CRIMEAN-CONGO HEMORRHAGIC FEVER: A REVIEW

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Summary

Crimean-Congo hemorrhagic fever is one of the most widely distributed viral hemorrhagic fevers with a high case fatality rate. This virus is a member of the genus *Nairovirus* in the family Bunyaviridae. The disease was first discovered in the Crimean region of Russia in the 1940s and is now reported in many regions of the world. The virus is transmitted to humans by the bite of Ixodid tick mostly of the Hyalomma genus or by contact with blood or tissues from human patients or infected livestock .Virus spreads from the initial infection site to regional lymph nodes, liver and spleen. At these sites, the virus infects tissue macrophages including Kupffer cells and dendritic cells. Horizontal transmission from a mother to her child has also been reported. Fever, headache, myalgia, arthralgia, abdominal pain and vomiting, sore throat, conjunctivitis, jaundice, photophobia and various sensory and mood alterations may develop after infection. Diagnosis is done with microscopic examination, immunoassay technique and nucleic acid detection test. Ribavirin orally and parenterally, specific immunoglobulin CCHF-Venin and vaccine for CCHF derived from inactivated mouse brain is used for treatment but the efficacy of this vaccine is not well quantified . Avoiding virus exposure, tick control, vertebrate control and barrier nursing of patients would be essential for prevention of disease.

Keywords: Bunyaviridae, Kupffer cells, Zoonotic Viral Disease

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Introduction

Crimean-Congo hemorrhagic fever (CCHF) is a zoonotic viral disease that is asymptomatic in infected animals, but a serious threat to humans. Human infections begin with nonspecific febrile symptoms, but progress to a serious hemorrhagic syndrome with a high case fatality rate. Although the causative virus is often transmitted by ticks, animal-to-human and human-to-human transmission also occur. [1] This disease is a particular threat to farmers and other agricultural workers, veterinarians, laboratory workers and hospital personnel. Crimean-Congo hemorrhagic fever is one of the most widely distributed viral hemorrhagic fevers. This disease occurs in much of Africa, the Middle East and Asia, as well as parts of Europe. Changes in climatic conditions could expand the range of its tick vectors and increase the incidence of disease. The CCHF virus is also a potential bioterrorist agent; it has been listed in the U.S. as a CDC/NIAID Category C priority pathogen. [2]

History

The first case of CCHF in South Africa was diagnosed in 1981. The virus was isolated from the blood of a school boy who died after being bitten by a tick in the North-West Province Internationally; [3] the disease was first recognized in the steppe region of western Crimea in 1944 when 200 peasants and soldiers developed a haemorrhagic disease.[4] In 1956, an identical virus was isolated from a child from the Congo. Later in 1969 the Congo and Crimean haemorrhagic fever viruses were shown to be identical, hence the name Crimean-Congo haemorrhagic fever (CCHF).[5] Crimean-Congo haemorrhagic fever is transmitted by the *Hyalomma* group of ticks (bont-legged) and is widespread. The virus has been found in Africa, Asia, the Middle East and Eastern Europe[1]. In order to control nosocomial infection, correct infection control procedures need to be followed to protect both the patients and the health- workers. [6]

