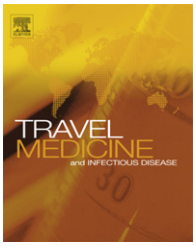
Travel Medicine and Infectious Disease (2010) **8**, 139–143

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevierhealth.com/journals/tmid



Crimean–Congo hemorrhagic fever: Risk for emergence of new endemic foci in Europe?

Helena C. Maltezou [a,*], Anna Papa [b]

[a] *Department for Interventions in Health-Care Facilities, Hellenic Center for Diseases Control and Prevention, Athens, Greece*
[b] *First Department of Microbiology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece*

Received 4 February 2010; received in revised form 27 April 2010; accepted 29 April 2010
Available online 26 May 2010

KEYWORDS
Crimean–Congo hemorrhagic fever;
Emergence;
Southeastern Europe;
Turkey;
Vector-borne disease

Summary During recent years, new foci of Crimean–Congo hemorrhagic fever (CCHF) have emerged in several Balkan countries, southwest Russia, and Turkey. Starting in 2002, Turkey experiences the largest ever recorded outbreak with more than 2500 cases. Potential reasons for the emergence or re-emergence of CCHF include climate changes which may have a significant impact on the reproduction rate of the vector *Hyalomma* ticks, as well as anthropogenic factors (e.g. changes in agricultural and hunting activities). Given the abundance of its vector, the numerous animals that can serve as hosts, and the favorable climate and ecologic parameters in other southern Europe Mediterranean countries, CCHF is an example of a vector-borne disease which may be knocking the door in this area. There are models which show probability of CCHF extending to other countries around the Mediterranean basin suggesting that the vector, veterinarian, and human surveillance should be enhanced.

Introduction

Crimean–Congo hemorrhagic fever (CCHF) is an acute, highly contagious viral zoonosis transmitted to humans not only by ticks, mainly of the genus *Hyalomma*, but also by direct contact with blood or tissues of viremic hosts. In cases of severe illness, prominent hemorrhagic manifestations occur at a late stage, with a fatality rate ranging from 5% to 50%.[1] Because of the potential of human-to-human transmission and the onset of nosocomial outbreaks, CCHF is a disease of immediate notification to public health authorities. CCHF is also included in the list of infectious agents for potential use as a biological weapon, and also in the list of diseases for which the Revised International Health Regulations call for assessment of the CCHF event for possible notification to the World Health Organization (WHO).[2]

CCHF was first recognized as a clinical entity during an outbreak which occurred in Crimea in 1944–1945.

---

* Corresponding author. Department for Interventions in Health-Care Facilities, Hellenic Center for Diseases Control and Prevention, 3–5 Agrafon Street, Athens 15123, Greece. Tel.: +30 210 5212 175; fax: +30 210 5212 177.
E-mail address: helen-maltezou@ath.forthnet.gr (H.C. Maltezou).

1477-8939/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tmaid.2010.04.008

Subsequently it was found that the causative agent was identical to an agent isolated in 1956 from a human case in The Congo, and the name CCHF was established.[1] At present, CCHF virus (CCHFV) is endemic in wide areas of Africa and Eurasia. During the recent years the emergence or re-emergence of CCHF was described in several Balkan countries, including Albania, Kosovo, Bulgaria, and recently in southwest Russia, Turkey, and Greece.[3–10] The epidemiology and ecology of CCHF, the current situation in southeastern Europe and neighboring areas are reviewed, and the risk for CCHFV becoming endemic in other European countries is discussed.

Epidemiological and biological aspects

In nature CCHFV circulates in a tick—vertebrate—tick transmission cycle, and humans are accidental intruders of this cycle. CCHFV infection has been detected in numerous wild and domestic vertebrates. The principal animal hosts include cattle, sheep, goats, and hares.[1,11] Ground-feeding birds are also a significant host of *Hyalomma* ticks and, at least in Africa, of CCHFV.[11]

