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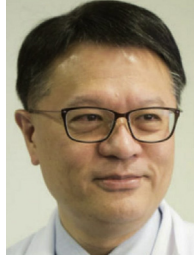


## Preface

# Emerging and Reemerging Infectious Diseases: Global Overview



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## BACKGROUND

New emerging and reemerging infectious disease outbreaks have continued to cause much human suffering and loss of life worldwide. During the past 2 decades, several landmark events in the field of infectious diseases with epidemic potential have occurred. The SARS (severe acute respiratory syndrome) pandemic (2002–2004), the Ebola virus disease (EVD) outbreak in West Africa (2013–2016), the cholera outbreak in Yemen (2015–2018), the Zika virus in the Americas and southeast Asia (2016–2018), Lassa fever (LF) in Nigeria (2018), diphtheria in Venezuela (2016–2017) and in Yemen (2017–2018), Yellow fever in Latin America and Africa (2016–2018), and Nipah virus in India and South Asia (2017–2018). The global media and World Health Organization (WHO) attention on Zika virus transmission at the 2016 Rio Olympic Games and the 2015 Ebola virus outbreak in West Africa had diverted the attention of global public health authorities from other lethal infectious diseases with epidemic potential. More recently, there has been growing concern of the increasing threat to global health security posed by a range of reemerging and emerging infectious diseases ([Box 1](#)) and the globalization of antibiotic-resistant bacterial infections.<sup>1</sup>

## INTRODUCTION TO INFECTIOUS DISEASE CLINICS OF NORTH AMERICA SERIES ARTICLES

### *Novel Coronavirus Infections of Humans*

Two new lethal zoonotic coronaviruses of humans with epidemic potential have emerged in the past 17 years. A novel  $\beta$  coronavirus, severe acute respiratory

Box 1

List of priority infectious diseases that threaten global health security

*Viral infections*

- Middle East respiratory syndrome<sup>a</sup>
- Severe acute respiratory syndrome<sup>a</sup>
- Pandemic influenza
- Marburg<sup>a</sup>
- Ebola<sup>a</sup>
- Lassa fever<sup>a</sup>
- Viral hemorrhagic fevers (including Crimean-Congo hemorrhagic fever<sup>a</sup>)
- Rift Valley fever<sup>a</sup>
- West Nile fever
- Dengue
- Polio (wild-type polio virus)
- Zika<sup>a</sup>
- Nipah and henipavirus diseases<sup>a</sup>
- Chikungunya<sup>a</sup>
- Measles
- Yellow fever
- Viral hepatitis

*Bacterial infections*

- Tuberculosis<sup>a</sup>
- Invasive meningococcal disease
- Invasive pneumococcal disease
- Drug-resistant bacterial, viral, and protozoal infections
- Cholera
- Typhoid
- Diphtheria
- Pertussis (whooping cough)

*Other*

- Drug-resistant malaria
- Antiretroviral-resistant human immunodeficiency virus/AIDS

<sup>a</sup> WHO Blueprint priority disease.

syndrome coronavirus emerged in November 2002 as a lethal zoonotic human pathogen in China and rapidly spread worldwide, disappearing in 2004, never to be seen again.<sup>2</sup> The Middle East Respiratory Syndrome coronavirus (MERS-CoV)<sup>3</sup> was first identified in 2012 in a lung sample of a 60-year-old patient who had died of respiratory and multiorgan failure in Jeddah, Saudi Arabia. Since then, MERS-CoV has remained on the radar of global public health authorities

because of recurrent nosocomial and community outbreaks, and its association with severe disease and high mortalities. From June 1 to July 31, 2015, MERS-CoV caused the largest outbreak outside of the Arabian Peninsula, occurring in the Republic of Korea and resulting in 186 confirmed MERS cases with 38 deaths. This occurred when a Korean traveler returning from a trip to Qatar, UAE, Saudi Arabia, and Bahrain became ill with a respiratory illness and visited several hospitals in Seoul before finally being diagnosed as having MERS-CoV infection. This outbreak clearly illustrated the epidemic potential of MERS-CoV, spreading from person to person. MERS-CoV continues to circulate in the Middle East and causes intermittent community and hospital outbreaks. As of July 2019, 2458 cases of laboratory-confirmed MERS-CoV cases (848 deaths, 34% mortality) were reported to the WHO.

