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CRIMEAN-CONGO HEMORRHAGIC FEVER VIRUS: AN EMERGING INFECTIOUS DISEASE

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ABSTRACT

Crimean-Congo Hemorrhagic Fever (CCHF) is a viral zoonotic tick-born disease with a mortality rate of up to 50% in humans. The CCHF Virus (CCHFV) is from the genus *Nairovirus* and family *Bunyaviridae*. After a short incubation period, the disease is characterized by sudden fever, chills, severe headache, dizziness, back, and abdominal pain. In severe cases, hemorrhagic manifestations, ranging from petechiae to large areas of ecchymosis develop. CCHF is transmitted to humans by the bite of infected tick and by direct contact with blood or tissue from infected humans and livestock. Since from 1999, establishment of a surveillance and laboratory detection system on viral hemorrhagic fevers particularly on CCHF has had benefits. One of which is the fact that a mortality rate approaching 6% in the year 2007. The present article reviews on the epidemiological and clinical features of CCHF; moreover, treatment, prevention and control strategies with a special focus on oral Ribavirin as a choice of medical treatment.

Keywords: Crimean Congo Hemorrhagic Fever, epidemiology, treatment, prevention.

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. 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 [1].

HISTORY:

Soviet scientists first identified the disease they called Crimean hemorrhagic fever in 1944 and established its viral etiology by passage of the virus through human "volunteers" (fatality rate unreported), but were unable to isolate the agent at that time [2]. In June 1967, Soviet virologist Mikhail Chumakov registered an isolate from a fatal case that occurred in Samarkand (on the ancient Silk Road in Central Asia, not the Crimea) in the Catalogue of Arthropod-borne Viruses [3]. Four months earlier, virologists Jack Woodall, D Simpson and others had published initial reports on a virus they called the Congo virus, first isolated in 1956 by physician Ghislaine Courtois, head of the Provincial Medical Laboratory, Stanleyville, and Belgian Congo [4, 5]. Strain V3010, isolated by Courtois, was sent to the Rockefeller Foundation Virus Laboratory (RFVL) in New York City and found to be identical to another strain from Uganda, but to no other named virus at that time. Chumakov later sent his strain to the RFVL, where it was found to be identical to the Congo virus [6].

The International Committee on Taxonomy of Viruses proposed the name Congo-Crimean hemorrhagic fever virus, but the Soviets insisted on Crimean–Congo hemorrhagic fever virus. Against all principles of scientific nomenclature based on priority of publication, it was adopted as the official name in 1973 in possibly the first instance of a virus losing its name to politics and the Cold War. However, since then Congo-Crimean or just Congo virus has been used in many reports, which would be missed in searches of medical databases using the official name. These reports include records of the occurrence of the virus or antibodies to the virus from Greece, Portugal, South Africa, Madagascar (the first isolation from there), the Maghreb, Dubai, Saudi Arabia, Kuwait and Iraq [7, 8, 9].

CLASSIFICATION AND STRUCTURE:

CCHFV is classified within the Nairovirus genus in the Bunyaviridae family. Five genera are recognized in this family: *Nairovirus, Orthobunya* virus, Hanta virus, *Phlebo* virus and *Tospo* virus. All infect animals, apart from the last mentioned genus which infects plants [10]. The Nairovirus genus consists of 34 viruses which are further divided

into seven serogroups. Out of these viruses, three are known to cause disease: CCHFV, Dugbe virus and Nairobi sheep disease virus [11, 12].

Viruses in the *Bunyaviridae* family are spherical, approximately 100 nm in diameter and contain two glycoprotein's embedded in the lipid bi layer [10, 13]. The viral genome consists of three RNA segments which are single-stranded and of negative sense polarity. All three segments contain one open reading frame (ORF) flanked by a non-coding region with partially complementary nucleotides at the end. Due to base-pairing of the terminal sequences, a non-covalent closed circular structure is predicted for each of the viral segments. The large segment (L) encodes the viral dependent RNA polymerase while the two glycoprotein's Gn, and Gc, are encoded by the medium (M) segment. The small segment (S) encodes the nucleocapsid protein (NP), which complex with all viral genomic RNA segments to form individual ribonucleoprotein particles [14]. Several viruses in *Bunyaviridae* also encode one or two nonstructural proteins (NS) from the S or the M segment, termed NSs or NSm, which is believed to function as an interferon antagonist, determine host range and possibly also serve as a regulatory function in replication [1]**.** The occurrence of such a protein has been shown for CCHFV but the function is currently unknown [15].

