



EMERGING INFECTIONS

8

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Cover photo: Bronchiole in the lung of a young infant with fatal *Bordetella pertussis* pneumonia, showing abundant bordetellae (staining red) attached to cilia of respiratory epithelial cells and free within luminal debris. Immunoalkaline phosphatase with naphthol-fast red and hematoxylin counterstain. Original magnification, $\times 100$. (Courtesy of Sherif R. Zaki and Christopher Paddock, National Center for Infectious Diseases, Centers for Disease Control and Prevention.)

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To Merle A. Sande, M.D. (1939–2007), esteemed infectious disease clinician, educator, investigator, mentor, and friend, for his tireless efforts spanning more than 25 years in North America and Africa in the fight against AIDS, the most important emerging infection of our time

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FOREWORD

Since the 14th century, when the city-state of Venice attempted to prevent outbreaks of plague by quarantine, requiring ships to stay at harbor for a period of 40 days, there has been great concern about the emergence and international spread of infectious diseases. This concern reached a peak during the 19th century, when international conventions were drafted in Europe and the Americas requiring quarantine for six infectious diseases: cholera, plague, relapsing fever, smallpox, typhus, and yellow fever. In the early 20th century, warnings of other infectious disease threats were noted when the 1918 influenza pandemic emerged and spread throughout the world. However, in that era, infectious diseases traveled slowly overland or by ship, and news traveled by telegram, telex, or telephone.

In the latter half of the 20th century, major changes occurred. These changes ranged from explosive population growth and rapid urbanization to human incursion into previously uninhabited areas; intensive farming and animal husbandry; environmental degradation; and discovery, development, and then misuse of antimicrobials. As a result, previously unidentified infectious diseases, or infectious disease-causing microbes resistant to antimicrobial agents, are emerging and being identified at historically unprecedented rates. These infections now travel around the world by air, not only in humans but in insects, animals, and improperly processed food. Airlines today carry more than 2 billion passengers a year, and international trade continues to expand, vastly increasing opportunities for rapid international spread of infectious agents. At the same time, news about infectious disease outbreaks spreads along the electronic highway in ways and at speeds not imagined just 30 years ago.

Emerging infectious disease outbreaks affect not only health; business continuity and economies also suffer. Vulnerability is universal. After the 2003 outbreak of severe acute respiratory syndrome (SARS) and its impact on human health and national economies, there could be no denial that new tools for collective defense and public health security were required. This highly publicized outbreak contributed to the rapid completion of the revision of the International Health Regulations (the 1969 convention that had required reporting of cholera, plague and yellow fever and laid out measures that were then thought to be required to stop the international spread of these infections).

The revised regulations are an international legal instrument designed to achieve maximum security against the international spread of diseases. They expand the focus of collective defense from just a few reemerging diseases to include any emergency with international repercussions for health, including outbreaks of emerging and epidemic-prone diseases, outbreaks of food-borne disease, natural disasters, and chemical or radionuclear events, whether accidental or caused delib-

erately. The long term vision of the revised regulations is for all countries to detect and stop infectious diseases where and when they occur by ensuring the necessary core capacities in surveillance and epidemiology. At the same time, the regulations provide for collective preparedness for any infections that threaten to cross international borders and for a rapid response if they do cross borders.

Given today's universal vulnerability, stronger public health security calls for global solidarity, working under the framework of the International Health Regulations, through diplomacy, cooperation, transparency, and preparedness. There has never before been a better opportunity for countries to work together to ensure a more secure world.

The 20 chapters in this volume provide concise and timely updates on the epidemiology, clinical features, and prevention and control strategies for a number of important emerging and reemerging infectious diseases and syndromes. They highlight the importance of disease surveillance and timely response as the best way to ensure that these diseases do not cause severe morbidity and mortality when and where they occur and to reduce the likelihood of international spread. The chapters also identify research priorities and emphasize the need for interdisciplinary collaboration in detecting and addressing emerging microbial threats.

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PREFACE

Despite progress in the prevention and control of infectious diseases during the past several decades, the early years of the 21st century provide continued evidence of the persistence and tenacity of infectious disease threats. The interplay of rapid globalization, demographic shifts, ecologic changes, and unprecedented movement of people and goods, while offering increased benefits in many arenas, also yields unexpected risks to health—often with attendant social and economic repercussions. The emergence and rapid global spread of severe acute respiratory syndrome (SARS), the widespread geographic diffusion of West Nile virus since its introduction into the Western Hemisphere and that of chikungunya virus from East Africa to islands in the Indian Ocean to India and then to Italy, and the stepped-up preparations for a seemingly imminent influenza pandemic provide dramatic evidence of the continued ability of microbes to emerge, spread, adapt, and challenge the global community.

