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Prevalence of Crimean-Congo Viral Infection and Usefulness of Available Vaccines and its Overview

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Abstract

Crimean-Congo hemorrhagic fever (CCHF) is a condition brought on by a virus (Nairovirus) that is spread by ticks and is a member of the Bunyaviridae family and the genus Hayalomma. This virus could travel across the Hayaloma genus. This species maintains two host-life cycles, changing from a larva to a nymph on its first host, which can be a tiny animal like a bird, and then from adult stages to humans, which serve as the second host. Currently, 27 distinct Hyalomma species are recognized. Geographically, CCHFV is spread throughout Asia, the Middle East, Southern Europe, and Africa, all of which have large tick populations. This virus is capable of spreading both horizontally and vertically. Animals like sheep, goats, cattle, and hares may act as hosts or reservoirs for the virus. Humans can contract this virus by coming into touch with infected ticks or animal blood. Due to contact with bodily fluids or infectious blood, medical personnel are most vulnerable in endemic areas. This virus can cause symptoms such as high fever, joint discomfort, headache, back pain, vomiting, and stomach pain in infected individuals. To identify this virus, scientists employ the ELISA and RT-PCR methods. The medicine ribavirin and some readily available vaccinations can also be used to treat this virus. The effectiveness of using the vaccines and medications that are now available to treat this virus cannot be proven. The effectiveness of the vaccine to protect against this virus was investigated using a small animal model, such as a knockout mouse.

Keywords: Crimean-Congo hemorrhagic fever (CCHF), Ribavirin, ELISA, PCR.

INTRODUCTION

Crimean-Congo hemorrhagic fever virus (CCHFV) is a tick-born lethal pathogen that causes fatal hemorrhagic fever in humans. The outbreaks caused by this lethal virus are geographically distributed in Asia, the Middle East, Southern Europe, and Africa where tick species are in abundance. The World Health Organization has now prioritized the research of this virus so that there is more improvement in diagnostics, vaccines, and therapeutics of CCHFV [1]. Crimean-Congo hemorrhagic fever (CCHF) is a disease caused due to a virus (Nairovirus) that is tick-borne and belongs to the family of Bunyaviridae. As it was first identified in 1944 in Crimea so for this reason it is given the name Crimean Hemorrhagic fever.

Then it was again identified as the main cause of disease in Congo and given the present name of Crimean- Congo hemorrhagic fever (CCHF). Apart from other countries, it is also present in the Indian Subcontinent [2]. Crimean- Congo hemorrhagic fever (CCHF) is a lethal disease caused by the virus CCHF (CCHFV) which requires a tick as a host. It is widely spread in the endemic areas of the Middle East, Asia, the African continent, and southern Europe [3]. It is also transmitted to humans when they come into contact with infected people or animals or by the bite of the tick directly. Many animals do not show any signs of disease after the infection of CCHFV leading to the lack of any disease model for studying disease progression. Numerous domestic and wild animals, such as cattle, goats, sheep, small mammals, rodents, and birds, in

which the infection is mainly asymptomatic, serve as amplifying hosts for the virus [4].

CCHF has been known as a tick-borne contamination. It can be transmitted among humans and vertebrates. Consequently vaccination in humans and animals might lessen the danger of infection. New studies showed that there is no worldwide approved therapeutics or vaccines for CCHF. Henceforth, the expansion of a new group of vaccines could contribute to better controlling of the disease [5].

Classification

CCHF in the order of Bunyavirales belongs to the family of Nairoviridae and the genus of Orthonairovirus [7]. Therefore, the correct name is actually "Crimean Congo hemorrhagic fever orthonairovirus", which is rarely used in common scientific practice and is thus often simplified as "Crimean-Congo hemorrhagic fever virus" Orthonairoviruses are tick-borne viruses, which are divided into different serogroups and characterized by a large L segment [8]. The unusually large size of the L-segment distinguishes them from other bunyaviruses. Together with the Hazaravirus, which is non-pathogenic for humans and has been isolated from 5 rodents in Pakistan, it makes up the CCHF serogroup [9].

