Zoonotic Diseases in Animal Agriculture and Beyond:
A One Health Perspective

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On the Front Cover:

This prehistoric rock painting from Tassili N'Ajjer, Algeria, was created during the Pastoral Period (from approximately 7,200 – 3,000 BP). It depicts the early domestication of animals, advent of agriculture, and the changing relationship between humans and animal diseases. The first group of zoonotic diseases emerged from this same era approximately 8,000–10,000 years ago. A second infectious disease era coincided with the evolution of the industrial age and was characterized by a decline in infectious diseases and the rise of chronic and degenerative diseases. Approximately three decades ago, a new infectious disease era was created with the resurgence of human infectious diseases and pandemics, the majority of which were, and are, zoonoses. We are currently living in the midst of this new era which was created by anthropogenic factors, population growth, and our unprecedented global interconnectedness. Photo courtesy of Dmitry Pichugin/Shutterstock.

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Contents

Figures

Tables

Foreword

While zoonotic diseases have been around for tens of thousands of years, the COVID-19 pandemic brought to public attention the increased interest of zoonotic diseases. News of the COVID-19 pandemic along with the recent Ebola virus outbreak in West Africa, sent the world searching for what zoonosis is, with Google searches for zoonosis doubling. Attention turned to animal agriculture as potential source of the next pandemic. The proposal to produce this paper was created within our Animal Agriculture and Environmental Issues work group as response.

Rather than focusing purely on zoonotic diseases, we wanted to highlight the importance of One Health. One Health recognizes that the health of people, animals, and the planet are connected and dependent upon each other. This tripartite is essential to the health and success as all.

More than a dozen expert authors, led by Dr. Lonnie King, came together to bring this proposal into a full publication. This publication is the result of many months of writing, editing, revising, and reviewing, not only by the authors, but also CAST staff and a group of peer reviewers. We thank each member of the task force for their dedication to this paper; it is not possible without an enthusiastic team of volunteers.

We hope that this publication highlights the importance of One Health in the context of animal agriculture and that our readers find value in it. Please share and spread word about this publication so we can spread further awareness on this important topic.

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Interpretive Summary

We live in a complex, interconnected, and fast-paced world that has created the conditions for a new epidemiologic era in which infectious diseases—especially zoonotic—have become an existential threat to our lives and well-being. For the first time in the history of our planet, driving forces, primarily generated by humans, have changed the earth's trajectory leading to declining natural systems and significant challenges to our health.

This publication focuses on a group of vignettes to help understand zoonotic diseases, the anthropogenic factors accelerating their emergence, and the consequences of these events. While human activities and behavior are mostly responsible for creating this new era, the world struggles to prepare, change behavior, and rethink strategies to effectively address the inevitability of more frequent occurrences and severity of disease outbreaks and pandemics. Although we know and have experienced the cost of failure, past disease outbreaks seem to be quickly lost from our collective memories and new innovative interventions have not been imagined or adopted. This publication highlights examples that challenge our traditional actions and thinking and emphasize the need to adopt new approaches to prevent or ameliorate zoonotic diseases. The consensus of the experts contributing to this publication is that One Health should be embraced to achieve these results.

The holistic, integrated, and collaborative strategies that characterize One Health make it an ideal framework to foster the convergence of diverse disciplines to help ensure new innovations and discoveries. Zoonotic diseases have become serious and vexing societal problems that cannot be solved by any single discipline or domain. One Health brings together experts and thinking in biomedicine and health but goes much further to include animal, environmental, climate sciences, social and behavior sciences, agriculture, business, engineering, and many more fields. It also promotes synergistic relationships among diverse communities and cultures that broaden the context of public health and span diverse boundaries to share insights and knowledge. Also underscored is the special opportunity for agriculture which has unique vulnerabilities, to further engage in One Health and expand its societal interests and impact.

Because zoonoses emerge from the dynamic confluence of people, animals and their products, environment, agriculture, wildlife, vectors, food, water, antimicrobial use, and changing ecosystems, experts and organizations must rethink and reimagine ways to integrate and coordinate their actions. These include adopting system thinking, committing new investments in prevention, improving public and animal health infrastructures and associated surveillance systems globally, expanding human capacity and skills and merging communities and resources across the domains of One Health. The growing costs and societal disruptions of outbreaks and pandemics demand that zoonoses be part of our national security planning and deserve commensurate investments in preparedness, prevention, research, and resilience. This publication highlights the necessity to fundamentally rethink and reestablish new relationships among institutions, organizations, and countries and especially between humanity and our natural systems worldwide.

Introduction: "Whereof What's Past is Prologue…"

"Whereof what's past is prologue," holds a well-known quote from Shakespeare's *The Tempest*. History not only sets the context for the present—through a prologue defined by preceding events—but it also sets the stage for us to influence our future. In today's world of escalating zoonotic diseases, infectious diseases that spread between animals and people, reflecting on the past as prologue offers an apt backdrop for better understanding the present and planning for the future

History is replete with stories and examples of zoonoses. In seminal events that occurred 10,000 years ago, the advent of agriculture and the domestication of animals enabled human communities to become more stable and live closer together. Since those early days, this new interface of humans, animals, and our shared environment has helped to introduce a new era of emerging and re-emerging zoonotic diseases, driven by a set of forces that have created a perfect microbial storm today. Zoonotic diseases now include numerous food-borne, waterborne, vector-borne, and parasitic infections, as well as diseases caused by viruses, *Rickettsia*, prions, fungi, and antimicrobial-resistant bacteria. Over the last few decades, approximately 75% of new emerging diseases infecting humans have come from or through animal populations or their products (Woolhouse and Gowtege-Squeria 2005), with an estimated average of two significant spillover events occurring each year over the last century (Dobson et al. 2020). Since the beginning of this century alone, the world has already experienced three major zoonotic coronavirus epidemics.