EPIDEMIOLOGY:

CCHF was first discovered in the Crimean region of Russia in the 1940s, the disease has been reported in many regions of Africa, the Middle East, Europe, and Asia. It has also been reported in parts of Europe including southern parts of the former USSR (Moldova, Ukraine and Transcancasus), and in central Asian countries (Tajikistan, Turkmenistan, Uzbekistan, Kyrgyzstan, and Kazakhstan) Turkey, Bulgaria, Greece, Albania and Kosovo, province of the former Yugoslavia. The initial recognition of hemorrhagic cases in Africa occurred in 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 [16, 17- 21].

A surveillance and control program of CCHF in Iran was established by three collaborating organizations in 1999 including the Center for Disease Control (CDC) at the Ministry of Health (MOH), Pasteur Institute of Iran (PII) (with the establishment of *Arboviruses* and viral Hemorrhagic- Fevers Laboratory known as a National Reference

Lab) and the Veterinary Organization, all organized at the National Level. These three organizations instituted a National Expert Committee on Viral Hemorrhagic Fevers (NECVHFs). This committee has been dedicated to all activities related to control, awareness, diagnosis, treatment, etc. Universities and public health centers located in different cities, categorized as Level II, have also been dictated lots of health care and administrative activities [22].

SYMPTOMS OF CCHF:

The onset of CCHF is sudden, with initial signs and symptoms including headache, high fever, back pain, joint pain, stomach pain, and vomiting. Red eyes, a flushed face, a red throat, and petechiae (red spots) on the palate are common. Symptoms distribution according to their frequencies is shown in table no.1.

TABLE 1: SYMPTOMS DISTRIBUTION ACCORDING TO THEIR FREQUENCIES

Symptoms	Number of patients (%)
Fatigue	659 (96%)
Fever	625 (91%)
Pain	650 (95%)
Gastrointestinal system	515 (75%)
Bleeding	213 (31%)

As the illness progresses, large areas of severe bruising, severe nosebleeds, and uncontrolled bleeding at injection sites can be seen, beginning on about the fourth day of illness and lasting for about two weeks [23]. Patient's distribution according to their frequencies is shown in table no.2.

TABLE 2: PATIENTS' DISTRIBUTION ACCORDING TO THEIR ADMISSION MONTHS.

Months.	Number of patients (%)
April	34 (5%)
May	103 (15%)
June	165 (24%)
July	254 (37%)
August	96 (14%)
September	27 (4%)
Other	6 (1%)

TRANSMISSION:

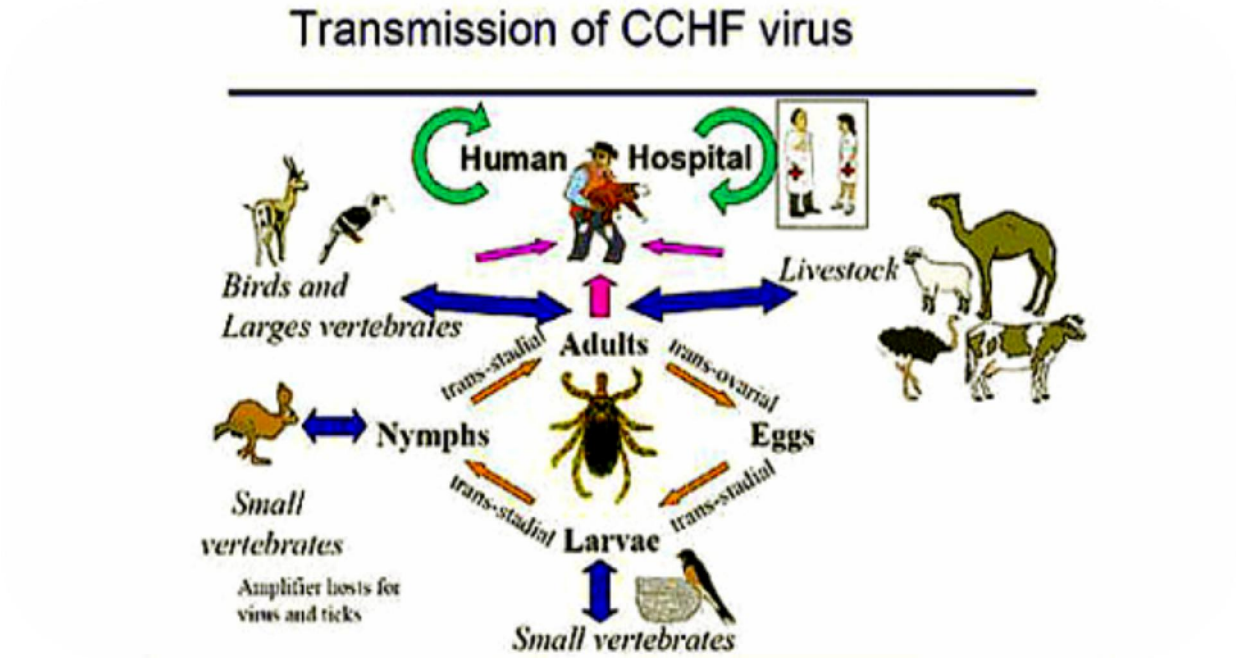

Figure 1
Showing transmission of CCHF virus

Community-acquired CCHF happens through transmission of the virus by direct contact with blood or other infected tissues of livestock or from an infected tick bite. Most of the human cases are slaughterhouses, and veterinary practice [24]. Humans can be infected incidentally by the bite of an infected arthropod or via aerosol generated from infected rodents' excreta. Infected humans can spread the disease via close contacts which may result in community outbreaks and Nosocomial infections. Possible horizontal transmission of CCHFV from a mother to her child indicates the importance of preventive measures for in-house outbreaks of CCHF [25].

Nosocomial transmission is well described in reports from Pakistan, Iraq, United Arab Emirates, South Africa and Iran [26, 27, 28]. CCHFV has repeatedly caused Nosocomial outbreaks with high mortality, and percutaneous exposure presents the highest risk of transmission [28, 29, 30, 31]. The most dangerous settings for acquiring CCHFV are interventions for controlling gastrointestinal bleedings, and emergency operations on patients who have yet to be diagnosed as having CCHF [32]. In general, these patients will be diagnosed after the operation, and injuries to the operating team

during the operation are usually under-reported. Risk of Nosocomial transmission can be minimized by proper and timely infection-control measures, careful management of infected patients, and, in some cases, providing prophylactic treatment to health-care workers after exposure [33, 34]. However, community-based control measures are necessary to decrease disease transmission and prevent further spread in the community [35].

PATHOLOGY:

Histopathologic studies in organs of deceased CCHF patients and in a recently established mouse model for CCHF pathogenesis consistently indicate infection of Kupffer cells, hepatic endothelial cells and hepatocytes. Necrosis of hepatocytes varied in extent, but generally the necrosis existed in multiple foci with association of viral antigen and no inflammatory infiltrates [36, 37, 38]. The extent of hepatocytes necrosis corresponded well with the association of elevated liver enzymes as a prognostic marker of fatality [36, 37, 39, 40]. The spleen is another important target for the course of disease characterized by lymphocyte depletion, splenocyte necrosis and dilated sinusoids [36, 38]. In other organs, the endothelial cells were sparsely infected; however hemorrhages, edema and/or necrosis were still present without inflammatory infiltrates [36, 37, 40, 41]. The necrosis in other organs besides the liver is supported by the clinical observation of a higher ratio of aspartate transferase (AST) to alanine transferase (ALT) in serum. A high ratio indicates whether there is necrosis in other organs besides the liver, and this ratio is almost always higher in CCHF cases [42].