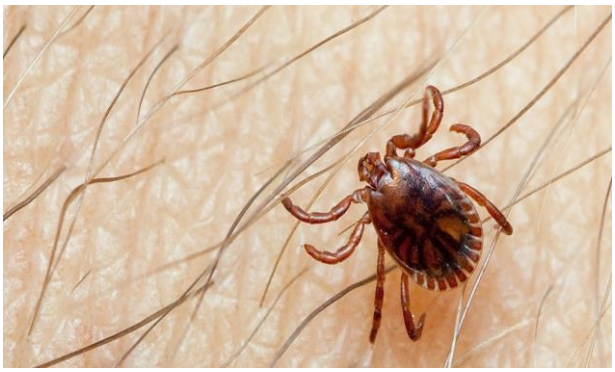


Figure 01: **Male Hyalomma specimen Crimean-Congo Viral Infection [6]**

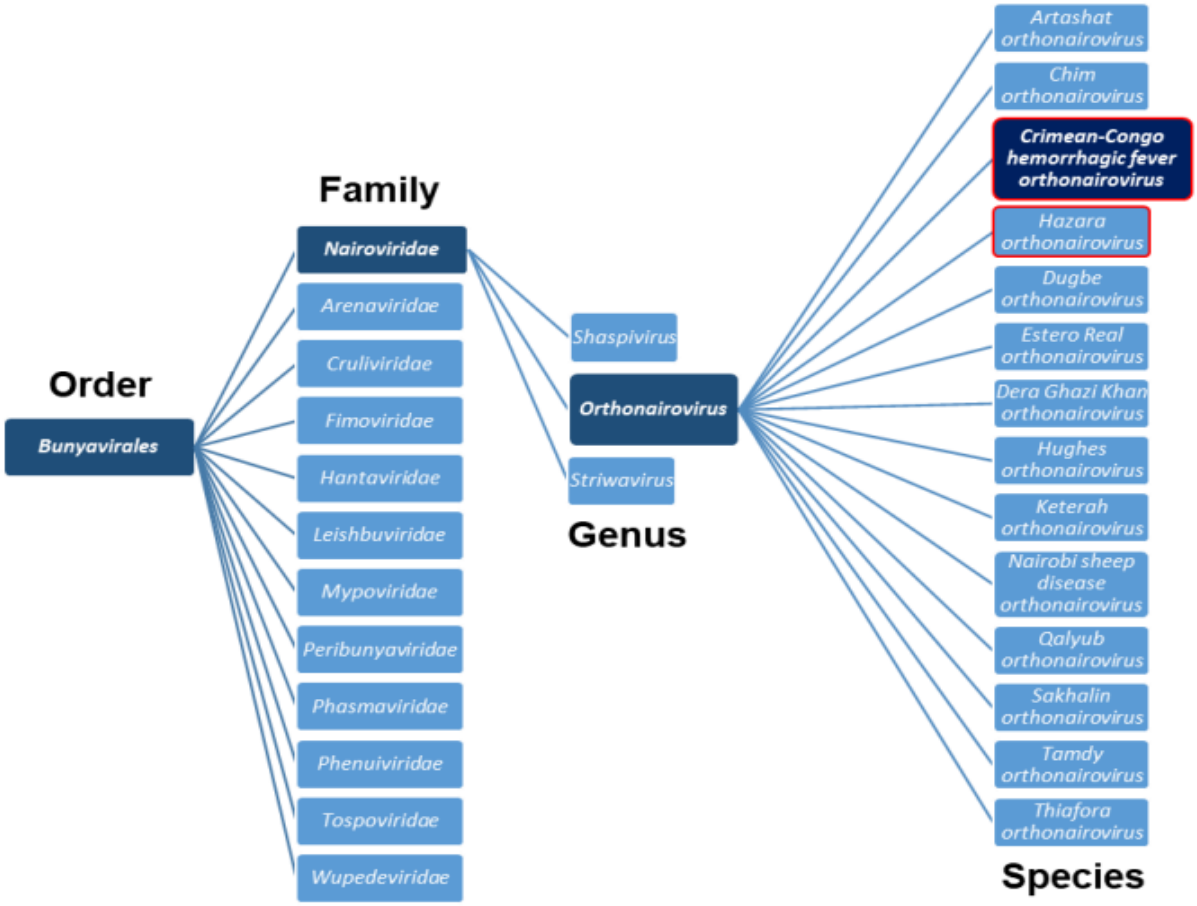


Figure 02: Phylogeny and classification of CCHFV [8]

Virus Transmission and Replication

Ticks of the genus i.e. Hyalomma act as a vector of the virus CCHF. There are different hosts for this virus which include animals such as sheep, goats, cattle, and hares [10]. This virus is transmitted to humans when humans get into contact with animal blood or infected ticks. In this way, one infected human can transmit it to the others when it comes into contact with the body fluids [11].