For the first time in the history of our planet, factors and driving forces predominantly created by humans are changing the earth's trajectory and leading to disruptions of our natural systems. Such anthropogenic factors and drivers that have directly shaped our current context include rapid growth in human and animal populations, destruction of habitats, changing land use and disruption of numerous ecosystems, loss of biodiversity, expansion of global travel and trade, urbanization, expansion and intensification of agricultural practices, globalization and diversification of the pet trade, globalization of the food system, advances in technology, and poverty. Other factors include the unique ability of microbes to adapt and evolve and infect multiple hosts and the lack of the political will to properly address these growing threats. (Smolinski, Hamburg, and Lederberg 2003). Ecological pressures and disruptions—coupled with the on-going expansion and growth of human populations—continue to bring animal pathways closer to people. As animals and

humans coexist in increasingly closer proximity, advances in technology combined with human behavior have enabled zoonotic diseases to spread more rapidly and with a wider global distribution. Humans have constantly eroded and disrupted key ecosystems that impact wildlife and create potential reservoirs and carriers of zoonotic diseases. Over the last two decades, in the United States alone, vector-borne diseases from ticks and mosquitoes have more than doubled and are spreading into new geographic settings. We are now aware of the substantial influence of climate on health including infectious diseases and the potential expansion and spread of disease vectors. Thus, climate change is another major factor that will likely drive cross-species disease transmission and potentially change the entire mammalian virome and the natural history of many bacteria and fungi. Moreover, the potential for establishment and movement of zoonoses has been accelerated and intensified both by our global interconnectedness and by the speed with which microbes, people, animals, and animal products can now travel and interact. For instance, microbes can now circumvent the globe faster than most of their incubation periods. Together, these factors contribute to the probability of increasing numbers of future spillover events and epidemics. The future is further complicated given that we have only discovered a small fraction of all zoonotic pathogens that can threaten people.

Our prologue has been written by these driving forces—mostly caused by human activities and behaviors—that have created an unprecedented context that threatens the health of people, animals, plants, and the environment. We now have the chance to take swift counteractions to shape a future where these threats and actions are minimized.

In 2003, the U.S. experienced concurrent cases of Severe Acute Respiratory Syndrome (SARS), Monkeypox, and West Nile Virus. None of these three zoonotic diseases had ever previously been found in the Western Hemisphere. Two decades later and considering our prologue, we again experience a global Monkeypox pandemic, a new corona virus—Severe Acute Respiratory Syndrome coronavirus-2 (SARS-CoV-2) and a rapid expansion of vector-borne diseases. The past is indeed prologue, and our zoonotic disease future will continuously be shaped by the same anthropogenic factors unless and until our thinking, investments and global collaborations are changed. Without swift counteractions, our world of microbial threats and zoonoses will become substantially more probable, perilous, and consequential. Old solutions and legacy systems are no longer adequate for ad-

dressing the global threats posed by zoonoses: different approaches are urgently needed. An existing approach known as "One Health" is an effective framework that can be used to better understand these dynamic drivers and reduce the risks of zoonoses and address complex issues such as antimicrobial resistance. One Health is a collaborative, multisectoral, and transdisciplinary approach—working at the local, regional, national, and global levels—with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment. This integrated and holistic approach involves working collaboratively and concurrently to improve health across its multiple domains: humans, domestic and wild animals, plants, and the environment in which these domains are embedded. The fundamental ethos of One Health is that the health of people, animals, plants, and their shared environment are inextricably connected, such that strengthening any of those domains can improve the others.

This report is not designed to cover the vast array of zoonotic disease topics but rather to present a few short vignettes to serve as examples to help explain zoonoses, emphasize key drivers, better understand the concept of One Health, and learn from these examples with the aim of synthesizing this information, drawing relevant conclusions, and proposing effective recommendations. This report also emphasizes the role and possibilities of agriculture to adopt One Health strategies and help reduce the risks of zoonoses. By looking through the lens of agriculture, we identify the lessons learned in zoonotic disease transmission and explore how agriculture can become an effective partner, leader, and positive influence. The past is prologue, but the arc of the future can still be bent toward new outcomes to create a safer world while concurrently improving the health of people, animals, plants, and our environment.

The objectives of this report are to:
- Raise the awareness and understanding of zoonotic diseases and the driving forces creating and impacting them;
- Introduce the concept of One Health and help to explain why it is an essential approach to address zoonoses and related health threats (e.g., antimicrobial resistance);
- Advocate for a collective, multisectoral, transdisciplinary approach to combat zoonoses with a special emphasis on the opportunity and need to involve agriculture as one of several relevant sectors; and
- Offer recommendations to advance interventions to reduce or eliminate zoonotic diseases and future pandemics.

Historical Perspective of Zoonoses and One Health

Agriculture is the foundation of civilization. Approximately 10,000 years ago at the end of the Ice Age, humans domesticated plants and animals which provided a relatively stable and secure food supply. But the benefits of food security came with costs—one of which has been zoonotic diseases.

Zoonotic diseases are diseases of animals that infect humans. For example, measles diverged from rinderpest, a deadly viral disease of cloven-hoofed livestock, particularly cattle and buffalo, around the sixth century BCE. Rinderpest means 'cattle plague' in German. The rinderpest virus might have spread into people and evolved into the measles virus because of the growth of large cities.

For centuries, the rinderpest virus devastated cattle populations, killing 95% of the herds, and resulting in widespread famine and death in human populations. In the early eighteenth century, rinderpest began killing the livestock of Pope Clement XI. He asked Dr. Giovanni Maria Lancisi, his personal physician, to stop the disease. Dr. Lancisi was familiar with the research of Dr. Bernardino Ramazzini, a physician at the University of Padua, who hypothesized that rinderpest spread by the animals' excretions, hide, and breath and not by astrology or other beliefs. Dr. Lancisi ordered that all the sick animals be slaughtered and buried in lime, and the healthy animals be kept separated from the sick. These measures stopped the disease from spreading.

Almost 50 years later, the first school of veterinary medicine was established in Lyon, France in

1761 to control rinderpest; and 163 years after that, the World Organization for Animal Health (WOAH; formerly OIE) was created to fight rinderpest. The WOAH predates the World Health Organization by almost a quarter of a century. In 2011, rinderpest was the second disease to be eradicated after smallpox, which had been declared eradicated in 1980 by the World Health Organization.