Epidemiology Information

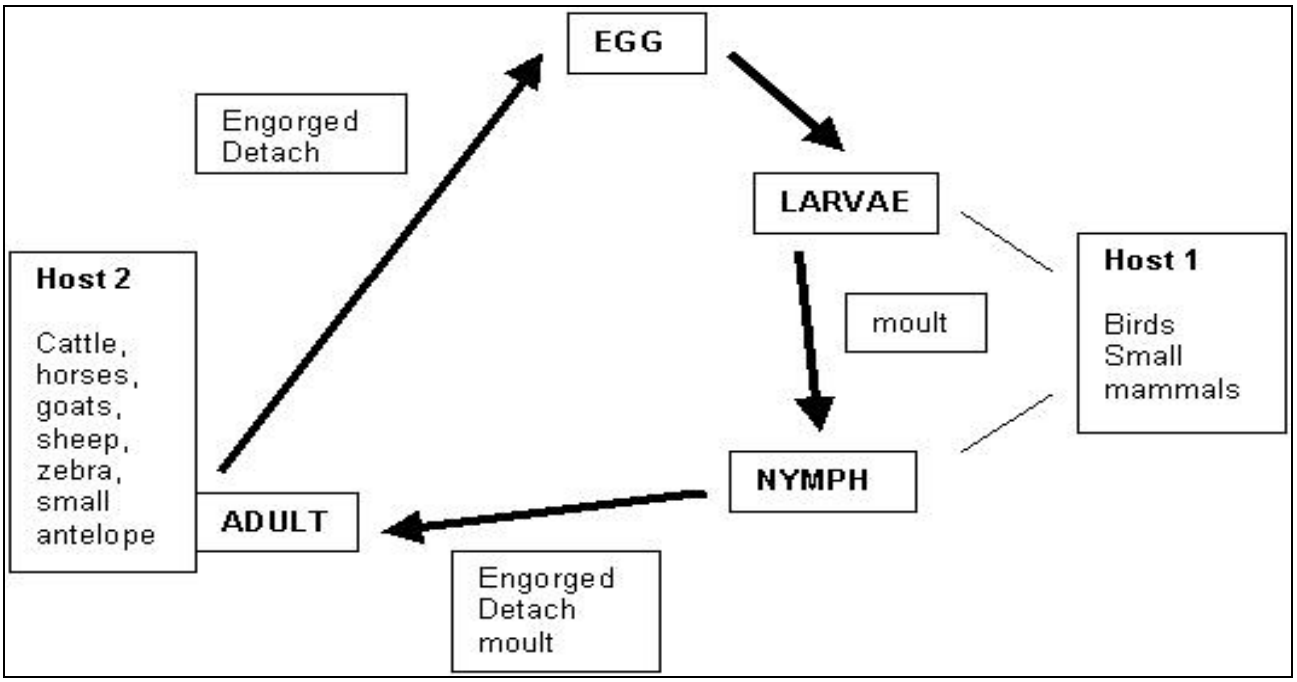
The geographic range of CCHF virus is the most extensive among the tick-borne viruses that affect human health and the second most widespread of all medically important arboviruses, after dengue viruses .The disease was first discovered in the Crimean region of Russia in the 1940s and is now reported in many regions of the world: Africa, the Middle East, Europe and Asia. In the territory of the former Soviet Union, disease outbreaks or the presence of the virus were reported in the southern regions of European Russia, in Mouldova, Ukraine and Transcaucasus and in Central Asian countries, in Tajikistan, Turkmenistan, Uzbekistan, Kyrgyzstan and Kazakhstan .[7] Published descriptions of major epidemics and outbreaks of CCHF have been reviewed extensively in the past. These reports illustrate the very wide distribution of CCHF virus. This distribution stretches over much of Asia, extending from the XinJiang region of China to the Middle East and southern Russia and to focal endemic areas over much of Africa and parts of south-eastern Europe. Thus, CCHF virus is the most widely distributed agent of severe haemorrhagic fever known. Before 1970, most cases were reported from the former Soviet Union (Crimea, Astrakhan, Rostov, Uzbekistan, Kazakhstan and Tajikistan) and Bulgaria, as well as virus circulation in parts of Africa such as the Democratic Republic of the Congo and Uganda. The initial recognition of haemorrhagic cases in Africa occurred in the 1960s, resulting in a series of in-depth studies in South Africa and reports of additional outbreaks from Congo, Mauritania, Burkina Faso, Tanzania and Senegal.[8] A substantial number of cases were also reported from Middle Eastern countries such as Iraq, the United Arab Emirates (UAE), Saudi Arabia and Oman and from Pakistan and China. By 2000, new outbreaks had been reported from Pakistan, Iran, Senegal, Albania, Yugoslavia, Bulgaria, Turkey, Kenya and Mauritania.

Serological evidence for CCHF virus has been reported from Greece, India, Egypt, Portugal, Hungary, France and Benin, although the virus was isolated only in Greece and the only reported human case was a Greek laboratory infection. CCHF virus is endemic in the Balkans, including Bulgaria, the former Yugoslavia and Albania. It is of interest that the strain that caused the laboratory-related infection in Greece was exceedingly mild, possibly reflecting chance variation; however, the virus has the greatest phylogenetic difference from other CCHF viruses and Greece is separated from Bulgaria by mountains approximately 1500-2500 m high. The common vector for CCHF virus is ticks of the genus Hyalomma. The virus is transmitted to humans either directly by Hyalomma ticks or by contact with infected domestic animals. CCHF virus is primarily a zoonosis, which means that the transmission cycle mainly involves ticks and wild or domestic animals. Cattle, sheep and goats do not become ill after infection but are viremic for about 1 week. During this period of time the virus may be transmitted to humans who have close contact to these animals such as agricultural workers, slaughterhouse workers and veterinarians. Furthermore, the virus may be spread into other geographical regions via infected livestock. The virus may also be transmitted from human to human who occurs primarily in the hospital setting. Health care workers are mainly at risk. [9]

