zoonotic diseases

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Editorial

Zoonotic Disease Threats: Are We Prepared?

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The coronavirus disease 2019 (COVID-19) pandemic caused great damage not only in terms of morbidity and mortality, but also intense social, economic, institutional and political disruptions, and costs that upended and challenged assumptions about our preparedness to deal with such global infectious disease threats. COVID-19 is an established, undoubtedly for the long term, evolving infectious disease threat that seems for many individuals to have become another aspect of the background noise of daily life. At five years after emergence of COVID-19, it seems that less information is now publicly available in a widely broadcast and timely manner, noticeably in the United States, regarding numbers and trends of cases, mortality, changing patterns of virus variants, and appropriate measures to prevent infection or other emerging zoonotic infectious disease threats on the horizon. Is this simply a matter of pandemic disease information fatigue; does it represent political decisions during a time of cultural division and social controversy regarding threats posed; and/or is there a lack of public confidence in public health agencies, vaccines, therapeutics, and increased skepticism of science by a significant portion of the population? No matter the reason for this decrease in information, it is not a matter of if, but rather a matter of when the next significant, potentially pandemic, zoonotic infectious disease threat will occur. Are we prepared with the expertise and tools needed for a timely and effective response? That is an open question with variations in preparedness around the world; however, the overall answer is likely no. There are essential elements that need to be in place to address the public health risks posed by established, resurging, and emerging zoonotic infectious diseases. Achieving preparedness is essential now.

The greatest source of zoonotic pandemic risk is virus spillover to humans from other animal species [1]. Highly pathogenic avian influenza (HPAI) H5N1 is an increasingly significant global public health threat with clear pandemic potential [2–4]. Influenza A virus H5N1 became established in Southeast Asia and has initiated infections from 2003 to 2019 that have resurged and evolved into the current panzootic wave of infections involving 26 countries and over 48 mammalian species that encompass both more individual animals and a greater geographic area [2,3]. The current outbreak of HPAI H5N1 clade 2.3.4.4b present in Europe, Africa, Asia, and the Middle East in 2020 spread to the western hemisphere by 2022, resulting in the largest recorded wild bird outbreak [5,6].

Resurgent HPAI H5N1 clade 2.2.4.4b spread rapidly around the world among birds, resulting in poultry outbreaks and infections that spilled over to multiple mammalian species, including commercially raised mink [7], marine mammals [8], and dairy cattle [9]. Experimental infection of swine with bird-derived HPAI H5N1 clade 2.3.4.4b resulted in the replication of all strains in the lungs with pathogenesis consistent with influenza A infection [10]. Significantly, nasal cavity infection and transmission were only evident with mammalian isolates of the virus [10]. That situation has changed. On 3 November 2024, the Centers for Disease Control and Prevention reported the first H5N1 bird flu naturally occurring infection of swine in the United States (https://www.cdc.gov/bird-flu/

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spotlights/h5n1-response-11012024.html, accessed on 15 December 2024). The infection of swine is significant, since swine are considered an optimal intermediary for avian influenza virus adaptation to mammals prior to acquiring mutations essential for human-to-human transmission [11]. More swine-to-human influenza infections occurred in the United States since 2011 than in any other country [12]. Multiple mammalian species adaptations now occurring with HPAI H5N1 increase the likelihood of different zoonotic pathways to a pandemic [2].

During the period from 2003 to mid-2023, the World Health Organization documented 878 human infections with HPAI H5N1 with a mortality rate of 52.2 percent [6]. Infections among dairy farm workers in North America are believed to represent the first mammalian species (cattle) to human transmission of HPAI H5N1 [9]. Cases arising among workers exposed to infected dairy cattle have been predominantly mild [9], whilst contact with infected wildlife resulted in human infections on multiple continents that caused diseases ranging from mild to severe to fatal pneumonia [4,13]. Recently, it has been unclear how a critically ill adolescent in British Columbia, Canada, and a child in California, USA, became infected with H5N1, when there was no apparent link to infected poultry, cattle, or wildlife [14]. Adding to the concern about human transmission is the increased incidence of detection of H5 virus in California wastewater samples reported by the Centers for Disease Control and Prevention National Wastewater Surveillance System for the period of 1–7 December 2024 (https://www.cdc.gov/nwss/rv/wwd-h5.html, accessed on 15 December 2024). The northern hemisphere is currently in flu season. Co-infections with seasonal influenza and HPAI H5N1 would increase the potential for genetic reassortment and the emergence of human transmission capability. In aggregate, these events represent a trajectory that is highly concerning.

The prevention of zoonotic infectious diseases should be prioritized through the development of government policies, coordination and collaboration across relevant agencies, and the utilization of individuals with appropriate expertise in relevant disciplines [15]. These priorities require a One Health approach necessary for pandemic prevention at the interface of interactions among wildlife, livestock, and humans to prevent pathogen spillover [16]. In response in part to the COVID-19 pandemic experiences, national initiatives were undertaken to assess current capabilities, gaps, and actions needed to respond to future transboundary infectious disease threats. The information gained resulted in strategy and implementation plans that include the United Kingdom Health Security Agency (UKHSA) Strategic Plan 2023–2026 (https://www.gov.uk/government/publications/ukhsa-strategic-plan-2023-to-2026, accessed on 15 December 2024) and the 2022 United States National Biodefense Strategy and Implementation Plan for Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security (https://www.whitehouse.gov/wp-content/uploads/2022/10/National-Biodefense-Strategy-and-Implementation-Plan-Final.pdf, accessed on 15 December 2024). What is needed is a continuous process of coordinated international, national, and regional assessment of policies, organization capabilities, resources, networks, strategies, and needs in a dynamic environment of ongoing and emerging zoonotic infectious disease and other biological threats.