Smallpox, one of the greatest scourges to afflict humanity, appears to be a zoonotic disease, emerging around from 3,000 to 4,000 years ago in east Africa. Its emergence coincided with the introduction of camels to the region. Camels and climate change might have triggered an evolution of an ancestral virus capable of infecting a wide range of animal hosts including rodents. Rodents might have spread the virus to camels, which subsequently spread it to humans. No other virus has affected history like smallpox, which has killed millions including pharaohs and kings. Although eradicated, there is concern today that it could be used as a bioweapon and samples are now kept frozen in a few government laboratories as an everpresent threat.

Zoonotic diseases continue to afflict humanity and animal health and welfare. Environmental degradation, ecosystem destruction, and intensive livestock production can promote zoonotic disease emergence. The HIV/AIDS and Ebola pandemics originated from animals. Bats, rodents and primates are particularly important hosts for potential zoonoses. Livestock and poultry can serve as intermediate or amplifier hosts facilitating zoonotic disease spread from wildlife to people. Some examples diseases that can be amplified by livestock and poultry include Avian influenza, Nipah virus, and hantavirus. Most recently, coronaviruses have caused the SARS, Middle East Respiratory Syndrome (MERS), and COVID-19 pandemics.

How Might Zoonotic Diseases Be Better Controlled?

Veterinarians play a key role in zoonotic disease detection in wild and domestic animals. The key is to listen to them and heed their findings. For example, during an outbreak of presumed St. Louis encephalitis in New York City in 1999, Dr. Tracey McNamara, the chief veterinary pathologist at the Bronx Zoo, was concerned that she might be dealing with a novel deadly zoonotic disease. If the disease had been St. Louis encephalitis, then the birds native to North America would have been healthy because they would have been naturally immune to the disease. Instead, they were dying. While conducting necropsies, the animal equivalent of autopsies, Dr. McNamara discovered that they were dying from severe meningoencephalitis and myocarditis. She contacted the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia and told them of her findings and concerns. She offered to send them her bird pathology specimens for testing, but instead, the CDC referred her to the National Veterinary Services Laboratories in Ames, Iowa. Dr. McNamara was ultimately proven correct: West Nile virus was identified for the first time in North America.

The CDC, along with other government agencies, subsequently established the National Center for Emerging and Zoonotic Infectious Diseases with a One Health Office that recognizes the links between human, animal, and environmental health. It encourages a One Health approach with collaborative efforts between physicians, veterinarians, epi-

demiologists, laboratorians, ecologists, and many other disciplines working across sectors. But much more needs to be done across the federal government.

As it is currently configured, the federal government is primarily focused on humans and much less so on animal, environmental, and ecosystem health. In 2019, the Department of Health and

Human Services' (HHS) budget was approximately $1.3 trillion of which 90% went to the Centers for Medicare and Medicaid Services which provides health insurance for the elderly and low-income, respectively. While extremely important, health insurance programs are not involved in preventative programs such as zoonotic disease surveillance or control. Less than 1% of HHS' 2019 budget was directly involved with disease surveillance, control, and prevention such as the CDC and the Food and Drug Administration (FDA).

Other departments and agencies involved with agricultural practices, wildlife, environments, and ecosystems, which are all key drivers of zoonotic disease emergence and spread include: the Departments of Agriculture (USDA), Homeland Security, Interior, and the Environmental Protection Agency (EPA). Their combined 2021 budgets were four times smaller than that of HHS' budget. Within these other departments and agencies, their resources for disease surveillance, control, and prevention are limited. Improved coordination and increased resources across these entities, such as the creation of a national, coordinated high level One Health Task Force, would help to address the gaps in the federal government's disease control capabilities.

The COVID-19 pandemic has demonstrated that a deadly airborne zoonotic disease has the capacity to kill millions around the world and bring societies to their knees. Earth is a microbial world, and recognizing this fact is an important first step in ensuring a sustainable civilization. Integrating human, animal, environmental, and ecosystem disease surveillance using a One Health approach will be absolutely critical to controlling the next pandemic which is sure to occur.

Prioritizing Zoonoses in the United States Using a One Health Approach

The U.S. CDC, U.S. Department of the Interior (DOI), and the USDA jointly hosted a One Health Zoonotic Disease Prioritization (OHZDP) workshop for the United States in December 2017. The specific workshop goals were two-fold: (1) To use a multisectoral, One Health approach to identify and prioritize endemic and emerging zoonotic diseases of greatest national concern for the United States that should be jointly addressed by human, animal, and environmental health sectors responsible for federal zoonotic disease programs in CDC/HHS, USDA, and DOI, and (2) To develop plans for implementing and strengthening multisectoral, One Health approaches to address these diseases in the United States. Participants representing 12 agencies from multiple departments agreed on a list of priority zoonotic diseases to be jointly addressed by U.S. federal agency programs working on human, animal, and environmental health using a One Health approach. Experts from the lead federal agencies responsible for zoonotic disease programs for people, animals, and the environment determined the final prioritized list of diseases. Advisors from multiple sectors from the federal and state level provided relevant subject matter expertise to inform the zoonotic disease prioritization process and worked with voting members to develop plans to strengthen One Health zoonotic disease prevention, detection, and response in the United States.

The priority zoonotic diseases for the U.S. included a mixture of emerging and endemic zoonoses including the following: (1) zoonotic influenza viruses, (2) salmonellosis, (3) West Nile virus, (4) plague, (5) emerging coronaviruses (e.g., MERS, SARS, and others), (6) rabies, (7) brucellosis, and (8) Lyme disease. These priority diseases impact public health, animal health (including animal agriculture and subsequently the nation's food supply, wildlife health, and the health of companion animals), biodiversity conservation, and our environment, the effects of which can be worsened by climate change and urbanization.