Life Cycle

The bont-legged ticks show a wide distribution. They have two stages in their life-cycle. The larvae attach themselves to a host where they feed and moult into the nymph stage. The larvae and nymphs feed on small mammals up to a hare size and ground-frequenting birds. The nymph feeds; once it is engorged it drops off onto the ground and moults into the adult. The adult attaches itself to a second host. The adults prefer to feed on large animals. Once it has fed, it detaches itself and drops to the ground where the female lays eggs. In South Africa there are three species. The unfed adults are dark brown to black in colour reddish or orange-brown and white-banded legs.[10]

Figure 1: Life Cycle Crimean-Congo hemorrhagic fever

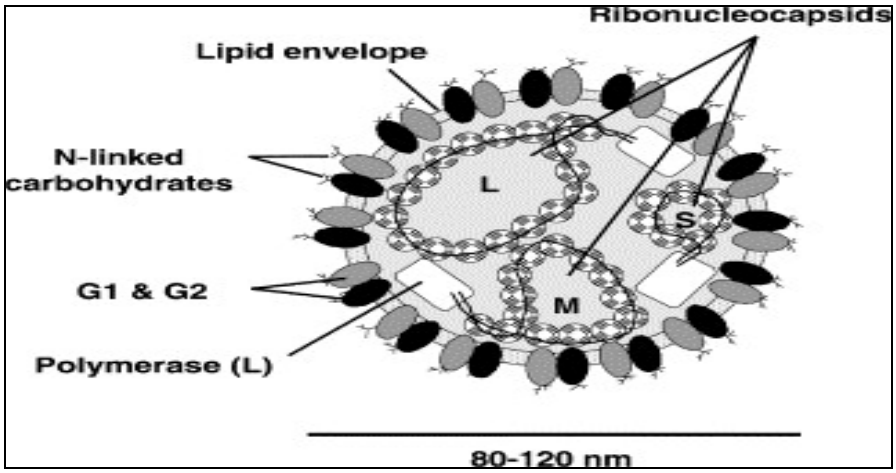


Etiology

Crimean-Congo hemorrhagic fever is caused by Crimean-Congo hemorrhagic fever virus (CCHFV). This virus is a member of the genus *Nairovirus* in the family Bunyaviridae. It belongs to the CCHF serogroup. Although early serological studies revealed very few differences between strains of CCHFV, nucleic acid sequence analysis has demonstrated extensive genetic diversity, particularly between viruses from different geographic regions. [11, 12]

Genome Summary

Figure 2: Genomic Structure of Bunyaviridae virion



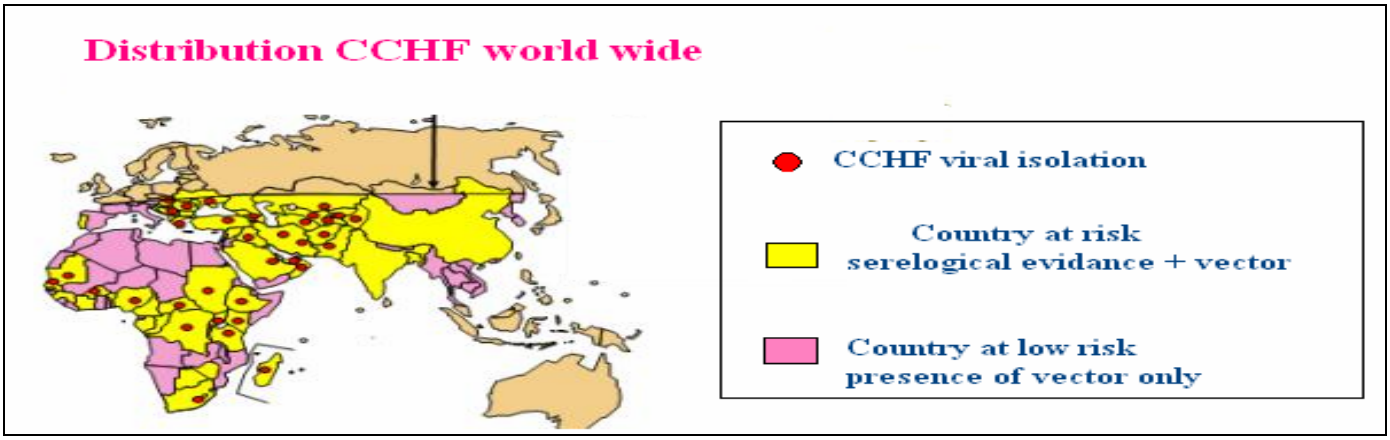
Schematic cross-section of a Bunyaviridae virion. The three RNA genome segments (S, M and L) are complexed with nucleocapsid protein to form ribonucleocapsid structures. The nucleocapsids and RNA-dependent RNA polymerase are packaged within a lipid envelope that contains the viral glycoproteins, G1 and G2 (also referred to as Gn and Gc, respectively) .[13]