CCHFV's intracellular replication cycle The internalisation of viruses occurs by clathrin-dependent, receptor-mediated endocytosis after they link to cell surface receptors (A) (B).When the endosomal pH is reduced, the viral glycoproteins undergo a conformational change that causes the membranes of the envelope and endosome to fuse, releasing the nucleocapsids into the cytosol [12]. RNA-dependent RNA-polymerase produces messenger RNA (mRNA) and complementary RNA (cRNA) following nucleocapsid dissociation (D) (RdRp).While the cRNA serves as a template for the generation of genomic vRNA, the mRNA is translated into viral proteins (E). To create new nucleocapsids, the vRNA, RdRp, and capsid proteins join forces. The endoplasmic reticulum (F), [13, 14] where glycoprotein translation takes place, is where the precursor protein is broken into the GN and GC precursor forms. The Golgi complex (G) receives the glycoproteins and performs further processing there (H). After final glycoprotein maturation, new virions are produced (I), transported to the plasma membrane, and released (J) [15, 16]. While H. marginatum of the Palearctic tick species is thought to be the primary vector in Europe, H. rufipes of the Afrotropical tick species is thought to be the primary vector in Africa [17].

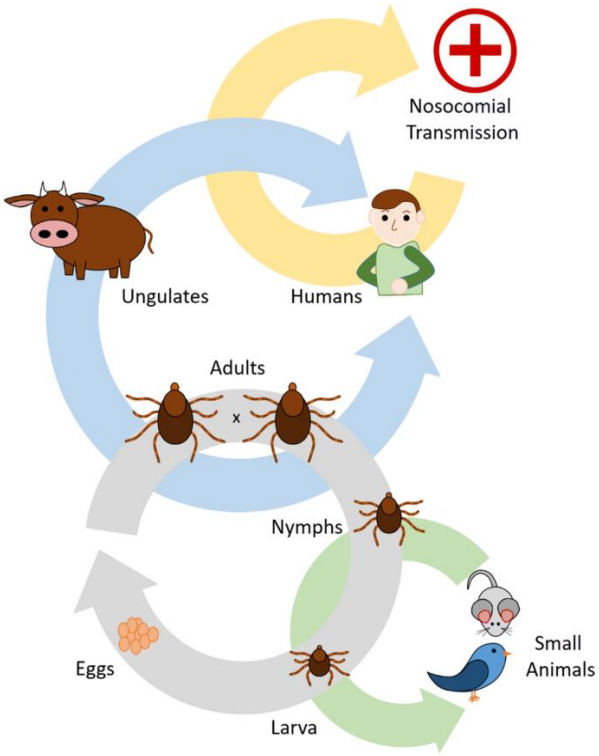


Figure 03: CCHFV transfer both vertically and horizontally, as well as the life cycle of Hyalomma species [12]