CLINICAL FEATURE AND PATHOGENESIS:

Human infection with CCHF virus results in severe hemorrhagic disease. The main course of CCHF has been noted by authors as progressing through four distinct phases including incubation, pre-haemorrhagic, haemorrhagic, and convalescence [43]. The incubation period is variable and influenced by the route of exposure from 1 to 3 days with a maximum of 9 days when infection is caused by the bite of a tick, and from 5 to 6 days with a maximum of 13 days when the infection is due to contact with infected tissue or blood [44, 45]. After the incubation period, the pre-hemorrhagic period is characterized by a sudden onset of fever, chills, severe headache, dizziness, photophobia, back and abdominal pain [44]. In severe cases, 3 - 6 days after onset of disease,

hemorrhagic symptoms rapidly manifest. These can range from petechiae to large areas of ecchymosed and often appear on the mucus membranes and skin, especially on the upper body and/or extremities. Mortality rates of Nosocomial infections are often much higher than those acquired naturally through tick bite and this may be due to viral load [46]. Symptoms may last from 1 to 7 days after incubation [47]. The primary cause of bleeding may be due to a cytokine storm that has been demonstrated by some documents [48]. Mortality rates for various CCHF outbreaks varied greatly. Convalescence period begins about 15- 20 days after onset of illness. The average fatality rate is often 30 - 50% [43, 49] but mortality rates of 10% to 80% have been reported in various outbreaks, e.g. 27.7 % and 80% from the United Arab Emirates and China, respectively [50, 51].

Pathogenesis of CCHF is not well understood yet. A common pathogenic feature of hemorrhagic fever viruses is their ability to disable the host immune response by attacking and manipulating the cells that initiate the antiviral response [52]. This damage is characterized by marked replication of the virus together with dysregulation of the vascular system and lymphoid organs [53]. In fatal cases, a fulminant shock-like syndrome occurs. It is suggested that inflammatory mediators may play an important role in the pathogenesis [47, 52] and some research is being done on this aspect of CCHF. The virus mainly infects endothelial cells and monocyte which cause the viremic phase of the disease. Endothelial damage, evidenced in the skin by a rash, contributes to stimulating platelet aggregation and activation of the intrinsic coagulation cascade. Organ lesions cause the release of pro coagulants and disruption of the capacity to regenerate the consumed clotting factors [54].

DIAGNOSIS:

CCHF infection should be suspected in any patient who have:

1. Clinical manifestations including acute onset of fever, headache, myalgia and bleeding.
2. Epidemiologic risk factors including a history of recent travel to an endemic region, living in an endemic area, history of tick bite, and exposure to blood or tissues of an infected patient or animal.

3. Laboratory findings such as leucopenia or leukocytosis, thrombocytopenia and increased level of creatine phosphokinase, transaminases, and prolongation of prothombin time (PT).

The laboratory for diagnosis Crimean-Congo hemorrhagic fever (CCHF) has been equipped with advanced molecular and serological techniques for diagnosis and research on the CCHF virus and other arboviruses and viral hemorrhagic fevers like the West Nile, Rift Valley Fever, Chikungunia, Hanta, Pumala, Dengue, Yellow Fever, Alkhorma, Lassa Fever, Tick Born Encephalitis, Onyog Nyoung, Sindbis, Mayaro and Ross River Fever.