Geographic Distribution

CCHFV is widespread in Africa, the Middle East and Asia. It has also been found in parts of Europe including southern portions of the former USSR (Crimea, Astrakhan, Rostov, Uzbekistan, Kazakhstan and Tajikistan), Turkey, Bulgaria, Greece, Albania and Kosovo province of the former Yugoslavia. Limited serological evidence suggests that CCHFV might also occur in parts of Hungary, France and Portugal. The occurrence of this virus is correlated with the distribution of *Hyalomma* spp., the principal tick vectors.[14]

Worldwide Distribution of CCHFV [15]

Figure 3: Distribution of CCHFV Worldwide



Distribution of Crimean-Congo hemorrhagic fever in various regions [16, 17, 18]

Table 1: Confirmed CCHF cases and deaths in Turkey, 2002–2008

Year	Cases	Death	CFR %
2002	17	0	0.0
2003	133	6	4.5
2004	249	13	5.2
2005	266	13	4.9
2006	438	27	6.2
2007	717	33	4.6
2008	688	41	6.1
Total	**2508**	**133**	**6.0**

Table 2: Confirmed CCHF cases and deaths in the Southern Federal District, Russian Federation, 2002–2008.

Year	Cases	Death	CFR %
2002	97	6	6.2
2003	77	3	3.9
2004	76	3	3.9
2005	137	4	2.9
2006	200	5	2.5
2007	234	4	1.7
2008	18	2	11.1
Total	**839**	**27**	**3.2**

Table 3: Suspect and confirmed cases of CCHF in Albania, 2001–2006.

Year	Suspected Cases	Confirmed Cases
2001	11	8
2002	9	4
2003	11	10
2004	15	9
2005	9	0
2006	5	1
Total	**60**	**32**

Table 4: Suspected and confirmed CCHF cases in Kosovo, 1995–2006

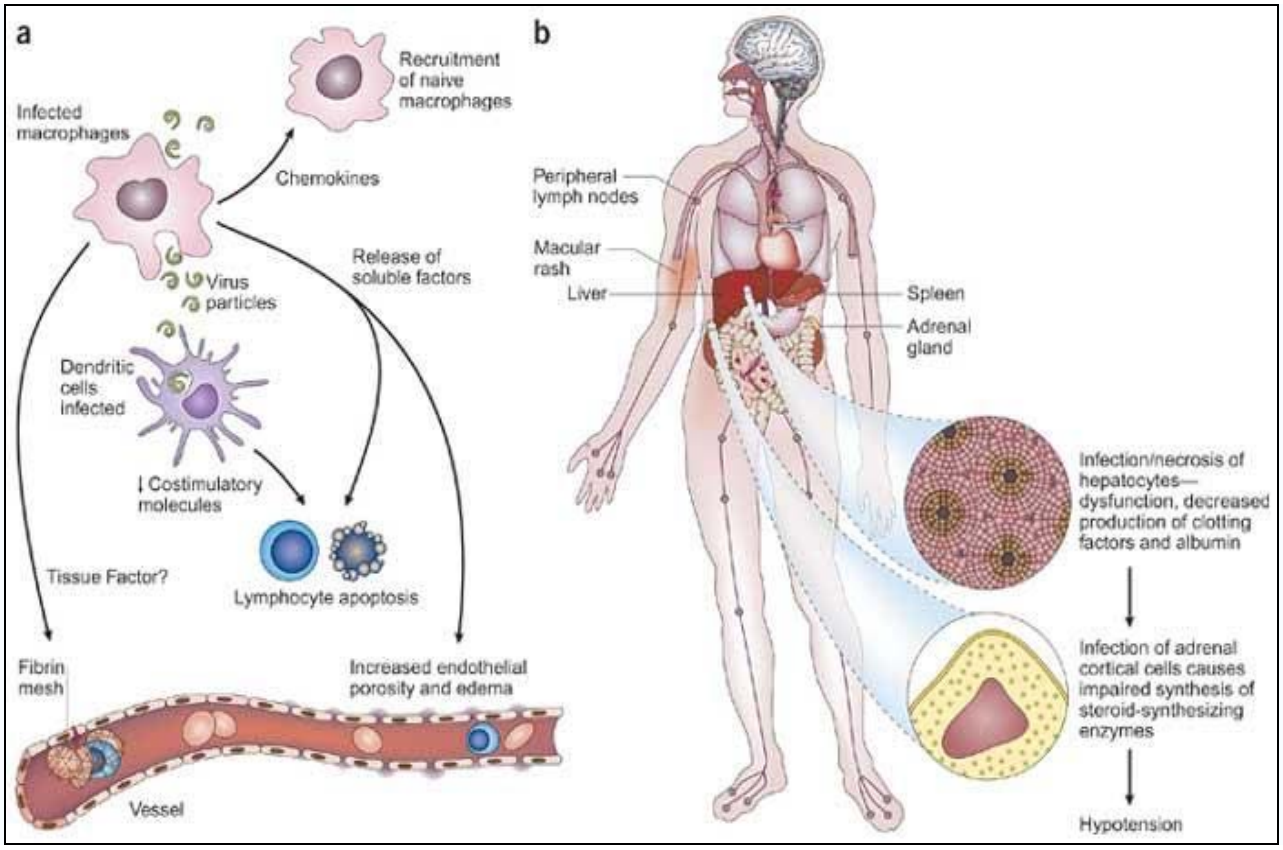
Year	Suspected Cases	Confirmed Cases	Death
1995	122	46	7
1996	23	9	5
1997	0	0	0
1998	1	1	0
1999	7	3	2
2000	2	1	0
2001	115	31	7
2002	114	14	3
2003	6	6	3
2004	17	12	2
2005	12	6	2
2006	11	5	2
Total	**430**	**134**	**33**