The U.S. OHZDP workshop report summarizes the risks of each of these priority zoonoses to public health, animal health, and environmental impacts and describes current work to address these diseases across the key federal agencies. Areas identified for improved One Health collaboration in the United States for the priority zoonotic diseases include:

(1) increasing and effectively leveraging leadership engagement, (2) creating a formalized One Health coordination mechanism at the federal level, (3) developing a National One Health Strategic Plan for the United States, (4) improving knowledge and data sharing for laboratory, surveillance, and response activities, (5) improving coordination during an outbreak response, (6) strengthening joint investment for One Health and prioritized zoonotic diseases, (7) increasing education and awareness through coordinated messaging on disease prevention, and (8) identifying research gaps and needs using a One Health approach. This workshop was the first-time multiple U.S. agencies worked together to prioritize zoonotic diseases of national concern, and the list of priority zoonoses represents a renewed commitment to improved communication, collaboration, and coordination between agencies and departments to use a multisectoral, One Health approach to address these zoonotic diseases.

This workshop was a critical step towards a unique U.S. approach to One Health, ensuring that all stakeholders have a shared vision and roadmap for implementing One Health strategies for disease surveillance, response, preparedness, workforce, and prevention and control activities in their current and future areas of focus. Strong and sustainable One Health collaboration with strong leadership is essential to protect health and security in the United States. These results highlight the power of One Health discussions as emerging coronaviruses were identified as priority zoonoses before the COVID-19 pandemic.

Looking toward the future, the House Appropriations Committee Report that accompanied the 2021 Omnibus Appropriations Bill directs CDC to work with DOI, USDA, and other interagency partners to (1) develop a National One Health Framework to improve the nation's response capacity to combat the threat of zoonotic diseases and advance emergency preparedness and (2) to develop a One Health coordination mechanism at the federal level to strengthen One Health collaboration related to prevention, detection, control, and response for the prioritized zoonotic diseases and related One Health work across the federal government. The outcomes of the U.S. OHZDP combined with the ongoing work will be critical to lay a strong foundation for One Health in the United States.

Global Phenomenon

A Threat Anywhere Is a Threat Everywhere

The emergence and reemergence of infectious diseases over the last few decades is largely due to the phenomenon of globalization. The distinction between national and international public and animal health systems is no longer relevant. Disease knows no borders in our increasingly interconnected and mobile world. The disease threats and consequences to everyone is enormous. Recent data demonstrates just how interconnected the U.S. has become with the rest of the world. Each day approximately 1 million people cross our borders (Improving the CDC Quarantine Station Network's Response to Emerging Threats; Consensus Study Report; p.9, National Academies Press, Washington, DC, 2022) and over 87,000 truck, rail, and sea containers enter the U.S. In 2020, Today more than one in five food items consumed in the U.S. are imported into the U.S. In 2021, the Customs and Border Protection issued 73,917 emergency action notifications where each notification represents an interception of a prohibited/restricted plant or animal product. (CPD 2022). New microbial threats, many zoonotic, are emerging more quickly, spreading more rapidly and becoming more consequential and more difficult to combat.

From an estimated 7.7 billion people worldwide in 2019, population projections estimate that the global population could grow to around 9.7 billion by 2050, of which sub-Saharan Africa, Asia, and the U.S. account for the majority of the growth (U.N., World Population Prospects 2022; Dept. of Economics and Social Affairs, 2022). According to UNICEF, everyday more than 370,000 babies are born. Further, the 47 least developed countries are among the fastest growing economies, intensifying the strain on resources and demand for livestock production and protein supply in these areas (United Nations 2019). These trends will only continue to intensify if current practices endure, and the human population continues to expand. In 2020, the United Nations reported 281 million international migrants which does not account for the large number of pastoralists movements across borders regularly with their livestock. (McAuliffe and Triandafilldou 2021)

The food supply is no exception to this globalization. The globalization of food supply has drastically reduced food costs in the U.S. and allowed worldwide access to a multitude of nutrients year-round. Global consumption of meat proteins over the next decades is projected to increase 14% by 2030, driven largely by poultry consumption followed by beef and pork (OECDFAO 2021). Such trends are driven not only by population growth but also by socio-economic changes including rising incomes, increased urbanization, and aging populations, whereby the contribution of protein to healthy aging is increasingly recognized (Henchion et al. 2017).

The processes that permit a globalized food chain and work to meet that demand also create a "microbial perfect storm" for emerging infectious diseases. It only takes one incident or error in the value chain, anywhere in the world, to cause a global outbreak. Considering the many steps in the global food supply chain from farm to fork in addition to an estimated 10,000 zoonotic viruses in mammals alone (Carlson et al. 2019), not accounting for other types of pathogens, the risk for such an event to occur becomes increasingly high. Zoonotic spill-over and emergence of infectious agents from wet markets from wild animal consumption has also been a global concern. Thus, a microbial threat anywhere is a threat everywhere. This truism supports the notion that zoonotic diseases will continue at an accelerated rate with significant consequences. Changes are needed in our policies, investments, preparedness, response and collaborations across our public, animal, and environmental sectors.

Risky Behaviors

Another condition that has resulted from the need to meet the increasing global demand for animal sources of protein is the movement towards intensive farming practices such as confined animal feeding operations (CAFO)s. Such practices, unless very well managed and monitored, could compromise health standards, and allow ample opportunity for rapid spread of infectious diseases. Intensification of food animal production is a global phenomenon that has been increasing in many of the developing regions, particularly in Asia. The consolidation of largescale, centralized food-processing operations and broad product distribution creates additional disease threats from the food supply (Institute of Medicine 2012). Compounding this problem is the unregulated use of antimicrobials in animal feed to serve as growth promoters as well as disease prevention. These antimicrobials drive the selection of antimicrobial resistant pathogens in addition to potential chemical pollution into the environment.

Yet another risky behavior that is practiced meeting the growing demand for protein are wet markets, or densely packed open air food markets where live animals (including wildlife species or bushmeat) are usually caged and slaughtered in close proximity to the sale of other food products, generate one of the most high-risk scenarios for cross-species pathogen transmission (Peros et al 2021). Unlike the intensive system of the Unites States and developed countries, globally animals are often confined together and/or mixed closely with different species during transport and at market, thus providing more opportunity for cross-species infectious disease transmission. There is strong evidence that the three coronavirus pandemics just in this century have links to wet markets in their origin.