### ***Influenza Viruses***

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Human infections due to highly pathogenic avian influenza A(H5N1) were initially detected in Hong Kong in 1997 before spreading to other continents, with a case fatality rate close to 60%. Influenza A(H1N1)pdm09 virus emerged and led to a pandemic in 2009 and has remained a common circulating strain. Human infections with the novel avian influenza A(H7N9) virus emerged in China in March 2013, whereas sporadic human cases of avian A(H5N6), A(H10N8) and A(H6N1) have been increasingly detected since 1997.<sup>4</sup> An outbreak of a novel H7N9 virus caused zoonotic disease in eastern China in the early spring of 2013. Six epidemics of human cases of H7N9 virus infection with 1564 laboratory-confirmed cases and 612 deaths occurred in China through September 2017, typically during the fall, winter, and spring months, including a large fifth epidemic during 2016 to 2017. As of May 2019, 1568 laboratory-confirmed H7N9 virus infections acquired in China had occurred since 2013. At least 10 human cases of infection with avian influenza A viruses acquired in China have traveled overseas and were diagnosed elsewhere.

### ***Zoonotic Viral Infections***

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EVD has focused global media attention ever since its first discovery due to its lethal nature and outbreak potential.<sup>5</sup> The first human case of EVD was described in 1976 near the Ebola River in the Democratic Republic of Congo (DRC), and the first outbreak of EVD affected 284 people, with a mortality of 53%. This was followed a few months later by the second outbreak of EVD in Yambuku, Zaire (now DRC). Until 2013, EVD outbreaks consisted of small numbers of cases that were contained by basic public health and containment measures. The largest EVD epidemic occurred in West Africa between 2013 and 2016, and detection of EVD cases in the United Kingdom, Sardinia, Spain, and the United States focused global attention on the epidemic. There is an ongoing EVD epidemic in the DRC. The first human case of LF was discovered in 1969 in Nigeria. Fifty years after its first discovery, LF outbreaks continue in West Africa. Annually, an estimated 300,000 to 500,000 cases of LF occur in West Africa with up to 5 to 10,000 deaths.<sup>6</sup> Travel-associated LF cases outside of West Africa have been recorded in the United States, Canada, United Kingdom, Netherlands, Israel, Sweden, and Germany.

Viral hemorrhagic fever can be caused by zoonotic viruses other than Ebola and LF viruses.<sup>7</sup> Viral hemorrhagic fevers represent a group of diseases caused by enveloped single-stranded RNA viruses belonging to 6 taxonomic families: Filoviruses (Ebola and Marburg); Arenaviruses (Lassa and other Old World arenaviruses and New World arenaviruses); Hantaviruses, Nairoviruses,

and Phenuiviruses (Congo-Crimean hemorrhagic fever, Rift Valley fever, Huaiyangshan virus, and Hantavirus); and Flaviviruses (Dengue, Yellow fever, Omsk hemorrhagic fever, Kyasanur Forest disease, and Alkhumra viruses). Chikungunya (CHIK) was first described in 1952 in southern Tanzania.<sup>8</sup> It is a disabling and debilitating zoonotic disease of humans caused by the Chikungunya virus (CHIKV), which is transmitted by infected *Aedes* spp mosquitoes, which sustain sylvatic and human rural and urban CHIK cycles. The past 5 years has witnessed an alarming global increase and spread of CHIKV to more than 100 countries across Asia, Europe, Africa, and the Americas. The virus is maintained in a complex sylvatic and rural cycle, progressing to an urban cycle every 5 to 20 years, causing global pandemics. Recently, the Indian Ocean and Indian epidemic CHIKV strains have emerged independently from the mainland of East Africa. This Indian Ocean Lineage caused repeated outbreaks from 2005 to 2014.

