

Book Review

Reviewed by Jens H. Kuhn

Harvard Medical School, Southborough, Massachusetts

Crimean-Congo Hemorrhagic Fever— A Global Perspective

Edited by Onder Ergonul and Chris A. Whitehouse
Dordrecht, The Netherlands: Springer (2007)
328 pp., \$198.00, hardcover
ISBN: 978-1-4020-6105-9

The tick-borne disease Crimean-Congo hemorrhagic fever (CCHF) was only known to a few expert arbovirologists until about a decade ago. This is reasonable, as the etiologic agent, Crimean-Congo hemorrhagic fever virus (CCHFV, family *Bunyviridae*, genus *Nairovirus*), seemed to be endemic mainly in rural areas of Africa and the former Soviet Union, where it caused disease outbreaks with low human case numbers. Due to its classification as a Risk Group 4 virus, research was limited to the few maximum-containment facilities around the world. This explains why: a) there is only very limited knowledge on the molecular biology of the virus; and b) the majority of the scientific literature on CCHF and CCHFV has been published in Russian.

In recent years, however, CCHF has been recognized as a truly emerging infectious disease. Recently, cases have been reported in the Middle East (e.g., Iran) and southeastern Europe (e.g., Turkey), and the number of cases appears to increase every year, although this observation could be due to an increased awareness among health-care professionals. CCHFV causes a severe disease in humans with a high case-fatality rate. Because of the absence of specific prophylactics and the lack of widely available specific and sensitive diagnostic capabilities, the virus is classified as a DHHS Non-Overlap Select Agent and a NIAID Category C Priority Pathogen in the United States.

Önder Ergönül and Chris A. Whitehouse have recently edited *Crimean-Congo Hemorrhagic Fever—A Global Perspective* to “present updated information on several key aspects of the disease and the virus” for a broader audience. (Oddly, Ergönül’s name is spelled without the diacritical marks throughout the book.) The editors have done a fantastic job in recruiting the world’s leading CCHF experts and in describing the disease and the virus in detail.

The introduction to the first section nicely summarizes the discovery of “Crimean hemorrhagic fever” in

1944 in the Crimea and presents tables with most known outbreaks up to 2006. However, although the editors do acknowledge the significant studies published in Russian, they state that the majority of “over 400 publications on CCHF” have been published in English. Regrettably, the author of this review is aware of over 700 Russian publications, many of which are seminal in CCHF research and most are not indexed in common electronic databases such as PubMed. Likewise, the editors’ statement in the preface that their book “is the first book written which is specifically devoted to CCHF” is misleading, as there have been several so far, published in Russian several decades ago.

The second chapter, written by B. Arda and A. Aciduman, is a fascinating journey into the history of the terms “illness,” “disease,” and “syndrome,” and nicely explains why it is difficult even for experts to assign a particular agent such as CCHFV to epidemics described in historical accounts hundreds or thousands of years old. J. P. Woodall, who first described “Congo virus” in 1967 in Uganda and who clearly is still unsatisfied with the current name of the virus, follows with a personal and historically insightful account of its characterization and the dispute that ensued when it was realized that the agent responsible for “Crimean hemorrhagic fever” and “Congo virus” were in fact the same.

In the second section, R. Flick presents current knowledge on the molecular biology of CCHFV, which is still very limited. The data are well presented, although the author strangely defied current practice and depicted the genomic segments of this trisegmented negative-stranded RNA virus in 5'→3' order, rather than vice versa. Also, this chapter clearly would have benefited from a comparison of CCHFV with other bunyaviruses, such as hanta-, orthobunya-, or phleboviruses, because some of those viruses are much better characterized on a molecular level and show great similarities to the genomic organization of CCHFV. The next chapter, written by R. Hewson, presents a concise and accurate overview of the molecular epidemiology and phylogeny of the many CCHFV strains isolated all over the world. His conclusions suggest that novel CCHFV strains will continue to emerge, that this emergence will most likely be the result of reassortments of the medium-size (M) genomic segment, and that studies should ensue to determine whether certain viral genotypes are associated with graver disease manifestations.

