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# Hantaviruses

Edited by C.S. Schmaljohn  
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With 24 Figures and 14 Tables



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*Cover Illustration:* Background: Immunofluorescent antibody staining of Seoul virus-infected Vero E6 cells with polyclonal sera to Seoul virus. Foreground: Schematic representation of a hantavirus particle showing the three genome segments complexed with the nucleocapsid and polymerase proteins and surrounded by a bilaminar envelope with two protruding viral glycoproteins.

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## Preface

Hantaviruses hit the headlines in 1993 when a large outbreak of hantavirus pulmonary syndrome (HPS), a previously unknown human disease with high mortality, erupted in the southwestern United States, and was quickly shown to be caused by a newly recognized virus, later named Sin Nombre virus, maintained in deer mice populations. Since this time there has been an exponential growth in studies and knowledge of these fascinating viruses, and many of these enlightening studies are highlighted in this volume. However, the roots of the field can be traced back to the early 1950s when United Nations troops were engaged in the Korean conflict. Over 3000 cases of an acute febrile illness were seen among the soldiers, about a third of which had hemorrhagic symptoms, and 5–10% died. The disease was initially called Korean hemorrhagic fever, but is now known as hemorrhagic fever with renal syndrome (HFRS). It took almost 25 years to identify the virus and the rodent reservoir, the field mouse, *Apodemus agrarius*. The virus was named Hantaan virus after the Hantaan river, which runs along the 38th parallel, and is close to the region where *Apodemus* first shown to harbor the virus were trapped. Hantaan virus became the prototype of the genus *Hantavirus* in the family *Bunyaviridae*, and included the only known members of the family that had no arthropod vector. Shortly after the isolation of Hantaan virus, other HFRS-associated viruses such as Seoul virus in rats and Puumala virus in bank voles were identified. In addition, a hantavirus that was not known to be pathogenic to humans, Prospect Hill virus, was discovered and isolated from infected meadow voles in the United States. These discoveries set the stage for the finding, more than ten years later, of the first pathogenic hantaviruses known to exist in the Americas. During the past seven years, HPS has been shown to occur throughout the Americas from Canada to Patagonia, and at least 10 different HPS-associated hantaviruses, each associated with a distinct rodent species, have been discovered. With the study of the many HFRS- and HPS-associated hantaviruses, an increasingly complex picture has emerged

with a spectrum of additional hantaviruses of unknown human pathogenicity detected in a variety of other rodent species.

This volume opens with a chapter by Karl Johnson describing the fascinating disease detective work done in the early years of discovery of these viruses. The next two chapters by Colleen Jonsson and Connie Schmaljohn, and Christina Spiropoulou, present a comprehensive overview of the recent advances in understanding hantavirus replication and maturation. Chapters 4 and 5 by Alexander Plyusnin and Sergey Morzunov, and Brian Hjelle and Terry Yates, describe the intricate long-term relationship that hantaviruses have maintained with their specific rodent reservoirs. Unlike the acute infection seen in humans, hantavirus infection of its primary rodent reservoir results in persistent infection with prolonged virus shedding in excreta. Also, phylogenetic data suggest these viruses have been associated with their rodent hosts for millions of years. Like other zoonotic diseases, studying the process of virus maintenance and transmission within rodent communities is critical to understanding hantavirus disease ecology and developing the ability to predict locations and periods of high risk of human exposure. Chapter 6 by Eric Mackow and Irena Gavrillovskaya describes exciting developments in attempts to identify host cell receptor usage and correlate these with viral pathogenicity. In Chapters 7 and 8, Delia Enria, Ana Briggiler, Noemi Pini, and Silvana Levis, and Mats Linderholm and Fredrik Elgh, provide up to date clinical descriptions of HFRS and HPS. The rapid progression and frequent severity of these diseases, make early detection and careful management of patients critical. The detailed descriptions of symptoms and disease parameters should be useful to clinicians that may encounter hantavirus-infected patients. Similarly, in chapter 9, Olli Vapalahti, Åke Lundkvist, and Antti Vaheri review important recent information correlating major histocompatibility alleles of HFRS and HPS patients, virus load and virus-specific antibody levels with severity of disease. Modulating this complex interaction of virus and host immune response is the focus of the final chapter by Jay Hooper and Dexin Li, which describes recent innovations in the development of vaccines for HPS and HFRS.

We have come a long way since the early days of the hantavirus field in the 1950s. The pace of discovery has accelerated enormously in the last 5–10 years. The application of polymerase chain reaction technology has allowed the rapid identification of an increasingly numerous and complex rogues gallery of disease-associated hantaviruses. The realization of the global nature of hantavirus-associated diseases, and the increas-

ing application of technologically advanced approaches to hantavirus study will further boost the rate of discovery and depth of knowledge of this important group of viruses and their associated diseases.

October 2000

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# List of Contents

K.M. JOHNSON Hantaviruses: History and Overview . . . . .	1
C.B. JONSSON and C.S. SCHMALJOHN Replication of Hantaviruses . . . . .	15
C.F. SPIROPOULOU Hantavirus Maturation . . . . .	33
A. PLYUSNIN and S.P. MORZUNOV Virus Evolution and Genetic Diversity of Hantaviruses and Their Rodent Hosts . . . . .	47
B. HJELLE and T. YATES Modeling Hantavirus Maintenance and Transmission in Rodent Communities . . . . .	77
E.R. MACKOW and I.N. GAVRILOVSKAYA Cellular Receptors and Hantavirus Pathogenesis . . . . .	91
D.A. ENRIA, A.M. BRIGGILER, N. PINI, and S. LEVIS Clinical Manifestations of New World Hantaviruses . . . . .	117
M. LINDERHOLM and F. ELGH Clinical Characteristics of Hantavirus Infections on the Eurasian Continent . . . . .	135
O. VAPALAHTI, Å. LUNDKVIST, and A. VAHERI Human Immune Response, Host Genetics, and Severity of Disease . . . . .	153
J.W. HOOPER and D. LI Vaccines Against Hantaviruses . . . . .	171
Subject Index . . . . .	193



## List of Contributors

(Their addresses can be found at the beginning of their respective chapters.)

BRIGGILER, A.M. 117

ELGH, F. 135

ENRIA, D.A. 117

GAVRILOVSKAYA, I.N. 91

HJELLE, B. 77

HOOPER, J.W. 171

JOHNSON, K.M. 1

JONSSON, C.B. 15

LEVIS, S. 117

LI, D. 171

LINDERHOLM, M. 135

LUNDKVIST, Å. 153

MACKOW, E.R. 91

MORZUNOV, S.P. 47

PINI, N. 117

PLYUSNIN, A. 47

SCHMALJOHN, C.S. 15

SPIROPOULOU, C.F. 33

VAHERI, A. 153

VAPALAHTI, O. 153

YATES, T. 77