Pathogenesis Mechanism [19, 20]

Table 5: Pathogenesis of Crimean-Congo hemorrhagic fever

(a)	(b)
Virus spreads from the initial infection site to regional lymph nodes, liver and spleen. At these sites, the virus infects tissue macrophages (including Kupffer cells) and dendritic cells. Soluble factors released from virus-infected monocytes and macrophages act locally and systemically. Release of chemokines from these virus-infected cells recruits' additional macrophages to sites of infection, making more target cells available for viral exploitation and further amplifying the dysregulated host response. Although none of these viruses infects lymphocytes, their rapid loss by apoptosis is a prominent feature of disease. The direct interaction of lymphocytes with viral proteins cannot be discounted as having a role in their destruction, but the marked loss of lymphocytes is likely to result from a combination of factors including virus infection of dendritic cells and release of soluble factors from virus-infected monocytes and macrophages. For example, virus infection of dendritic cells impairs their function by interfering with the upregulation of costimulatory molecules, which are important in providing rescue signals to T lymphocytes. Additionally, release of soluble factors from infected monocytes and macrophages results in deletion of lymphocytes, both directly by release of mediators such as nitric oxide and indirectly by contributing to upregulation of proapoptotic proteins such as Fas and TRAIL. The coagulation abnormalities vary in nature and magnitude among the VHFs. For example, Ebola virus induces the overexpression of tissue factor, which results in activation of the clotting pathway and the formation of fibrin in the vasculature. In contrast, coagulation disorders are less marked in Lassa fever and impairment of endothelial function contributes to edema, which seems to be a more prominent finding in Lassa fever than in other VHFs.	The hemodynamic and coagulation disorders common among all of the VHFs are exacerbated by infection of hepatocytes and adrenal cortical cells. Infection of hepatocytes impairs synthesis of important clotting factors. At the same time, reduced synthesis of albumin by hepatocytes results in a reduced plasma osmotic pressure and contributes to edema. Impaired secretion of steroid-synthesizing enzymes by hemorrhagic fever virus-infected adrenal cortical cells leads to hypotension and sodium loss with hypovolemia. Macular rashes are often seen in VHFs.

Figure 4: Pathogenesis of Crimean-Congo hemorrhagic fever



Reservoirs and Vectors [21, 22]

- The CCHF virus may infect a wide range of domestic and wild animals. Many birds are resistant to infection, but ostriches are susceptible and may show a high prevalence of infection in endemic areas. Animals become infected with CCHF from the bite of infected ticks.
- A number of tick genera are capable of becoming infected with CCHF virus, but the most efficient and common vectors for CCHF appear to be members of the Hyalomma genus. Trans-ovarial (transmission of the virus from infected female ticks to offspring via eggs) and venereal transmission have been demonstrated amongst some vector species, indicating one mechanism which may contribute to maintaining the circulation of the virus in nature.
- However, the most important source for acquisition of the virus by ticks is believed to be infected small vertebrates on which immature Hyalomma ticks feed. Once infected, the tick remains infected through its developmental stages and the mature tick may transmit the infection to large vertebrates, such as livestock. Domestic ruminant animals, such as cattle, sheep and goats, are viraemic (virus circulating in the bloodstream) for around one week after becoming infected.
- Humans who become infected with CCHF acquire the virus from direct contact with blood or other infected tissues from livestock during this time, or they may become infected from a tick bite. The majority of cases have occurred in those involved with the livestock industry, such as agricultural workers, slaughterhouse workers and veterinarians.

