfsph.iastate.edu/Factsheets/pdfs/crimean_congo_hemorrhagic_fever.pdf.
[19] European Centre for Disease Prevention and Control. (n.d.). Hyalomma marginatum. Retrieved from http://ecdc.europa.eu/en/healthtopics/vectors/ticks/Pages/hyalomma-marginatum-.aspx.
[20] Estrada-Peña, A., Jameson, L., Medlock, J., Vatansever, Z., & Tishkova, F. (2012). Unraveling the ecological complexities of tick-associated Crimean-Congo hemorrhagic fever virus transmission: a gap analysis for the western Palearctic. *Vector-Borne and Zoonotic Diseases*, *12*(9), 743–752.
[21] CFSPH, Iowa State University. (2007). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cfsph.iastate.edu/Factsheets/pdfs/crimean_congo_hemorrhagic_fever.pdf.
[22] Wilson, M.L., et al. (1991). Transmission of Crimean-Congo haemorrhagic fever virus from experimentally infected sheep to *Hyalomma truncatum* ticks. *Research in Virology*, *142*(5), 395–404.

1.4.5 Personnel

Those in the livestock and agricultural industry, butchers, slaughterhouse employees, hospital workers, or individuals that practice veterinary medicine have the highest risk of infection with CCHF.[23] Hiking, camping, and other outdoor activities can increase risk of coming in contact with ticks.

1.4.5.1 Symptoms

Four stages are typically observed in CCHFV infected patients: incubation, prehemorrhagic, hemorrhagic, and recovery. Incubation lasts 1–9 days depending on how an individual was exposed.[24] Influenza-like symptoms (fever, chills, headache, and myalgia) present first. As symptoms worsen patients may experience rash, vomiting, abdominal pains, and diarrhea. The hemorrhagic phase, typically 2–3 days, consists of bleeding from the nose, gastrointestinal tract, uterus, and/or urinary tract.[25] Neurological symptoms such as reduced alertness, agitation, mood swings, and lack of clear thinking or ability to concentrate can develop.[26] Supportive therapy is the main form of treatment. Ribavirin is sometimes prescribed, but randomized human clinical trials showing its efficacy have never been published. Survivors can expect recovery to start 10–20 days after the first onset of symptoms.[27] Depending on hospitalization and treatment received, mortality rates can range from 5–80 percent.[28]

1.5 Environmental Persistence of CCHF

CCHF is susceptible to both heat and disinfectants.

Table 1. Resistance of CCHF to Physical and Chemical Action[29,30]

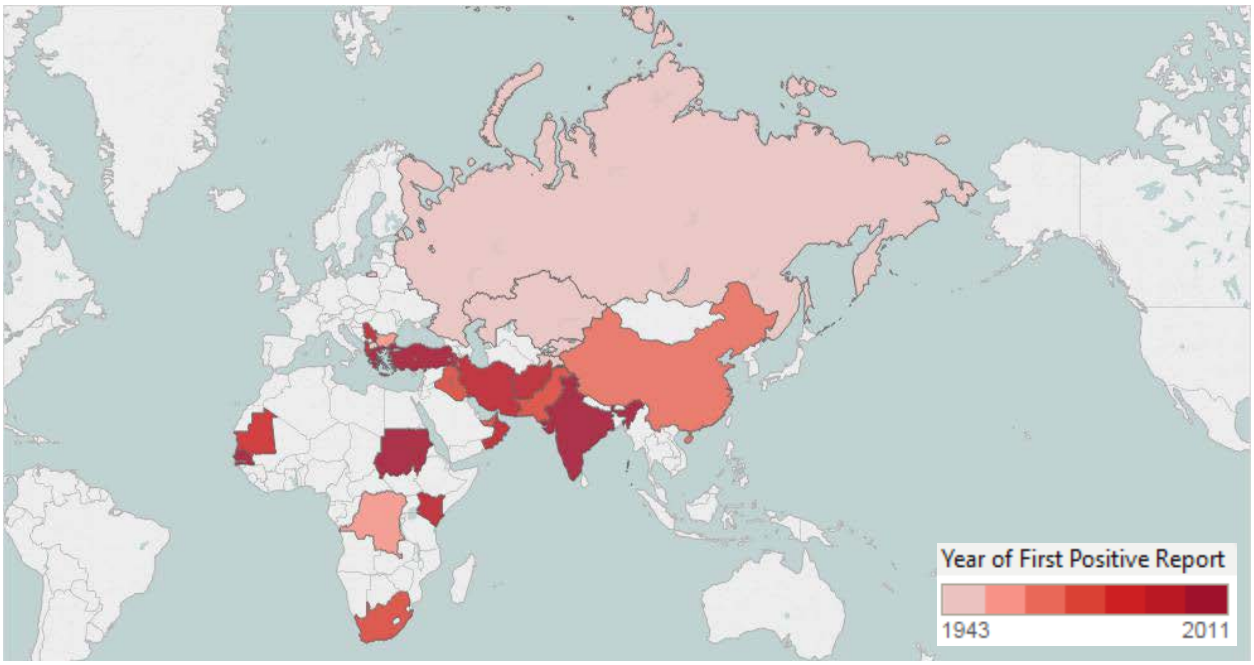
Action	Resistance
Temperature	Inactivated within 30 minutes at 56°C for 15 minutes at 60°C.
Chemicals/disinfectants	Inactivated by 1% hypochlorite and 2% glutaraldehyde.
pH	Inactivated by a pH less than 6.
Survival	Virus stable in blood up to 10 days at 40°C. In wet conditions stable for 7 hours at 37°C, 11 days at 20°C, and 15 days at 4°C. In dry conditions for 90 minutes to 24 hours.