1. Serological Assay: Serum samples are analyzed by specific ELISA for IgM and IgG detection. In IgM detection, the ELISA plates are coated with the goat IgG fraction to human IgM (anti μ chain) diluted in PBS 1 X and incubated overnight at 4˚C. Then the serum sample is diluted in PBS containing Tween (PBST) and 3% skim milk (PBSTM) and the plates are incubated for 1 hour at 37˚C. After dilution of the antigen in PBSTM, the plates are incubated for 3 hours at 37˚C. Diluted immuno ascites then is added and the plates are incubated for 1 hour at 37˚C. Peroxidase- labeled anti-mouse immunoglobulin is added and the plates are incubated for 1 hour at 37˚C. The plates are then washed 3 times with PBST containing 0.5% Tween. Finally, hydrogen peroxide and TMB (3, 3′, 5, 5′ Tetra Methyl Benzedrine) is added and the plates are incubated for 15 minutes at room temperature. The enzymatic reaction is stopped by the addition of 4, N, sulfuric acid. The plates are read by ELISA reader at 450 nm. In IgG detection; the ELISA plates are coated with the mouse hyper immune ascetic fluid diluted in PBS 1X and incubated overnight at 4˚C. The native or recombinant antigen (which is produced in this lab) diluted in PBSTM is added and the plates incubated for 3 hours at 37˚C. Diluted serum in PBSTM is added and the plates are incubated for 1hour at 37˚C. After adding the diluted Peroxidase-labeled anti-human or animal immunoglobulin in PBSTM, the plates are incubated for 1 hour at 37˚C. The plates then are washed 3 times with phosphate-buffered saline (PBST) containing 0.5% Tween after each incubation. Finally, hydrogen peroxide and TMB is added and the plates are incubated for 15 minutes at room temperature. The enzymatic reaction is stopped by the addition of 4, N, sulfuric acid. The plates are read by ELISA reader (Anathos 2020) at 450 nm.

2. Molecular Assay: Viral RNA is extracted from 140 µl of serum or from phenol extracted tick suspensions using QIAamp RNA Easy Mini kit according to manufacturer's instructions (QIAgen, GmbH, and Hilden, Germany). The extracted viral RNA is analyzed subsequently by Real-time RT-PCR using the one-step RT-PCR kit (QIAgen, GmbH, and Hilden, Germany) and using specific primers which amplify a 536 bp fragment of the S-segment of the CCHFV genome. The PCR reaction is done in 50 µl of total volume in sequence of 30 minutes at 50˚C, 15 minutes at 95˚C , and 40 cycles including 30 seconds at 95˚ C, 30 seconds at 50˚C, 45 seconds at 72˚C , and finally 10 minutes in 72˚C as final extension [55, 56, 57].

TREATMENT:

The mainstay of treatment of CCHF is supportive, with careful maintenance of fluid and electrolyte balance, circulatory volume, and blood pressure. In addition, treatment of other suspected possible causes, such as bacterial sepsis, should not be withheld while awaiting confirmation or exclusion of the diagnosis of CCHF. In an outbreak in the former USSR, soviet physicians found little clinical benefit from administration of immune plasma in convalescence phase, although plasma with high neutralizing antibody titers has been reported as potentially useful [58].

Pharmacotherapy:

There are no antiviral drugs approved by the United States Food and Drug Administration (FDA) for the treatment of CCHF [59]. Ribavirin is a guanosine analogue that has an incomplete purine ring rather than an acyclic ribose moiety. After intracellular phosphorylation, Ribavirin triphosphate interferes with early events in viral transcription, such as capping and elongation of messenger RNA, and inhibits ribonucleoprotein synthesis [60]. It has a broad spectrum of activity in vitro against RNA viruses. The concentration of its major metabolite-1, 2, 4-triazole-3-carboxamide is higher in urine after oral administration than after intravenous administration, implying that the drug is degraded in the gastrointestinal tract and liver [61]. Aerosolized Ribavirin is absorbed systemically, as indicated by the presence of measurable concentrations in the plasma [62]. Clinical efficacy has been demonstrated for the treatment of infections caused by hemorrhagic fever viruses (with oral and intravenous formulations of Ribavirin) [63, 64].The CCHFV is susceptible in vitro to Ribavirin. In some uncontrolled studies on both

sporadic and outbreak cases of CCHF, Lassa fever, Bolivian hemorrhagic fever, and hemorrhagic fever with renal syndrome caused by Hanta virus, Ribavirin has been reported to have some anecdotal benefit when administered either parenterally or orally[64,65,66]. Paragas and colleagues[67] screened drugs for potential activity against CCHFV and found that Ribavirin inhibited the replication of CCHFV, Ribamidine had antiviral activity that was 4.5- to 8- fold less than that of Ribavirin. Three other drugs (6-azauridine, selenazofurin, and tiazofurin) had no significant antiviral activity.