Transmission

Human to Human

The virus is transmitted to humans by the bite of Ixodid tick (mostly of the Hyalomma genus) or by contact with blood or tissues from human patients or infected livestock. Transmission to humans can occur either through tick bites or possibly by crushing engorged infected ticks. Direct contact with virus-contaminated blood or tissues from infected animals or humans is another source of virus transmission and is generally characterized by more severe clinical symptoms and high mortality. The virus may also be transmitted from human to human who occurs primarily in the hospital setting. Hospital health-care workers are at serious risk of transmission of CCHF infection when caring for patients with haemorrhages from the nose, mouth, gums, vagina and injection sites[7]. The transmission of the CCHF infections and deaths among health-care workers has been reported in parallel with outbreaks in the general population. The most dangerous settings for acquiring CCHF virus are interventions to gastrointestinal bleedings and emergency operations on patients that have yet to be diagnosed with CCHF. In general, these patients were diagnosed after the operation and injuries to the operating team during the operation are usually under-reported. Airborne acquisitions of the infection was suspected in several cases in Russia, but were not documented. Horizontal transmission from a mother to her child has also been reported. [22]

Tick to Human

CCHF virus is transmitted to humans by bites from Ixodid ticks, especially the genus of Hyalomma. The virus is also transmitted to humans either by direct contact with blood or tissues from infected animals, mainly sheep, or by patient's blood, vomit containing blood, or respiratory secretions.[23] The latter human-to-human infection sometimes causes nosocomial outbreaks of CCHF. The virus is transmitted to humans by the bite of infected ticks, direct contact with blood or infected tissues from viremic animals and direct contact with the blood or secretions of an infected person .[24]Transmission also may occur from aerosol contact of blood from patients with advanced stages of the disease.[25]

Animal to Human

The virus is also transmitted to humans either by direct contact with blood or tissues from infected animals, mainly sheep. [26]Cattle, sheep and goats do not become ill after infection but are viremic for about 1 week. During this period of time the virus may be transmitted to humans who have close contact to these animals such as agricultural workers, slaughterhouse workers and veterinarians.[27] Asymptomatically viremic sheep and cattle have been implicated in the transmission to abattoir workers, even outside of known endemic area and crushing infected ticks may also be hazardous. 28

Animal to Tick

Immature ticks acquire the virus by feeding on infected small vertebrates. Once infected, they remain infected throughout their development and, when they are mature, transmit the infection to large animals, such as livestock .[26]

Tick to Tick

Among invertebrates, CCHF viral infection has been demonstrated only in ticks, including viral isolations from numerous species/subspecies of seven genera of the family Ixodidae and two species of the family Argasidae. An especially important biological feature of ticks in general as potential vector/reservoirs of arboviruses is their ability to transmit arboviruses transovarially. Evidence of this phenomenon for CCHF virus in nature is based mainly on limited isolations from eggs of H. marginatum and *Dermacentor* marginatus .[29]

Incubation Period

The incubation period for CCHF is about 2-9 days. If the virus is transmitted via tick bite, the incubation period appears to be shorter (1-9 days) than after transmission via infected animals (5-13 days). The incubation period is usually 5-6 days after contact with blood. In general, the incubation period after a tick bite can be as short as 1-3 days, but can much longer, depending on several factors including route of exposure. For example, in South Africa, among 21 patients for which reliable data were obtained, the time to onset of disease after exposure by tick bite was 3.2 days, to blood or tissue of livestock was 5.0 days and to blood of human cases was 5.6 days. It has been hypothesized that different hosts can induce phenotypic changes in CCHFV strains that modulate viral virulence. It is unclear whether the variation observed in incubation times and ultimately disease outcome, may be due to this phenomenon or other factors, such as viral dose.[29] During this period of time and whilst first non-specific symptoms are present, the infection may be unperceived imported into non-endemic regions. [30]

Morbidity and Mortality

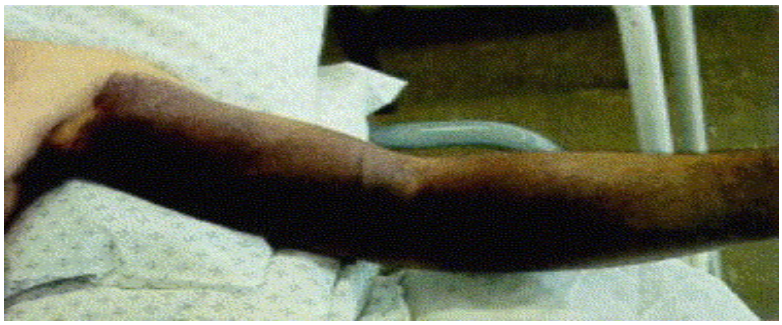
Climatic factors can influence the numbers of ticks in the environment and the incidence of disease. In some countries, Crimean-Congo hemorrhagic fever tends to be seasonal. This disease is most common in Iran during August and September and in Pakistan from March to May and August to October. Most cases are the result of occupational exposure. CCHF is particularly common in farmers, shepherds, veterinarians, abattoir workers and laboratory workers.[31] Healthcare workers are also at high risk, particularly after exposure to patients' blood. During one nosocomial outbreak at a hospital in South Africa, 33% of medical personnel exposed via needle stick injuries became ill. Approximately 9% of those who had other forms of contact with infected blood also developed CCHF. In the general public, activities that increase tick exposure such as hiking and camping increase the risk of infection. The average case fatality rate is 30-50%, but mortality rates from 10% to 80% have been reported in various outbreaks. The mortality rate is usually higher for nosocomial infections than after tick bites; this may be related to the virus dose. Geographic location also seems to influence the death rate. Particularly high mortality rates have been reported in some outbreaks from the United Arab Emirates (73%) and China (80%). Geographic differences in viral virulence have been suggested, but are unproven. The mortality rate may also be influenced by the availability of rigorous supportive treatment in area hospitals.[32]