[23] CFSPH, Iowa State University. (2007). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cfsph.iastate.edu/Factsheets/pdfs/crimean_congo_hemorrhagic_fever.pdf.
[24] Keshtkar-Jahromi, M. et al. (2011). Crimean-Congo hemorrhagic fever: Current and future prospects of vaccines and therapies. *Antiviral Research*, *90*(2), 85–92.
[25] World Organization for Animal Health (OIE). (2014). Crimean-Congo Hemorrhagic Fever. *Terrestrial Manual*. Retrieved from http://www.oie.int/.
[26] Bhanot, A., Khanna, A., and D. Talwar. (2015). Crimean-Congo hemorrhagic fever: An emerging threat for the intensivist. *Indian Journal of Critical Care Medicine*, *19*(9).
[27] CFSPH, Iowa State University. (2007). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cfsph.iastate.edu/Factsheets/pdfs/crimean_congo_hemorrhagic_fever.pdf.
[28] OIE. (2014). Crimean-Congo Hemorrhagic Fever. *Terrestrial Manual*. Retrieved from http://www.oie.int/.
[29] OIE. (2014). Public and Animal Health Importance of Crimean-Congo Hemorrhagic Fever and Other Tick-Transmitted Diseases of Animals in the Middle East. Retrieved from http://www.oie.int/doc/ged/D2954.PDF.
[30] Public Health Agency of Canada. (2011). Crimean-Congo Hemorrhagic Fever Virus. Retrieved from http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/crim-congo-eng.php.

1.6 Geographic Distribution

CCHFV has been detected in Africa, the Middle East and Asia. It has also been found in parts of Europe including southern portions of the former Soviet Union (Crimea, Astrakhan, Rostov, Uzbekistan, Kazakhstan, and Tajikistan), Turkey, Bulgaria, Greece, Albania, and the Kosovo province of the former Yugoslavia.[31] A more detailed map of countries with historic CCHF detections can be found in Figure 1; countries are color coded by year of first CCHF identification.

Figure 1. Map of Countries with CCHF, by Year of First Detection[32]



Geographic distribution of CCHF is correlated to the distribution of *Hyalomma* ticks worldwide.[33] Factors that influence tick populations and distributions include weather, climate change, vertebrate host populations, and vegetation. For example, extended cold weather inhibits larva and nymph development. Changes in these factors can alter tick survival, maturation, and egg production.[34]

It has been suggested that the extinction of camelids 5–2.5 million years ago along with the lack of species diversity of cloven-hoofed, ruminant mammals is responsible for the absence of *Hyalomma* ticks in North and South America.[35]

[31] CFSPH, Iowa State University. (2007). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cfsph.iastate.edu/Factsheets/pdfs/crimean_congo_hemorrhagic_fever.pdf.
[32] CABI. (2015). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cabi.org/isc/datasheet/87383.
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[34] CABI. (2015). Crimean-Congo Hemorrhagic Fever. Retrieved from http://www.cabi.org/isc/datasheet/87383.
[35] Sonenshine, D. and T. Mather. (1994). Ecological Dynamics of Tick-Borne Zoonoses. Oxford University Press.

1.7 CCHF in the United States

There is a risk that ticks could enter the United States on an imported host animal or travelers and/or their pets. *Rhipicephalus sanguineus* (brown dog tick), the most wide spread tick species in the world, is found throughout the United States. This indigenous arthropod species may be competent to transmit CCHFV. One study found that 55 percent of brown dog ticks collected from a sample of livestock in Hamadan Province in Iran were reverse transcription polymerase chain reaction positive for CCHFV.[36] Furthermore, CCHF susceptible domestic animals and wildlife hosts are present in the United States.

[36] Keshtkar-Jahromi, M., Sajadi, M. M., Ansari, H., Mardani, M., & Holakouie-Naieni, K. (2013). Crimean–Congo hemorrhagic fever in Iran. *Antiviral Research, 100*(1), 20–28.

Attachment 1.A References and Resources

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Attachment 1.B Abbreviations

APHIS	Animal and Plant Health Inspection Service
CABI	Center for Agriculture and Biosciences International
CCHF	Crimean-Congo hemorrhagic fever
CCHFV	Crimean-Congo hemorrhagic fever virus
CFSPH	Center for Food Security and Public Health
FAD PReP	Foreign Animal Disease Preparedness and Response Plan
OIE	World Organization for Animal Health
SOP	standard operating procedure
USDA	U.S. Department of Agriculture