CCHFV infection is a two-stage vector-borne disease: small herbivores are infested by the immature stages of *Hyalomma* ticks and serve as amplifying hosts, while adult *Hyalomma* ticks feed mainly on large herbivores, which have the greatest prevalence of CCHFV infection. CCHFV infection of animals is not associated with evolution to clinically overt disease, chronic infection, or death. In particular, following a tick bite, animal hosts remain viremic and thus infectious for only a few days.[12] For this reason, the CCHFV cycle is sustained by concomitant attachment and feeding on a specific animal by more than one stage of ticks, which in turn allows for CCHFV transmission from mature to immature ticks during feeding and before dropping to the ground.[12] This limits severely the potential for amplification; infected nymphs arising from any infected unfed larva can only infect the same host on which the larva fed. Furthermore, the infected nymphs develop after feed as adults on different types of hosts, so the cycle can only be maintained by transovarial transmission, which is essential, but apparently is of unknown limited efficiency. Infected ticks have also been detected in migratory birds and their implication in the spread of CCHFV appears likely on the basis of phylogenetic studies showing lineage links of CCHFV over long distances.[13]

Hyalomma ticks are well-established vectors of CCHFV. The genus *Hyalomma* consists of 30 species of which *Hyalommamarginatum marginatum* is the almost exclusive CCHFV vector in Europe. *H. marginatum* is abundant in almost all Balkan countries, and also in Turkey, Russia, Ukraine, Italy, Spain, and Portugal. This species is also found in southern France, Cyprus, Israel, and along the northern seaside of all Mediterranean African countries.[1,14–19] In 2006 *Hyalomma* ticks were detected for the first time in the Netherlands and southern Germany.[20,21] Although CCHFV has been detected in other tick species (e.g. *Dermacentor*, *Rhipicephalus*, *Ixodes*, *Boophilus*), CCHFV cycle in nature is sustained almost exclusively by *Hyalomma* ticks. It is unknown whether these species play a significant role in CCHFV cycle, if non-biologic environmental factors change.

Geographical distribution and ecological factors

In contrast to almost all other hemorrhagic fever viruses that have relatively narrow geographical ranges, CCHFV demonstrates the widest geographical distribution among all tick-borne diseases, being detected in more than 30 countries across Africa, central and southwestern Asia, Middle East, and southeastern Europe. The distribution of CCHFV coincides with the distribution of *Hyalomma* ticks, with a 50° north latitude limit. The numerous animal species that can serve as hosts for CCHFV indicate that non-biological factors are more likely to determine the patterns of epidemiological risk.[12]

Temperature and humidity are major determinants for the geographical range and survival of ticks. Warmer temperatures have an impact on tick populations and their annual and seasonal patterns, mainly by shortening their inter-stadial development period which may affect their lifecycle. The key predictor variable for the presence of CCHF identified by stepwise forward selection is a minimum land surface temperature of 18.91 °C, whereas a value of 18.16 °C predicts CCHF absence.[12] These temperature limits explain the consistent association of CCHF cases with warmer temperatures and the season. Compared to other ticks, *Hyalomma* ticks adapt better to dry climates. These characteristics are in accordance with activation of *Hyalomma* ticks in temperate areas in late spring and their continuous activation throughout summer to early autumn.[1,12] *Ixodes ricinus* also shows this seasonal pattern of activity, however it is extremely sensitive to low humidity. The CCHF outbreaks which occurred in Albania and Kosovo in 2001 were preceded by mild winters.[5,22] Micro-ecological factors (e.g. vegetation, microclimate) may also influence the tick—host dynamics and may provide an explanation for the heterogeneity in infection levels which may occur even within endemic regions. For example, in several Balkan countries, endemicity of CCHF occurs in well-confined areas. *Hyalomma* ticks are found mainly in areas of small and relatively dry vegetation that are relatively easily accessible by humans, and not in forest-type vegetation.

Humans may affect the ecology of CCHFV and thus modify the risk for transmission. Disruption of agricultural activities, changes in land use from floodplains to agricultural land, abandonment of hare hunting followed by reintroduction of livestock, and war conflicts have been associated with large CCHF outbreaks in the former Soviet Union, Bulgaria, Kosovo, and Turkey.[11,23] Recreational activities may also account for the onset of CCHF cases. Animal trade may account for importation of infected *Hyalomma* ticks from endemic to non-endemic areas.[1] There is a phylogenetic evidence of movement of CCHFV lineages over large distances, which may be explained by movement of CCHFV-infected or infested livestock, for example there is considerable movement of sheep and goats between Africa and Asia in the context of religious festivals.[13] Major migratory bird fly paths may explain CCHFV lineage links between West and South Africa.[13] Increased awareness and improvements in diagnosis of CCHF may also contribute to the apparent emergence of CCHF.