A newly identified molecule known as MxA, which is a member of the interferon-induced GTPases that belong to the dynamic super family prevented replication of CCHF viral RNA when presented intracellularly and inhibited production of new infectious virus particles by interacting with a component of the nucleocapsid [68].

Recommendation for drug therapy has not been approved by the FDA and it should always be administered under an investigational new drug protocol. In an epidemic situation, these requirements may need to be modified to permit timely administration of the drugs [58].

In a situation which a modest number of patients require treatment, it is recommended that an intravenous regimen of Ribavirin be given in accordance with the recommendations of Center for Disease Control (CDC) for treating patients with suspected VHF of unknown cause, pending identification of the agent[69]. A similar dose has been used in the treatment of Lassa fever [63].

Ribavirin is contraindicated in pregnancy and because most of patients with CCHF have self limited diseases, direct observation and supportive treatment is recommended (unpublished data).However, in the context of VHF of unknown cause, it is believed that the benefits of treatment with Ribavirin outweigh the fatal risks, and Ribavirin is therefore recommended [70].

The use of oral or intravenous Ribavirin has not been approved by the FDA for children. Only aerosolized Ribavirin has been approved by the FDA for children, to treat respiratory syncytial virus infection. Ribavirin is available as 200-mg capsules. However, Schering-Plough Corp. has produced a pediatric syrup formulation, which is not commercially available yet [58].

Acarides (chemicals intended to kill the tick vectors) in the livestock production facilities is another measure of protection in CCHF [71].

PREVENTION AND CONTROL STRATEGIES:

Although an inactivated, mouse brain derived, vaccine against CCHF virus has been developed, there is currently no effective vaccine available for human use. The aforementioned vaccine was used in 1974 during an immunization programme applied to medical workers and military personnel in CCHF endemic areas [72]. After the programme introduction, the incidence rates and the case fatality rates of the disease were both reduced. However, the vaccine could not be applicable in many countries due to its method of preparation.

At present, there are few preventive measures for CCHF that mainly consist on personal protection against tick bites and limitation of exposure to infected livestock or humans. In this regard, persons living or travelling in endemic areas should use personal protective measures that include the avoidance of areas where ticks are abundant and predominantly when the tick vector population is particularly active[73]; to minimize tick exposure light-colored clothing –that facilitates tick identification- and covers legs and arms is recommended. On the other hand, the regular examination of clothing and skin for ticks, the application of tick repellent diethyltoluamide to the skin or permethrin to the clothing are mainstays of prevention [74]. Acarides (chemicals intended to kill the tick vectors) in the livestock production facilities is another measure of protection. Acarides can be used on animals before slaughter or export; human outbreaks have occurred after exposure to infected ostriches during slaughter; these infections seem to be preventable by keeping the birds free of ticks 14 days before slaughter. In endemic for CCHF virus it has been suggested to subject the ostriches to a 30-day quarantine period before slaughter. Persons who work with livestock (butchers, farmers, veterinarians) in the endemic areas should take practical measures to protect themselves; these include the use of repellents and on the skin and clothing, the use of gloves or other clothing to prevent skin contact with the infected tissue or blood [75].