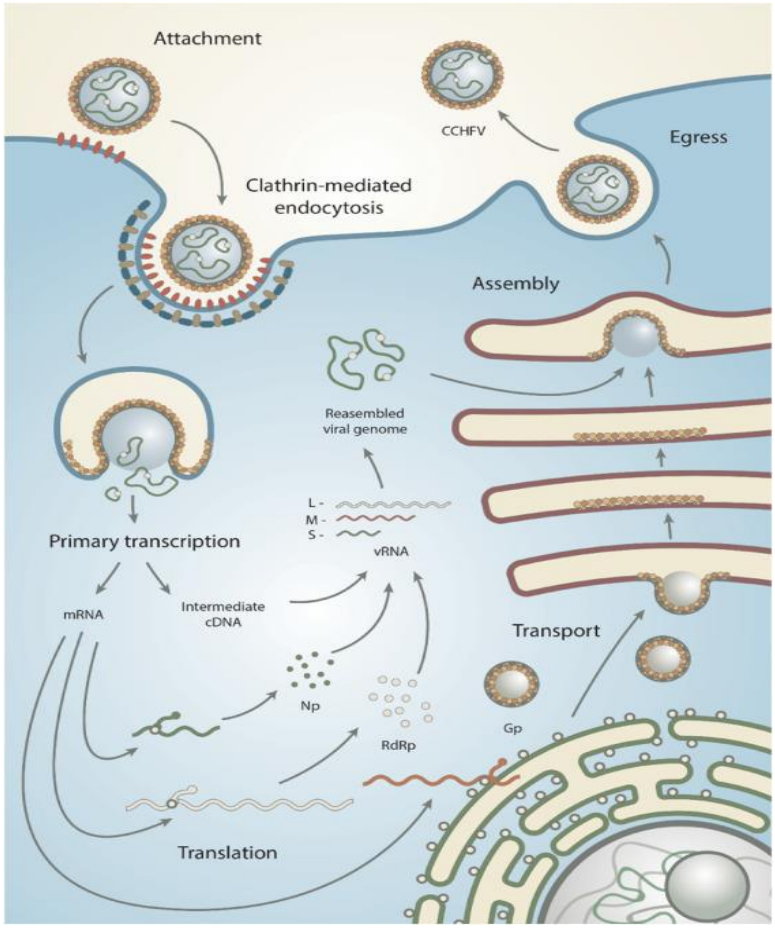
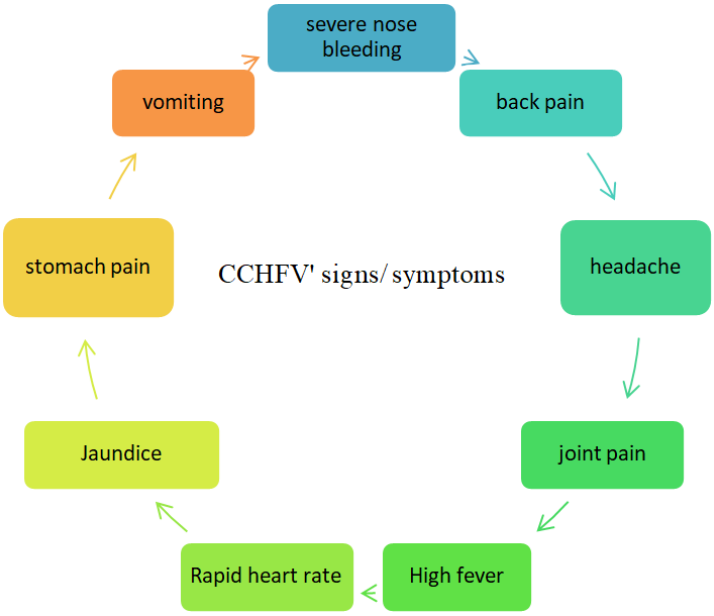


Figure 03: CCHFV's intracellular replication cycle [18]

Signs and Symptoms



Diagnosis, Prevention & Treatment

There are different laboratory tests that are used to diagnose CCHF which include Enzyme-linked Immunosorbent assay (ELISA) of both types one of which captures antigen and the other type that detects antibodies i.e. IgG and IgM. Real-Time Polymerase chain reaction (RT-PCR) can also be used to diagnose it. For a patient which has a history of CCHF in them the combination of ELISA and RT-PCR can be used to diagnose. Immuno-histo-chemical staining can also be used to detect the viral antigen [19]. RT-PCR and the detection of IgG/IgM antibodies, which are far more sensitive, secure, and rapid diagnostic methods, are currently the gold standard in people and animals. About a week after infection, IgM antibodies against CCHFV can be found in patient sera, and IgG antibodies can be found soon after [20]. Either immunofluorescence tests (IFA) or enzyme-linked immunosorbent assays (ELISA) are used to detect antibodies. The RT-PCR is thought to be more accurate since CCHF patients who have severe symptoms may not elicit an antibody response. Due to the enormous genetic diversity of CCHFV, it is more challenging for a single test to detect all strains using a PCR [21].

Treatment

Treatment includes correction of fluid balance as well as electrolyte abnormalities. There is an antiviral drug available that is ribavirin which has shown some benefits for patients infected with CCHF. Favipiravir, alone or in combination with ribavirin, appears to be promising in animal models but had not been tested in humans [22-24].