Post-harvest, the bundling or batching of large quantities of single ingredients or mixing of multiple ingredients of various origins can amplify the effects of a single contamination event (Institute of Medicine 2012). Estimates show that one infected beef carcass can lead to contamination of eight tons of ground beef (Nestle 2003). This is just a small selection of conditions that generate the microbial perfect storm. This could cause a very costly incident with potential outbreak and health consequences during importation of animal source food. Another important global phenomenon threatening the health of people, animals and causing environmental contamination is the growing challenge of antimicrobial resistant microbes. Jones, et al, reported that from 1950 to 2010, 335 new diseases were reported, of which, almost 21% were considered antimicrobial resistant (AMR) pathogens. It is estimated that globally, from 2000–2018 the total global consumption of antimicrobials in people increased by 46% and in people located in LMIC, there was a 76% increase. (Browne et al. 2021). The use of antimicrobials globally for all livestock in 2013 was estimated to be 131,109 tons with an estimated increase to over 200,000 tons by 2035. (Van Boeckel et al. 2015). The relationship between antimicrobial use and the development and spread of AMR has been well documented. With the unprecedented movement of people, animals and their products, AMR is rightly referred to as the quintessential One Health challenge with the transmission of AMR microbes and their genetic materials intermingling among all domains.

Breaches to Control

The perfect storm of conditions for emergence and propagation of pathogens has resulted in countless outbreaks with significant impacts both locally in the United States and globally. There are several examples of the impact that these events have had both from a health and economic perspective, some of which can be found in Table 1 (The World Bank 2017). As our world become even most closely connected economically, socially, politically, and emotionally, costs will continue to rise dramatically. The total cost of SARS-CoV-2 has been estimated at $16 trillion (Cutler and Summers 2020) and the Congressional Budget Office has estimated another $7.6 trillion loss in productivity over the next decade. These amounts were unthinkable just a few years ago.

Transboundary Diseases

Transboundary diseases are defined as highly contagious or transmissible epidemic diseases with the potential to spread across the globe and the potential to cause substantial socioeconomic public health consequences. Transboundary diseases can also refer to livestock and poultry diseases with the same characteristics. Many of the same anthropogenic factors helping to determine zoonotic disease outbreaks, are influencing the geographic distribution and spread of transboundary infections. While many of these diseases are not zoonotic, they can very much impact human and public health. Diseases such as African swine fever, foot-and-mouth Disease and avian influenza often have significant impacts on the morbidity and mortality of livestock and poultry. Even diseases like Citrus Greening Disease that was imported into the U.S., is devastating the Florida citrus industry. Animals, plants, and crops are susceptible to transboundary diseases resulting in losses to the global food system and to the livelihoods and nutritional needs of people. This is especially true for food animals in LMIC where small livestock keepers are key to local production and an important source of income to this population. Widespread transmission of these diseases can be detrimental to the economy and crippling to tourism, export markets, and supply chain disruptions. Dr. Delia Grace estimated that between 750 million and 1 billion poor livestock keepers who produce several billion head of livestock and poultry rely on this production for nutrition, income, and food security and to help alleviate poverty; yet they represent some of the world's most susceptible populations for both zoonotic and transboundary diseases.

Shifting Priorities to Address Global Microbial Threats

Surveillance

Functioning surveillance systems within sectors with data and information sharing across sectors are essential for the detection and prevention of global and domestic outbreaks and pandemics. Functioning surveillance systems within each sector, with coordinated data and information sharing between sectors, are essential. One of the largest gaps in the current surveillance regulatory framework is the reliance on global animal disease surveillance systems with limited ca-

Table 1.   Examples of the cost and burden of a few selected zoonoses

Disease	Situation	Financial Cost	Health Burden	Human-Animal Environment Interface	Source
Highly pathogenic avian influenza	January 2004–January 2009, Asia public and animal health service costs, compensation, production and revenue losses to the livestock sector; some primarily affecting smallholder producers in East Asia and imposing social impacts (livelihoods, trade opportunities, food and nutrition security and safety)	$20 billion	486 human cases with 282 deaths	Wild birds mixing with backyard poultry; agricultural intensification without sufficient biosecurity; food challenges	WHO 2015; FAO 2005
Antimicrobial resistance	Cumulative impacts by 2050	$100 trillion (up to $6.1 trillion/year in high-impact scenario)	10 million human deaths annually	Agriculture/aquaculture contribute to direct transmission of resistant strains and antimicrobial dispersion; reduced efficacy threatens both health and food production	Review on Antimicrobial Resistance; World Bank 2017a
Severe acute respiratory diseases (SARS)	November 2002–July 2003; trade and travel disrupted in China; spread to 29 countries	$41.5 billion	8,500 cases, 813 deaths	Bat-human contact facilitated disease emergence, live markets may have had an amplification role	World Bank 2012b
East coast fever	Annually for Tanzania, Zambia, Malawi, and Kenya from endemic disease; death or reduced growth and productivity	More than $200 million		Tick-borne agricultural disease (cattle, sheep, and goats); threat to livelihood, food and nutrition security	Minjauw and McLeod 2003; DFID and GalvMED 2010
Schistoso-miasis (zoonotic)	Based on estimated 14% total schistosomiasis (zoonotic and non-zoonotic) burden; heavily impacting parts of Southeast Asia, some Africa		10 million DALYs annually	Ecological changes from anthropogenic activity (damming and irrigation) create favorable habitat for vector; non-zoonotic forms can also reduce livestock productivity	Torgerson and MacPherson 2011
Top 13 neglected zoonotic diseases of importance to poor livestock keepers	Zoonotic gastrointestinal disease; leptospirosis; cysticercosis; zoonotic tuberculosis; rabies; lesihmaniasis; brucellosis; echinococcosis; toxoplasmosis; Q fever; zoonotic trypanosomosis, hepatitis E; and anthrax		2.4 billion cases and 2.2 million deaths annually	Various environmental determinants and agricultural exposures	Grace et al 2012

pacity. If country-based surveillance systems are unable to detect priority or novel pathogens circulating in their animal populations, then the United States has no way of knowing to place restrictions on imports coming from those countries. The regulatory structure described above places a significant level of trust and control in the hands of foreign governments to be able to oversee and maintain oversight at the level that meets U.S. standards. Ultimately, if the surveillance capacity in another region falters and is unable to detect an emerging threat, there is a subsequent threat to other nations. Investment in strengthening surveillance capacity abroad will be vital to national security.