Suspected or diagnosed patient with CCHF should be isolated in a private room, preferably in a negative-pressure room; the subjects should be treated and cared for using barrier-nursing techniques that include disposable gloves, masks, shoe covers and

goggles [76]. The patient should be attended only by designated medical/Para-medical staff and all used material such as syringes, gloves, tubing etc. should be collected in autoclave-able bag and autoclaved before incinerating. All instruments should autoclaved before re-use and all surfaces should be decontaminated with liquid bleach. The patients' samples should be collected, labeled, sealed and decontaminated from outside with liquid bleach and packed in triple container packing. After the patient is discharged, all room surfaces should be treated with liquid bleach and the room should be fumigated. By using these measures transmission in the Nosocomial setting could be prevented. In case of death of the CCHF patient, the dead body should be sprayed with 1:10 liquid bleach solution and then placed in a plastic bag which should be sealed with adhesive tape and the vehicle used for the body's transportation should be disinfected with 1:10 liquid bleach solution. The clothing of the deceased should be burned [77].

In case of direct contact with the patient's blood or secretions the recommended procedure is the rigorous daily follows up of the person that came in contact by checking white blood cell counts and biochemical tests for at least 14 days after exposure and the administration of oral high dose Ribavirin. In this regard, prophylactic Ribavirin was administrated in a health care worker who had a needle-stick injury and it has been shown that the subject did not develop CCHF [78].

PROGNOSIS:

The case-fatality rate has been estimated to range from 15% to 70% in various studies [79, 80, 81]. The lowest case-fatality rate of CCHF (2.8%) in the medical literature is reported from Turkey. This could be due to vigorous supportive treatment and administration of Ribavirin within 24 hours after admission to their patients. Another explanation could be the geographical variation of the virus. However, to reach such a conclusion, additional reports from different centers are necessary [82]. Swanepoel's evaluation[83] of 15 fatal and 35 non-fatal CCHF patients in South Africa showed that the patients with fatal infections had thrombocytopenia, and markedly elevated levels of AST, ALT, gamma-glutamyltransferase, LDH, creatine kinase (CK), bilirubin, Creatinine, and urea. Total protein, albumin, fibrinogen, and hemoglobin levels were depressed. Values for prothombin, activated PTT, thrombin time, and FDPs were grossly elevated, which indicated the occurrence of DIC. Many of the clinical pathological

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.

The data obtained from 60 cases in Turkey [84] also showed that the rates of fever during hospitalization, confusion, neck stiffness, bleeding from multiple sites, and presence of petechia/ecchymosed were higher in CCHF patients who died compared to those who survived. Mean values of ALT, AST, LDH, CK, PTT, INR, and urea were higher, and mean PLT count was lower in patients who died. Another study in Turkey indicated impaired consciousness and splenomegaly as independent predictors of adverse outcome. [85] Of particular importance is the fact that in fatal cases there is little evidence of an antibody response [86]. These data show that hemorrhagic manifestations, confusion, and laboratory evidence of DIC are predictors of fatal outcome.

CURRENT SCENARIO IN INDIA:

Two persons, including the husband of the 30-year-old woman who died of Crimean-Congo hemorrhagic Fever recently at a private hospital in Ahmadabad have tested positive for the fatal virus causing the disease, in Gujarat. The National Institute of Virology (NIV) is going to test the samples sent by Kasturba Hospital for 7-8 viruses causing viral hemorrhagic fever. The 48-year-old Bhiwandi resident was shifted from Jaslok Hospital to Kasturba Hospital on after those doctors found that the clinical symptoms indicated viral hemorrhagic fever. Doctors and nurses in the region have been warned to take utmost precautions when treating patients showing symptoms of the deadly fever.

CONCLUSION:

Crimean Congo hemorrhagic fever disease (CCHF) may create a serious health problem in our country. The disease takes place among hemorrhagic viral diseases. Prevalence needs to be measured in animals and in at-risk humans in endemic areas; and a useful animal model needs to be developed. Further research is needed to determine the efficacy of specific treatment with Ribavirin and other antiviral drugs, and develop a safe and effective vaccine for human use. Early diagnosis and treatment of CCHF are potentially associated with a lower mortality and decreased chance of secondary spread of infection. In this regard, the implementation of alert systems in endemic areas in slaughterhouses and hospitals has been shown to be useful. In addition, a strong

laboratory capacity is important in endemic areas and areas where the virus could be expected to circulate. No real need to panic about this fever we can battle against it.

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