Since zoonotic infectious diseases are not restricted by international borders, it is important to leverage the experience and resources of the existing global networks of the World Health Organization (WHO) and the World Organization for Animal Health (OIE), and to create new flexible, responsive intergovernmental networks of collaboration. The success of such networks depends upon competent, experienced leadership, effective management practices coordinating multiple agencies with diverse operational cultures, development of an international framework to provide stable core funding, shared technical expertise, standardized methods for field and laboratory studies/analyses, uniform data collection and analysis, timely reporting, readily accessible data, and the transparency of operations.

There are questions to consider regarding the existing structure and ongoing operations of international and national multiagency programs. What is currently being done to actively or passively monitor existing or potential human and veterinary disease threats? What is the nature of existing surveillance networks and the range of tools being employed? To what degree is there sampling and sequencing of clinical isolates of recognized pathogens and novel microbes? How are data sharing and communications standardized and conducted across the hierarchy of agencies (international, national, local), public health officials, care providers, other relevant stakeholders, and the public? What are the existing criteria used to determine what constitutes a threat as well as the initial and evolving magnitude of a threat? Who is responsible for determining the nature and course of integrated, actionable responses at different stages of an emerging infectious disease or actual pandemic threat? Who is responsible for determining and managing the appropriate coordinated responses to the outbreak of a zoonotic disease threat at the local, state, and national levels? Are there uniform collection, analysis, and shared reporting mechanisms that function in real time?

Laboratories should be designated and equipped with core technological capabilities and relevant infrastructure as a network of interconnected centers strategically positioned at multiple locations around the world. What are some of the key considerations in developing such a network? (1) Establish regional surveillance networks for disease-causing agents in humans and other vertebrate animal species. (2) Realizing that zoonotic infectious diseases can occur in many forms, it is important to maintain diverse, adaptable platforms that incorporate genomics (next-generation sequencing), proteomics, and bioinformatics analyses for microbe characterization, the development of diagnostic tests, and screening arrays for antimicrobial and antiviral agent activity determinations. (3) Physical infrastructure should include high-security BSL-3 and BSL-4 laboratories as well as animal resource facilities at the appropriate biosafety levels. At least one site should have a BSL-3 insectary with an ability to implement a BSL-4 insectary if needed. (4) Have in place timely communications policies and practices that are accurate, understandable by target audiences (politicians, the public), and transparent. (5) In addition to core scientific staff, establish a network of specialists across diverse disciplines that can be consulted and actively engaged in response efforts on an ad hoc basis.

A communication-related consideration that is often overlooked, but is essential to success in addressing a public health threat, is the scientific literacy of decision makers and the public. This is a challenging topic for multiple reasons. Increasing public mistrust and distrust of science, scientists, and facts are evident in Western society, particularly since the start of the COVID-19 pandemic. Large amounts of information about the pathogen, diagnosis, clinical course, treatments, and control procedures were emerging rapidly and resulting in changing response strategies, as is expected to occur when considering new discoveries. Sorting out the truth from misinformation and disinformation can be overwhelming and confusing, particularly when large amounts of all three are emerging rapidly. Adding to the confusion is the increasing complexity and rapid development of the scientific principles underpinning the responses to infectious disease threats. The novel technology platform of RNA vaccines is one example. Topics such as this often need to be demystified for non-specialist scientists as well as the public, whose scientific knowledge might be limited and anachronistic. Additional factors contributing to this situation include social division, political polarization, mistrust in institutions, and as stated—the continuous flow of conflicting information.

What are the roles of *Zoonotic Diseases* (ISSN 2813-0227) and companion biomedical journals in this era of rapid change? Traditionally, their role has largely focused on the dissemination of new information ranging from basic science studies and clinical research to providing up-to-date, comprehensive reviews of existing knowledge, and perspectives pieces. Those critical roles are foundational to *Zoonotic Diseases* as an advanced global research forum. The scope and aims of *Zoonotic Diseases* are deliberately broad in an attempt to capture and offer new insight into any aspects that impact this evolving and complex field, including public policy and factors that influence zoonotic diseases in a changing world—climate, technology, economics, and society. *Zoonotic Diseases* provides a timely peer-review process to first decision and rapid publication after acceptance. We encourage you to submit your manuscripts for consideration for publication. Consider contributing manuscripts to our shared Special Issues with other MDPI journals: Zoonotic Vector-Borne Diseases of Companion Animals (participating journals are *Animals*, *Pathogens*, *Veterinary Sciences*, *Zoonotic Diseases*) and Animal Diseases in Agricultural Production Systems (participating journals are *Agriculture*, *Animals*, *Veterinary Sciences*, *Antibiotics*, *Zoonotic Diseases*). We welcome topic suggestions for Special Issues from both our Editorial Board Members and the community of our readers.

As *Zoonotic Diseases* enters the fifth year of publication, the valuable contributions of the global community of Editorial Board Members are recognized for their commitments and contributions to the development of the journal, for reviewing manuscripts, and for their advancement of zoonotic diseases research. I recognize the critically important role and excellent contributions of the Managing Editor and the MDPI staff to the continued growth and success of *Zoonotic Diseases*.

The Editorial Office and Editorial Board look forward to receiving your manuscript submissions and to working with you to disseminate new knowledge and perspectives about zoonoses.

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