Since 1995, the program committees of the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) and the Infectious Diseases Society of America (IDSA) have organized sessions on new and emerging pathogens during ICAAC and the IDSA annual meetings. These sessions are designed to address the spectrum of new and emerging bacteria, viruses, fungi, and parasites of recognized or potential scientific and public health importance, with discussions of strategies for their prevention and control. The chapters in *Emerging Infections 8* are derived from recent sessions and focus on a range of infections that pose challenges for the clinical, laboratory, research, and public health communities. Some of these are newly recognized diseases, whereas others are previously known pathogens presenting new challenges. Some are described as domestic threats, whereas others affect populations elsewhere. However, as has been clearly demonstrated, infectious agents know no borders: every local threat is potentially a global threat.

Our experiences in responding to the outbreaks of the recent past, many of which are of zoonotic origin, provide important lessons for the future and highlight the importance of the One Health Initiative, which calls for closer collaboration between the medical and veterinary communities. Most importantly, a global threat requires a coordinated, interdisciplinary global response. In today's world, detection and control of infectious diseases call for a wide-ranging and multifaceted international approach that includes strong leadership and political will; a robust network for global disease detection, monitoring, containment, and control; and cooperation, collaboration, and seamless communication among nations and leaders. The recently revised International Health Regulations, which were promulgated by the World Health Organization in 2005 and became effective on 15 June 2007, provide a global framework for addressing these threats. Because weakened public

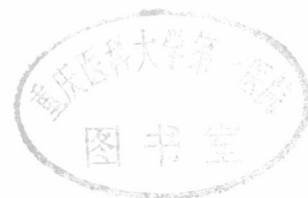
health systems and health services in many areas of the world pose threats to all, investments in national public health institutions and systems, health services, and response capacity, as well as workforce development, can yield substantial returns for the health and security of the global community. Finally, in addition to the necessity of managing the immediate and specific risks and vulnerabilities posed by infectious diseases, there is a critical need to tackle the underlying factors that contribute to disease emergence and spread; key among these are poverty, social inequities, malnutrition, and lack of clean water and adequate sanitation.

Future infectious disease challenges are difficult to predict but certainly include continued problems with antimicrobial-resistant infections, diarrheal diseases, and influenza and other respiratory diseases, as well as continued and new threats for immunocompromised populations. Additional links between chronic diseases and infectious agents will likely be discovered, providing new opportunities for disease prevention and treatment. In addition to preparing for naturally occurring infectious disease outbreaks, we will continue to strengthen our ability to detect and respond to potential acts of bioterrorism. Publication of this volume, the eighth in the *Emerging Infections* series, coincides with the 2008 joint ICAAC-IDSA meeting. We hope that the contents will serve as a valuable source of current information for those responsible for these and other microbial threats to global health and security.

W. Michael Scheld
Scott M. Hammer
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Chapter 1

Novel Non-SARS Coronaviruses

Larry J. Anderson and Lia M. Haynes

Until 2003, because the only two coronaviruses (CoVs) known to infect humans, 229E and OC43, were associated with the common cold, CoVs were thought to not cause serious disease in humans. In 2003, the outbreak of severe acute respiratory syndrome (SARS) changed this perspective on human CoV disease. SARS was shown to be caused by a novel CoV, SARS-CoV (18, 50, 76). The discovery of SARS-CoV and the recognition that CoVs can cause serious disease generated renewed interest in efforts to detect CoVs, understand the diseases they cause, and treat and prevent infections. This renewed interest plus availability of new molecular tools to detect novel viruses have led to discovery of a number of new CoVs, including ones from bats and humans (16, 23, 58, 62, 79, 93, 97, 103, 104). It is likely that other novel CoVs will be detected in the future. These novel CoVs as well as other novel viruses present clinicians, epidemiologists, and laboratory investigators with the challenge and opportunity to determine what diseases they cause. The non-SARS novel human CoVs identified to date appear to cause illness similar to that of the previously described human CoVs, 229E and OC43.

The first human CoVs (HCoVs) were isolated in the 1960s and noted to be morphologically similar to avian infectious bronchitis virus, mouse hepatitis virus, and transmissible gastroenteritis virus of pigs isolated in the 1930s and 1940s (4, 10, 17). The electron microscopic features of these viruses, i.e., circular structures of 100 to 160 nm with surface spikes, were considered crown-like and led to their being named coronavirus (Fig. 1). Subsequently, viruses with similar electron microscopic features have been detected in a wide range of animals, birds, and humans. Their genome organization and replication strategies are similar, and these viruses have been placed in the *Coronavirus* genus in the family *Coronaviridae* (88). Members of the *Coronavirus* genus tend to cause species-specific infections and are associated with a wide range of diseases, including respiratory, gastrointestinal, liver, neurologic, and fetal diseases in their respective host species (Table 1).

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