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The role of ticks in the maintenance and transmission of Crimean-Congo hemorrhagic fever virus: A review of published field and laboratory studies

Aysen Gargili [a, b, c], Agustin Estrada-Peña [d], Jessica R. Spengler [e], Alexander Lukashev [f, g], Patricia A. Nuttall [h], Dennis A. Bente [a, b, *]

[a] Department of Microbiology & Immunology, University of Texas Medical Branch, Galveston, TX, USA
[b] Galveston National Laboratory, University of Texas Medical Branch, Galveston, TX, USA
[c] Faculty of Health Sciences, Marmara University, Istanbul, Turkey
[d] Veterinary Faculty, University of Zaragoza, Zaragoza, Spain
[e] Viral Special Pathogens Branch, Centers for Disease Control and Prevention, Atlanta, USA
[f] Chumakov Institute for Poliomyelitis and Viral Encephalitides, Moscow, Russia
[g] Institute of Molecular Medicine, Sechenov First Moscow State Medical University, Moscow, Russia
[h] Department of Zoology, Oxford University, UK

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ABSTRACT

This manuscript is part of a series of reviews that aim to cover published research on Crimean-Congo hemorrhagic fever (CCHF) and its etiological agent, CCHF virus (CCHFV). The virus is maintained and transmitted in a vertical and horizontal transmission cycle involving a variety of wild and domestic vertebrate species that act as amplification hosts, without showing signs of illness. These vertebrates have traditionally been considered reservoirs of CCHFV, but in fact they develop only a transient viremia, while the virus can persist in ticks for their entire lifespan, and can also be transmitted vertically to the next generation. As a result, ticks are now considered to be both the vector and the reservoir for the virus. CCHFV has been detected in a wide range of tick species, but only a few have been proven to be vectors and reservoirs, mainly because most published studies have been performed under a broad variety of conditions, precluding definitive characterization. This article reviews the published literature, summarizes current knowledge of the role of ticks in CCHFV maintenance and transmission and provides guidance for how to fill the knowledge gaps. Special focus is given to existing data on tick species in which vertical passage has been demonstrated under natural or experimental conditions. At the same time, we identify earlier reports that used unreliable methods and perceptions to ascribe a vector role to some species of ticks, and have contributed to confusion regarding viral transmission. We also examine epidemiological pathways of CCHFV circulation and discuss priority areas for future research.

Contents

* Corresponding author. University of Texas Medical Branch, 301 University Boulevard, Galveston, TX, 77555-0610, USA.
E-mail address: dabente@utmb.edu (D.A. Bente).

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1. Scope of this review

This manuscript is part of a series of reviews that aims to cover all published research on Crimean-Congo hemorrhagic fever (CCHF), a frequently severe disease produced by Crimean-Congo hemorrhagic fever virus (CCHFV; family *Bunyaviridae*, genus *Nairovirus*). Previous reviews have focused on epidemiology, molecular characterization, seroepidemiological studies, and the role of wild and domestic vertebrate animals in CCHFV maintenance and amplification of the infection (Bente et al., 2013; Spengler et al., 2016a, b; Zivcec et al., 2016).

CCHFV has been detected in a wide range of tick species, but only a few have been definitively identified as vectors and reservoirs. In this paper, we discuss four main research questions:

1. the role of ticks in the maintenance and transmission of CCHFV in nature (e.g., vector competence and viral persistence in ticks);
2. the role of tick factors (e.g., gut barrier and saliva-assisted transmission) on CCHFV transmission and evolution;
3. vector-vertebrate host dynamics (e.g., host pattern, host species, host selection in experimental studies); and
4. the geographic distribution of tick vectors able to maintain CCHFV, potential introduction of CCHFV into new areas and the emergence of new disease foci.

We address these questions by providing a collective, comprehensive compilation of data on the role of ticks in the ecology of CCHFV, including those species that have been conclusively shown to play a role in CCHFV maintenance and transmission. We also establish an epidemiological context for the reported data, providing definitions and terms regarding the role of both ticks and vertebrates in CCHFV circulation. We identify studies that have reported the detection of CCHFV in feeding ticks, a method which is suitable to detect the presence of the virus in a territory, but not for discerning the vectorial capacity of the tick, and discuss the consequences of using unreliable methods for either the identification of the tick or the construction of unsubstantiated conclusions based solely on detection of viral RNA.

The data compiled in this review have been obtained by a search in both PubMed and Web of Science. A deliberately relaxed query was done in both datasets, to capture a larger than required set of papers. The query included the terms “CCHF”, “CHF, “CCHFV”, CHFV, “Congo virus” or “Crimean-Congo”, plus the terms “tick”, “Ixodidae”, “Argasidae” or the name of every genus of tick. We purposely avoided the inclusion of search terms in the query regarding countries and common or scientific names of vertebrates, so as not to restrict the search to a geographic region or group of hosts. This query produced a large number of papers including clinical manifestations or treatment of the disease in humans, that we removed after reading the abstract and/or the body of the text. We also included data from references that are not recorded by these datasets, the majority of which are Russian reports translated into English (e.g., NAMRU-3 translations).

2. Background

2.1. Epidemiology of Crimean-Congo hemorrhagic fever

Among the tick-borne viruses, CCHFV is the most important cause of severe and fatal human hemorrhagic disease. CCHF has a variable case fatality rate of 3% to over 50%. However, based on improved diagnostic capabilities and data from cases in Turkey in the last decade, it is likely that the range is much smaller and the higher rates reflect a failure to recognize less severe infections in