Connecting Systems and Organizations

On a global scale, a major gap in the current framework is a lack of standardization and coordination of existing surveillance platforms. Not only is there a lack of standardization and coordination among different administrative levels (e.g., community, subnational, national, regional, and global levels), but there is a lack of standardization and coordination among human, animal, and environmental sectors. Many countries have multiple surveillance platforms that run parallel to one another, with each being controlled by a different sector and little communication and lack of data exchange and interoperability among them. Generating structures that minimizes redundancy and establishes interoperable platforms for data sharing among all sectors and administrative levels will be an important step for effective surveillance and early detection moving forward.

One recent activity in support of One Health is an encouraging development. The FAO, WOAH, WHO and the U.N. Program on the Environment have formed a quadripartite organization termed the One Health High-Level Expert Panel (OHHLEP). This newly formed organization is working to ensure a sustainable and healthy future. This group is broadening the definition of One Health to be more inclusive of environmental/ecological sciences and activities, building a more optimal surveillance system and creating tools to mitigate drivers of zoonotic spillover.

Funding One Health Initiatives

Minimizing the conditions that generate the threats of pathogen emergence and filling the gaps that result in outbreaks of pandemic potential all require One Health solutions targeting upstream prevention and control measures. The One Health approach is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems and recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and interdependent (World Organization for Animal Health 2021). This has widely been recognized as the way forward

for food safety and security, among other issues, however challenges to implementation still arise (Atlas et al. 2010).

One challenge is the lack of resources dedicated to strengthening capacity for implementation of One Health. In recent years, through the Global Health Security Agenda, global partners conducted in-country Joint External Evaluation (JEE). The results indicated that no country was fully prepared to handle a major epidemic or a pandemic. The findings clearly showed the world remains severely underprepared as we witnessed when SARS-CoV-2 pandemic emerged. More countries are now establishing a One Health coordination structure or platform at their national level that serves as the inter-ministerial contact point to coordinate efforts. These platforms facilitate communication channels and partnerships within and between sectors as well as stakeholder alignment. However, these structures often lack a common funding mechanism without which implementation can be difficult.

The One Health Operational Framework developed by the World Bank has made significant progress, having an entire section on the value of investing in One Health; however, costs and benefits of capacity building and research are not fully addressed (The World Bank 2018). The lack of a centralized One Health infrastructure, including a system for ethical conduct of multisectoral research and regulatory activities, remains a major challenge in most parts of the world. Infrastructure for policy and finance, surveillance, and education also remain limited in many countries. Through the One Health Operational Framework developed by the World Bank, there has been movement towards establishing a global framework for such political and financial infrastructures as well as strong incentives to do so (The World Bank, 2018).

The World Bank has approved the establishment of a Financial Intermediary Fund (FIF) for Pandemic Prevention, Preparedness, and Response. This FIF is designed to mobilize significant financial support and engender collaborative actions to strengthen health systems and security capacities especially for LMIC and regions. Activities related to One Health will be eligible for funding as the FIF recognizes that a multi-sectoral One Health approach is central to preventing disease and pandemic risks. It is anticipated that the FIF could be launched in late 2022. This is an encouraging development.

Importance of Education

Education systems are beginning to understand the importance of One Health, with a set of recommended core competencies having been established, new One Health Academic Degree programs emerging (Togami et al. 2018), and the development of One Health university networks such as the One Health Workforce Next Generation Project aimed at building upon the Africa One Health Univer-

sity Network (AFROHUN) and Southeast Asia One Health University Network (SEAOHUN) (United States Agency for International Development 2022). However, most One Health education occurs within the veterinary, public health and medical programs after at least three or more years of study (Villanueva-Cabezas et al. 2022). Moving forward, One Health education must begin earlier than postgraduate education and include system thinking principles and diverse student cohorts, beyond medical and veterinary students, to share world views, life experiences, cultural backgrounds, and knowledge systems (VillanuevaCabezas et al. 2022). Expanding One Health education should truly be multi- and transdisciplinary including social and behavioral, environmental and climate sciences and agriculture. Previous discussions suggest that emerging zoonotic diseases qualify as "wicked "problems because of their complexity, dynamic interconnectedness, and lack of contemporary solutions. As we face more "wicked" problems in our future, researchers, scientists, and One Health practitioners will need to develop the professional and interpersonal skills to enable them to successfully collaborate, and work with diverse teams and

stakeholders. The National Science Foundation Scientists recently awarded a grant to Ohio State University researchers who proposed that graduate and professional courses and curricula need to be redesigned to ensure that new graduates not only have deep disciplinary training but also have transdisciplinary competencies and thinking skills to address today's grand challenges. To accomplish this, they suggest that a new generation of "wicked" scientists need to be developed to prepare them for a volatile world of intractable problems. (Kawa and Biwer 2021).

Movement towards a One Health approach to mitigate emerging zoonoses including food-, water- and vector-borne diseases and antimicrobial resistant pathogens provides great hope as these frameworks and strategies develop. It will be the implementation of these strategies that will allow us to discover the full scope of factors underlying emergence, trace and disrupt pathways, and establish a system capable of predicting, preventing, and controlling adverse health impacts associated with emergence and propagation of novel, emerging, and reemerging diseases (Institute of Medicine 2012).

Foodborne Disease

Although foodborne illness outbreak detection has improved in the last 25 years, comprehensively quantifying the disease burden and societal effects of foodborne illness in the United States has proven to be a challenge. The CDC predicts that approximately 9.4 million people annually are infected with foodborne pathogens, 56,000 are subsequently hospitalized, and 1,300 ultimately die (Scallan et al. 2011). *Salmonella* and *Campylobacter* are estimated to cause 75% of illnesses related to animal-sourced foods in North America (Li et al. 2019). Models establish an economic burden of foodborne illness to be between $50.1 and $77.7 billion in the United States yearly (Scharff 2012).