Sign and Symptoms

For CCHF, initial symptoms are nonspecific and sometimes occur suddenly. They include fever, headache, myalgia, arthralgia, abdominal pain and vomiting. Sore throat, conjunctivitis, jaundice,

photophobia and various sensory and mood alterations may develop. A petechial rash is common and may precede a gross and obvious hemorrhagic diathesis, manifested by large ecchymoses, bleeding from needle-puncture sites and hemorrhage from multiple other sources.[33] The case-fatality rate has been estimated to range from 15% to 70%, but mild or inapparent infections occur. Crimean-Congo hemorrhagic fever infection is usually associated with profound disseminated intravascular coagulation (DIC). Patients with Crimean-Congo hemorrhagic fever may bleed profusely; and since this occurs during the acute, viremic phase, contact with the blood of an infected patient is a special concern.

Figure 5: Massive cutaneous ecchymosis on the arm of a CCHF patient, 7-10 days after clinical onset.



Diagnostic Tests: [35,36,37,38]

1. Organism Detection Tests:
   a) Microscopy.
2. Immunoassay Tests:
   a) Enzyme-Linked Immunosorbent Assay (ELISA)
   b) Indirect immunofluorescence assay
   c) Reverse Transcription Polymerase Chain Reaction (RT PCR)
   d) ELISA and Reversed Passive Hemagglutination (RPHA)
   e) Recombinant Nucleoprotein-Based Enzyme-Linked Immunosorbent Assay
3. Nucleic Acid Detection Tests:
   a) One-step RT-PCR with real-time SybrGreen detection
   b) Test One-step Real-Time RT-PCR Assay
   c) One-step Real-Time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR)

Treatment

Table 6: Treatment of Crimean-Congo hemorrhagic fever

Blood, platelet and plasma replacement	Blood, platelet and plasma replacement may be useful for CCHF
Ribavirin - Intravenous treatment	The intravenous preparation of ribavirin is recommended for treatment of viral hemorrhagic fevers and the oral form for post exposure prophylaxis. Intravenous ribavirin should be administered within 6 days of illness onset as follows: 30 mg/kg loading dose, followed by 16 mg/kg 4 times a day for 4 days, then 8 mg/kg 3 times a day for 6 days. A parenteral preparation of ribavirin currently is not commercially available in the US, but is available for compassionate use protocols for the treatment of Lassa fever, Hantavirus infections, Crimean-Congo hemorrhagic fever and other viral hemorrhagic fevers. Clinicians should contact the Special Pathogen branch at CDC (404-639-1115) for information on the management of CCHF and the use of ribavirin in this infection (AHFS Drug Information, 2006). [39, 40]
Ribavirin - Oral treatment	Ribavirin therapy was started early (within 4 days after the onset of the disease) for 7 patients and none died. Ribavirin therapy was initiated late (at least 5 days after the onset of the disease) for 5 patients and 3 died. In another report, oral ribavirin was used in the treatment of 3 patients in Pakistan with nosocomial CCHF, administered at a dosage of 4 g daily for 4 days and then 2.4 g daily for the following 6 days. The 3 patients were not expected to respond to therapy, but this treatment saved their lives . [39, 40]
Immunotherapy	A new specific immunoglobulin CCHF-Venin has been prepared the plasma pool of boosted donors, by a combined ethanolpolyethyleneglycol fractionation method with an ion-exchange purification step. The final product is free from immunoglobulin aggregates, vasoactive substances and polyethyleneglycol and meets national and international requirements for intravenous immunoglobulin. It contains antibodies to CCHF virus of a titre of 8. [41]
Vaccination	A vaccine for CCHF derived from inactivated mouse brain is used in Bulgaria, but is not available outside of that country. Furthermore, the efficacy of this vaccine is not well quantified .[41]