Previously thought to be rare and self-limiting diseases, monkeypox has not attracted much attention since its discovery 70 years ago.<sup>9</sup> More recently, monkeypox is being recognized as an increasing public health threat, particularly in regions in West Africa, where there is close interaction between humans and wild animal reservoirs. Global concern has been raised about its emergence as well as the resemblance of its clinical presentation to that of smallpox, a deadly disease globally eradicated by vaccination 40 years ago. During outbreaks, it has been challenging to clinically distinguish monkeypox from chickenpox, an unrelated herpesvirus infection. Outbreaks of buffalopox have occurred with multiple human cases in India. Similarly, during outbreaks of vaccinia virus infection in cattle in Brazil, there is documented evidence of human infections.

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### **Viral Hepatitis**

Viral hepatitis affects hundreds of millions of people worldwide.<sup>10</sup> Five biologically unrelated hepatotropic viruses cause most of the global burden of viral hepatitis: hepatitis A virus, hepatitis B virus (HBV), hepatitis C viruses (HCV), hepatitis D (delta) virus (HDV), and hepatitis E viruses (HEV). A large proportion of deaths from viral hepatitis is due to hepatitis B and hepatitis C. Globally, an estimated 257 million people were living with HBV and 71 million people were living with HCV. In 2017, 1.4 million people died of the consequences of viral hepatitis infection, and 90% of this burden was due to cirrhosis and hepatocellular carcinoma, which are consequences of chronic hepatitis B and chronic hepatitis C. HBV, HCV, HDV, and occasionally HEV, can also produce chronic infection.

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### **Antibiotic-Resistant Bacterial Infections**

The global spread of antibiotic-resistant pathogens now threatens global health security and is a priority global public health issue. Multidrug-resistant tuberculosis (MDR-TB) affects more than half a million people worldwide, causing significant morbidity and mortality. In 2018, there were an estimated 558,000 new MDR-TB cases globally, and only a fraction of them were diagnosed. Of concern is that the number of MDR-TB cases continues to increase every year. Recent advances in rapid point-of-care diagnostics and introduction of all oral and shorter treatment regimens provide hope for improving treatment outcomes.<sup>11</sup>

*Streptococcus pneumoniae*, *Mycoplasma pneumoniae*, *Staphylococcus aureus*, *Legionella pneumophila*, and Enterobacteriaceae are common pathogens causing community-acquired pneumonia (CAP) globally. *Klebsiella pneumoniae*, *Burkholderia pseudomallei*, and *Acinetobacter baumannii* are also important causes

of CAP in the Asia Pacific regions. The prevalence of antimicrobial resistance in *S pneumoniae* and *M pneumoniae* has been documented over the years, impacting the need for more prudent use of antibiotics. Antimicrobial resistance associated with the common bacterial infections causing CAP and the known mechanisms of resistance are reviewed by Margaret and Jeffery.<sup>12</sup>

Enteric infectious diseases cause an estimated 1.7 million deaths annually, the highest burden being borne by developing countries. Antibiotic-resistant bacterial enteric infections<sup>13</sup> have been reported from across the world due to travel and a convergence of multiple risk factors, including mass gathering events, conflict zones, and displaced populations.

Despite dramatic advances in the prevention of pneumococcal and meningococcal disease worldwide, case fatality rates remain static, and vaccination programs struggle to keep up with the bacterium's ability to adapt and spread.<sup>14</sup> Preventing further resistance by improving antimicrobial stewardship is essential. Future developments are focused on the development of universal vaccines and improved diagnostic tools rather than novel anti-infectives.