The third section is the highlight of the book. Z. Vatanserver et al. review the epidemiology of CCHFV in Turkey, which has been hit by successive CCHF outbreaks since 2002. This chapter, like several of the subsequent reviews, summarizes important data published in languages other than English and comes to the important conclusion that human changes to the environment probably caused a population increase of the principal CCHFV vector, *Hyalomma marginatum marginatum*—a warning to other countries with similar landscapes and climates. T. Avšič-Županc follows suit with an historical and status-quo description of CCHFV in Albania, Bulgaria, Greece, and Kosovo, succeeded by S. Chinikar's account of the history of CCHF research in Iran. The next chapter, written by A. M. Butenko and G. G. Karganovo, is a superb overview of the epidemiological data on CCHFV in the area of the former Soviet Union. The subsequent two chapters, written by M. Saijo and F. J. Burt et al., respectively, describe how western China and South Africa were affected by CCHF outbreaks. M. J. Turell then clarifies the differences between “vectors” and “reservoirs” and provides comprehensive information on tick species that were found to be naturally infected with CCHFV and others that could be infected experimentally. He concludes with a small but important paragraph on the role of birds in the spread of transovarially infected larval ticks or infected nymphal ticks to different areas. This understudied topic is also discussed by A. Nalca and C. Whitehouse in a very informative chapter on animals infected either naturally or experimentally with CCHFV. S. E. Randolph and D. J. Rogers further discuss the role of climate on the ecology

of tick-borne diseases in general and suggest taking a closer look at global climate change and tick movements. The section ends with B. S. Cooper's explanation of mathematic models of CCHFV transmission.

The book's next two sections describe the measures to be taken to diagnose and control CCHF. Chapters 16 and 17 by O. Ergönül and M. Bray, respectively, nicely summarize the current understanding of CCHF as a disease, whereas H. Zeller contributes a very detailed summary of the advantages and disadvantages of available diagnostic assays. O. Ergönül et al. then describe current treatment protocols for CCHF patients with particular emphasis on ribavirin. C. Whitehouse adds a chapter on tick control, especially in livestock. A. Tarantola et al. describe the risk of CCHFV infection to health-care workers, but unfortunately omit the Russian data in their analysis. The book ends with a must-read contribution by P. Formenty et al. on international CCHF surveillance and intervention strategies in case of new outbreaks.

In conclusion, this book contains a wealth of useful information compiled by experts in the field. There could have been more color images; some chapters (such as Chapter 16) and figures or figure legends (such as Figures 2-3 and 5-1) should have been edited more carefully in regard to the English language; and I would have liked to have seen a chapter on maximum-containment facility research and on how to work with infected ticks under such conditions. Despite these minor shortcomings, the book is an absolute must for arbovirologists and emerging infectious disease experts, as well as for high-containment biosafety professionals who want to acquaint themselves with CCHF and CCHFV.

EPA Issues Guidance to Pesticide Manufacturers for Registration of “Anthrax-related” Products

EPA Pesticide Program Updates
from EPA's Office of Pesticide Programs 09/03/08
www.epa.gov/pesticides

EPA has issued Pesticide Registration Notice (PRN) 2008-2 to provide guidance to registrants who may want to register “anthrax-related” products (products that inactivate *B. anthracis* spores on inanimate surfaces such as in contaminated buildings). This guidance should help the United States be prepared to respond to incidents involving anthrax spores by assuring that anthrax-related products are registered, bear appropriate labeling, and are effective when used as directed. This guidance will help protect public health from the risks posed by anthrax spores by employing terms and conditions of registration that limit the use of anthrax-related products to those who are properly trained and determined to be competent in their use.

In a parallel effort to this PR Notice, EPA is also developing guidance for the efficacy test methods that registrants should use to demonstrate the effectiveness of their anthrax-related products.

The PR Notice, public comments on the draft PR Notice, and EPA's responses to those public comments will be filed in Docket ID # EPA-HQ-OPP-2006-1004. The PR Notice can be found at www.epa.gov/PR_Notices/pr2008-2.htm, and the Federal Register Notice of Availability can be found at www.epa.gov/fedrgstr.