In attempts to encapsulate the symptoms and severity of foodborne disease, studies have generated estimates of disability-adjusted life years (DALYs) which represent years of healthy life lost to premature death or long-term disability from foodborne disease. DALYs data related to foodborne illness caused by animal-derived products predicts approximately 65,000 years of healthy life were lost in 2010 in the United States (Li et al. 2019). Analyses of available data have repeatedly demonstrated that incidence of foodborne illness and associated multistate outbreaks of disease have risen over time (Braden and Tauxe 2013; Nguyen et al. 2015; Tack et al. 2019), indicating that the impact of foodborne disease continues to be underestimated. There is often a lack of comprehensive data available to understand effects of foodborne illness beyond disease incidence such as societal and economic impacts.

Further complicating this issue, new challenges in foodborne disease surveillance and control have arisen through the growth of a globalized food system. In the last century, agricultural practices have evolved in response to influences from the environment and climate, advancing technologies, and dietary demands of growing populations. Reliable food sources produced through modernized agricultural practices have supported the increasing global human population. More efficient production increased food surpluses, which spurred trade of food and fiber overseas and led to increased availability and diversification of food throughout the world. As a result, food products served in one country are now often produced or sourced from another. This has also meant that it is possible for contaminated food items to cause illness among consumers in multiple parts of the world at once. Pathogens and the characteristics of those pathogens, such as novel antibiotic resistance genes, are found on the plates of consumers thousands of miles away from the source of production. Distribution of food products over a global landscape has necessitated changes in foodborne illness outbreak detection and response.

Historically, foodborne illnesses have primarily affected individuals at a county level, associated with food preparation or handling proximal to consumption (Braden and Tauxe 2013). As production and distribution has increased globally and become more complex, pathogens that contaminate foods upstream in the production process subsequently become more disseminated (Antunes, Novais, and Peixe 2020). These dispersed human illness outbreaks might even occur linked to food products not for human consumption such as pet food. For example, in 2019, the CDC detected a multidrug-resistant strain of *Salmonella* I 4,[5],12:i:- among dog owners in the United States. Upon further investigation it was noted that several ill people fed their dogs pig ear pet treats prior to illness onset, and multiple ill dogs were also reported. Testing of pig ear pet treats revealed significant levels of contamination with numerous strains of *Salmonella* (CDC 2019c). More than 150 cases of human illness resulted. *Salmonella* serotypes uncommonly found in the United States were detected, including *Salmonella London* isolates with an antibiotic resistance gene (*qnrE1*) that had been reported to the CDC only once prior. The detection of uncommon serotypes and the introduction of a novel resistance gene into the United States prompted traceback of pet treats to production sources.

Traceback activities in this investigation indicated pig ear pet treats originated from Brazil, Argentina, and Colombia (CDC 2019c). Examination of the literature in these countries indicated that some of the serotypes uncommonly documented in the United States but seen in this outbreak had been reported among swine herds and pork products previously (Colello 2018; Rodrigues et al. 2020). Outbreaks of this nature highlight both the diversity of routes through which foodborne disease may spread and the challenges in preventing illness in an international market.

In recent years, technological advancements have enabled efforts to protect public health. As of 2019, PulseNet, the national molecular subtyping network for foodborne disease surveillance, transitioned from using pulsed field gel electrophoresis (PFGE) to detect outbreak-related cases of foodborne disease to using whole genome sequencing (WGS). WGS provides more detailed and precise data for identifying outbreaks than PFGE. Instead of comparing bacterial genomes using 15-30 bands that appear in a PFGE pattern,

WGS allows for the comparison of millions of nucleotides. This is analogous to comparing two books by using all the words in the books to see if they are the same, instead of comparing just the number of chapters. Using WGS has allowed detection of illness outbreaks when they are smaller in size and has helped to determine the degree of relatedness of bacterial isolates from human, animal, and environmental sources. It has been found that some bacteria that appeared to be similar using PFGE are genetically distinct, and the greater level of detail provided by WGS allows epidemiologists more accuracy in both including and excluding cases within an outbreak investigation (Carleton 2019; Oakeson et al. 2018). This change has also proven integral in enhancing the ability of detecting multistate outbreaks that span wide geographic distances; genetic sequences of bacteria can be uploaded to databases and shared internationally (Gerner-Smidt et al. 2019).

WGS also provides information regarding genes that correlate with certain forms of antibiotic resistance; this "predicted" or genotypic resistance, based on the presence and expression of certain genes, correlates well with the phenotypic resistance found using traditional antibiotic susceptibility testing for enteric pathogens (McDermott et al. 2016). Despite the numerous advantages, there are also new challenges for WGS data analysis and interpretation. Persistence of pathogens in animal or environmental reservoirs allows for replication and genetic diversification that evades thresholds of bacteria isolate relatedness used to detect outbreaks (Gerner-Smidt et al. 2019). Similarly, specific genetic strains of bacteria can recur, reemerge, and persist over time, which presents difficulties in parsing distinctions between bacteria that result in endemic foodborne disease and those causing outbreaks. Ultimately, epidemiologic data collection is vital in interpreting the significance of WGS findings in the context of outbreaks. Integrating these with the sampling of food, animals, and the environment in a comprehensive One Health approach has proven to be vital for outbreak investigations (Gerner-Smidt et al. 2019).

Global spread of disease during the COVID-19 pandemic impacted surveillance of foodborne disease outbreaks in the United States. The height of COVID-19 infections in the United States brought on a spike in Americans avoiding or delaying medical care for other acute or emergent conditions (Czeisler et al. 2020), and simultaneously, PulseNet noted a 22% drop in clinical *Salmonella* isolates reported by state and local health departments in 2020 compared to isolates reported from 2017–2019 (Ray et al. 2021). Despite this, outbreak-associated *Salmonella* connected to ownership of or contact with non-commercial (also known as "backyard") poultry reached an all-time high (Nichols et al. 2021). Backyard poultry ownership has contributed a sizable and growing proportion of live-animal associated *Salmonella* cases in

the United States for decades (Basler et al. 2016). However, the COVID-19 pandemic also ignited new interest in understanding how food is produced and participation in poultry raising in backyard chicken coops across the United States. A record number of Americans purchased poultry for food production or pet ownership in 2020 and subsequently more than 1,700 *Salmonella* illnesses were linked to backyard poultry contact (Nichols et al. 2021).