Prevention

- The risk of acquiring Crimean-Congo hemorrhagic fever from ticks can be decreased with repellents such as DEET, clothing that minimizes skin exposure (e.g., longsleeved shirts, long pants tucked into boots) and avoidance of tick habitats [24].
- Environmental modification around dwellings (e.g., removal of brush and long grass, insecticides) might be appropriate in some circumstances. Clothing and skin should be examined regularly for tick's Protective clothing and gloves should be worn during exposure to viremic animals, particularly when blood and tissues are handled, and the hands should be washed immediately afterward [25].
- CCHFV is thought to be inactivated in meat by post-slaughter acidification; Holding meat at 4-8ºC for 24 hours after slaughter has been recommended. It is safest to always cook meat and other animal tissues thoroughly, and to use good hygiene (e.g., hand washing, avoidance of mucous membrane contact) when preparing them for cooking [26].
- Some countries may recommend higher standards. The use of a N95 or equivalent respirator, eye protection, and single airborne precaution room or well-ventilated setting has been advised during any medical procedure that may produce aerosols or droplets. Safe burial practices have been published for fatal cases [20].
- Laboratory workers must follow stringent biosafety precautions. People who have had high-risk exposures are often treated prophylactically with ribavirin, and a recent retrospective analysis suggests it has been effective in preventing illnesses [20, 21].

Vaccine

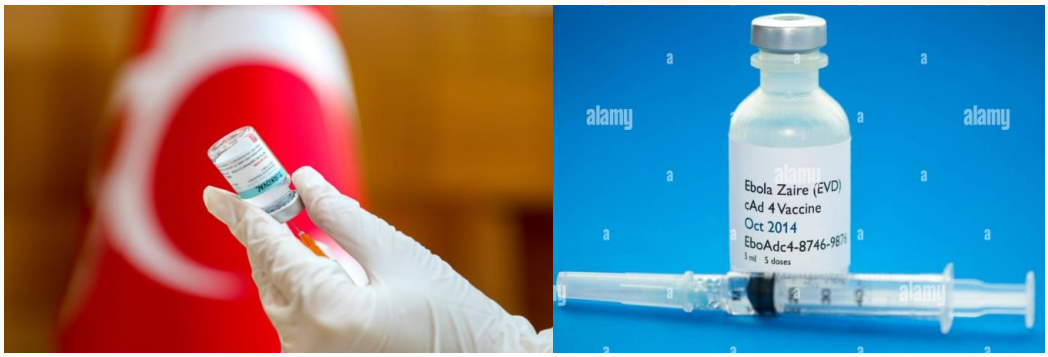


Figure 04: Crimean-Congo hemorrhagic fever vaccine [29]

Antiviral compounds such as ribavirin have not acted effective in treating CCHFv. Only available vaccine has been produced in Bulgaria which was made in the mouse brain which was inactivated by chloroform. It has shown immunity [30]. Another vaccine that can protect against the disease is a DNA-based vaccine.

Transgenic tobacco leaves has also been used to provide oral immunization to the mice when presented as food. It provides humoral response for the glycoprotein. This vaccine is safe for the human use as well [29]. Pakistan is a country in which Crimean-Congo hemorrhagic fever (CCHF) causes deadly infections. It is a tick-borne viral infection and a robust plant needs to be implemented early detection, surveillance system, proper treatment preventive measures and timely response [31].

CONCLUSION

Crimean-Congo hemorrhagic fever (CCHF) is a condition brought on by a virus (Nairovirus) that is spread by ticks and is a member of the Bunyaviridae family and the genus Hayalomma. Congo Virus infection CCHF is a clear and growing health threat in the WHO EMR as well as the efficacy of several vaccinations. Treatment includes correction of fluid balance as well as electrolyte abnormalities. There is an antiviral drug available that is ribavirin which has shown some benefits for patients infected with CCHF. Favipiravir, alone or in combination with ribavirin, appears to be promising in animal models but had not been tested in humans. In order to advance in the development of a vaccine that considerably improves our ability to regulate the situation of CCHF on a global basis; the current review assesses the prevalence of Congo viral infection overview. The various distinctive animal models can be utilized. A strategic framework for the prevention and control of CCHF is important to curb the ongoing and new threats posed by CCHFV. The CCVax responses protective against CCHFV showed promising results and for providing protection.

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