### ***Opportunistic Infections in Transplant Recipients***

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Organ transplants are routinely performed worldwide. Worldwide, more than 120,000 estimated solid organ transplants are performed, with kidney, liver, heart, and lung being the top four. Despite proactive implementation of prevention and management guidelines by organ transplantation units, the threat of opportunistic known and novel infections is ever present. Advances in molecular microbiology are enabling diagnosis of an increasing number of donor and community-acquired pathogens in transplant recipients.<sup>15</sup>

## **SUMMARY**

This issue of *Infectious Disease Clinics of North America* on “Emerging and Reemerging Infectious Diseases” illustrates the constant threat of a range of pathogens that can present to the physician worldwide in a variety of clinical settings. It is imperative that clinicians and other health care workers worldwide have a high degree of awareness of the possibility of an infection with pathogens with outbreak potential or antibiotic resistance. This series of up-to-date articles, written by authoritative and renowned experts in their specialist areas, is aimed at a global readership of health care practitioners, infectious disease and tropical medicine internal medicine trainees, pulmonologists, microbiologists, family physicians, and public health practitioners in both western and developing countries.

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## REFERENCES

1. WHO. List of blueprint priority diseases. 2018 annual review. 2019. Available at: <https://www.who.int/blueprint/priority-diseases/en/>. Accessed August 16, 2019.
2. Hui DS, Zumla A. Severe acute respiratory syndrome (SARS)—historical, epidemiological, and clinical features. *Infect Dis Clin North Am* 2019;33(4):869–89.
3. Azhar EI, Hui DS, Memish ZA, et al. The Middle East respiratory syndrome (MERS). *Infect Dis Clin North Am* 2019;33(4):891–905.
4. Uyeki TM, Peiris M. Novel avian influenza A virus infections of humans. *Infect Dis Clin North Am* 2019;33(4):907–32.
5. Nicastrì, Kobinger G, Mboera L, et al. Ebola virus disease (EVD): epidemiology, clinical features, management and prevention. *Infect Dis Clin North Am* 2019;33(4):953–76.
6. Asogun D, Gunthner S, Akpede G, et al. Lassa fever—epidemiology, clinical features, diagnosis, management and prevention. *Infect Dis Clin North Am* 2019;33(4):933–51.
7. Iannetta M, Di Caro A, Nicastrì E, et al. Viral hemorrhagic fevers other than Ebola and Lassa. *Infect Dis Clin North Am* 2019;33(4):977–1002.
8. Vairo F, Haider N, Kock R, et al. Chikungunya—epidemiology, pathogenesis, clinical features, management and prevention. *Infect Dis Clin North Am* 2019;33(4):1003–25.
9. Petersen E, Kantele A, Koopmans M, et al. Human monkeypox—epidemiological and clinical characteristics, diagnosis and prevention. *Infect Dis Clin North Am* 2019;33(4):1027–43.
10. Lanini S, Ustianowski A, Pisapia R, et al. Viral hepatitis: aetiology, epidemiology, transmission, diagnostics, treatment and prevention. *Infect Dis Clin North Am* 2019;33(4):1045–62.
11. Tiberi S, Zumla A, Migliori GB. Multi-drug/extensively drug resistant tuberculosis. *Infect Dis Clin North Am* 2019;33(4):1063–85.
12. Margaret IP, Jeffery HO. Antibiotic resistant community-acquired bacterial pneumonia. *Infect Dis Clin North Am* 2019;33(4):1087–103.

13. Shakoor S, Platts-Mills JA, Hasan R. Antibiotic resistant enteric infections. *Infect Dis Clin North Am* 2019;33(4):1105–23.
14. Fitzgerald D, Waterer GW. Invasive pneumococcal and meningococcal disease. *Infect Dis Clin North Am* 2019;33(4):1125–41.
15. Kumar R, Ison M. Opportunistic infections in transplant patient. *Infect Dis Clin North Am* 2019;33(4):1143–57.