Prevention

Table 7: Prevention against Crimean-Congo hemorrhagic fever

Avoid or minimize virus exposure	The best means of preventing disease is to avoid or minimize exposure to the virus. This can be accomplished in a number of ways. Persons in high-risk occupations (i.e., slaughterhouse workers, veterinarians, sheep herders, etc.) should take every precaution to avoid exposure to virus infected ticks or virus-contaminated animal blood or other tissues. For example, wearing gloves and limiting exposure of naked skin to fresh blood and other tissues of animals are effective practical control measures . Tick-avoidance measures are important in the prevention of C-CHF, especially for backpackers and hikers and include the use of protective clothing, with trousers tucked into socks and boots. Frequent body searches should be made to find and remove ticks .[42]
Tick control	Vector control on domestic animals can best be accomplished by direct chemical use. Acaricide treatment of cattle with Sevin during the period of adult attachment was found to be the most efficient control measure for H. m. marginatum in Astrakhan Oblast. Application of acaricides only to specific body regions where adults are known to attach can increase treatment efficiency (Watts *et al.*, 1988). Applying commercially available insect repellents (i.e., diethyl toluamide [DEET]) to exposed skin and the use of clothing impregnated with permethrin can give some protection against tick bites .[13]
Vertebrate control	The density of tick vectors of CCHF may be reduced by controlling the primary vertebrate hosts of the immature ticks. Suppression of rodent populations apparently reduced the numbers of D. marginatus in Europe and H. a. asiaticum in the Asian deserts and semideserts. Hyalomma ticks were reduced in Europe by controlling hares and hedgehogs. Control of birds could also limit the dispersion of tick vectors .[29]
Environmental control	Environmental modification has been shown to be effective in controlling vector population density and CCHF viral activity. Clearing areas around resorts, woodlots and path sides of shelters where ticks may survive has been stressed as a useful measure to reduce H. m. marginatum population density and the chances of human contact with the ticks. The recommended strategy for controlling H. a. anatolicum was the removal of vegetation on hill slopes, floodplain meadows and abandoned alfalfa fields in Kazakhstan. Environmental modification which increases larval tick exposure to sunlight and to winter temperature causes mortality. Irrigation and plowing were also considered effective in reducing the density of H. a. anatolicum .[29]

Barrier nursing	Strict barrier-nursing techniques should be enforced: all persons entering the patient's room should wear disposable gloves, gowns, masks and shoe covers. Protective eye wear should be worn by persons dealing with disoriented or uncooperative patients or performing procedures that might involve the patient's vomiting or bleeding (for example, inserting a nasogastric tube or an intravenous or arterial line). Protective clothing should be donned and removed in the anteroom. Only essential medical and nursing personnel should enter the patient's room and anteroom. Isolation signs listing necessary precautions should be posted outside the anteroom .[33]
Vaccination	A suckling mouse brain, formalin-inactivated vaccine has been used in Bulgaria and other parts of Eastern Europe and the former Soviet Union. However, with the relatively small target population of persons at-risk for contracting CCHFV, the large-scale development and production of a CCHF vaccine by modern standards seems unlikely. [13]

Prognosis

Deaths occurred on days 5-14 of illness. Patients with fatal infections had thrombocytopenia and markedly elevated levels of serum aspartate and alanine aminotransaminases, gamma-glutamyltransferase, lactic dehydrogenase, creatine kinase, bilirubin, creatinine and urea. Total protein, albumin, fibrinogen and hemoglobin levels were depressed. Values for prothrombin ratio, activated partial thromboplastin time, thrombin time and fibrin degradation products were grossly elevated, findings that indicate the occurrence of disseminated intravascular coagulopathy. Many of the clinical pathologic changes were evident at an early stage of the disease and had a highly predictive value for fatal outcome of infection. Changes were present but less marked in nonfatal infections. CCHF has an infection rate of 20-100% and a 15-30% fatality rate. Individuals who survive and do not experience specific sequelae typically return to their premorbid state.[42]

Conclusion

Crimean-Congo hemorrhagic fever is a zoonotic viral disease that is asymptomatic in infected animals, but a serious threat to humans. This disease is a particular threat to farmers and other agricultural workers, veterinarians, laboratory workers and hospital personnel. Clinical findings indicate the occurrence of disseminated intravascular coagulopathy. Environmental modification has been shown to be effective in controlling vector population density and CCHF viral activity. Clearing areas around resorts, woodlots and path sides of shelters where ticks may survive has been emphasized as a useful measure to reduce virus density and the chances of human contact with the ticks. Treatment with ribavirin, immunoglobulins and specific vaccine is possible. There is need of community awareness regarding this disease for better control of the epidemics.

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