Consumers reported purchasing poultry for eggs and meat after hearing about potential interruptions to food supply chains and outbreaks in meat and poultry processing plants (Chappell 2020; Danovich 2020). Many were also first-time poultry owners seeking to provide children who were home while schools were closed with an opportunity to learn more about food production. Unfortunately, new poultry owners are more likely to be unaware of the potential for *Salmonella* transmission from poultry or may participate in high-risk practices such as keeping poultry inside the house instead of using appropriate biosecurity measures known to more experienced poultry owners (Nichols et al. 2021). Shifts in food preference and food-seeking practices will continue to be subject to international influences, and this will subsequently further shape the epidemiology of foodborne disease in the United States.

Climate change is another major influencer of foodborne disease worldwide. Because of the complex interplay of climate and food production, it is challenging to predict exactly how rising temperatures, more frequent natural disasters, and changes in precipitation will impact either the process of producing food or the pathogens transmitted via food (Lake 2018). Availability of resources such as water and nutrient-rich soil impact crop yields or arability of land, both of which might have downstream consequences on how food is distributed and the security of food access. Livestock agriculture might also see major change in the face of challenges such as decreased productivity because of prolonged seasonal heat stress. Similarly, political regulation or cultural shifts away from meat consumption for the sake of lowering greenhouse gas emissions and mitigating climate change could also impact the size and scope of this industry and its role in the average American diet (Lake et al. 2012). Foodborne pathogens will also change in distribution and prevalence in response to climate. Because each species grows ideally in its own unique external conditions, certain factors associated with climate change might promote foodborne disease proliferation while others will hinder it. For example, *Salmonella* is more likely to be detected or shed from animal hosts and spread by insect vectors in summer months and therefore might become more prevalent in a warming world (Hellberg 2016, Lake 2018).

In response to climate change, new methods of food production are being developed and used. These methods

are often innovative and may consider the need to produce food in an environment that requires more efficient use of resources but pose new questions with respect to foodborne disease risks. For example, during 2021 an outbreak of *Salmonella* Typhimurium infections occurred among 31 people across four states. The outbreak was linked to hydroponically grown salad greens and was the first outbreak resulting from hydroponic production without the use of soil. This outbreak might have been linked to contaminated water; the outbreak strain of *Salmonella* Typhimurium was isolated from an outdoor storm water drainage pond located beside the farm (CDC 2021).

Though there is no clear trajectory for foodborne disease in context of the shifting climate, it will inevitably impact disease burden and attribution, potentially giving rise to new public health challenges or food security threats. Arguably, all foodborne illness is preventable, but food production is a dynamic system subject to the diverse tastes and demands of an ever-growing population and shifting global climate. Movement of food, both within the United States and internationally, necessitates bolstered infectious disease surveillance for transported goods and collaboration between trade partners to ensure food safety from start to finish. Harmonizing and accepting international food safety regulations and strengthening compliance and enforcement could greatly help disease prevention and bolster outbreak detection and control efforts. Integration of epidemiologic investigation, traceback of food products, and laboratory testing of clinical, environmental, and animal isolates will continue to serve as the cornerstone of outbreak response. However, technological advancement will be needed to scale up investigations of international scope. This will predominantly necessitate building capacity and allocating resources that allow for sharing data rapidly between countries in order to detect and respond to cross-border outbreaks. Public communication and education about the risks of disease transmission from animals and food products will continue to be integral, especially as we learn of new disease threats. Consumer education on safe food preparation and handling are especially important in preventing foodborne infections. Acknowledging and studying the global influences on foodborne disease will simultaneously aid in preventing disease across borders and mitigating outbreaks in a changing world.

Zoonotic Vector-borne Diseases:
An Emerging One Health Threat in the United States

Zoonotic vector-borne diseases are caused by a diverse group of pathogens that are transmitted to humans by infected arthropod vectors, such as mosquitoes, ticks, and fleas. The pathogens causing these diseases are maintained in the environment by infected animal hosts, most often wildlife, which makes control of these diseases difficult. In the United States there is a long list of endemic vector-borne zoonoses that are capable of causing mild to severe and even fatal disease, such as Rocky Mountain spotted fever which has a case-fatality rate of 7% in endemic areas (Regan et al. 2015). In addition to known endemic diseases, recent advancements in molecular diagnostics have aided in the identification of several newly described vector-borne pathogens that cause novel human disease including Bourbon virus, Heartland virus, *Borrelia miyamotio* and *Ehrlichia muris eauclairensis* (Brault et al. 2018; Kosoy et al. 2015; Prit et al. 2011; Scoles et al. 2001). Additionally, a small subset of vector-borne diseases pose a potential severe biothreat to public health. These include plague, tularemia, and Eastern equine encephalitis (CDC-USDA 2021).

Over a 13-year period, between 2004 and 2016, human tick-borne disease cases reported to CDC's National Notifiable Disease Surveillance System (NNDSS) more than doubled and accounted for 77% of all vector-borne disease reports (Rosenberg et al. 2018). During this same time, Lyme disease accounted for 82% of all tick-borne diseases reported with estimates of 30,000 infections annually, although only a portion of these are captured through national surveillance (Hinckley et al. 2014; Nelson et al. 2015). Other tick-borne diseases, such as spotted fever rickettsiosis, anaplasmosis, and ehrlichiosis, continue to increase in burden across the United States (Nichols et al. 2016, Heitman et al. 2019). The national surveillance of vectorborne disease is an imperfect system (see Table 2 for list of zoonotic vector-borne diseases under national surveillance), and most certainly an underestimate of the true burden of these diseases. Several key contributors are responsible the underestimation of our national surveillance data, including dependency on clinician awareness and use of appropriate diagnostic tests, completeness of data, and timely reporting to public health officials. Even less is known about the burden and geographic patterns of zoonotic vector-borne diseases not included in our national surveillance system, such diseases include bartonellosis, Heartland virus disease, Chagas disease, flea-borne typhus, and babesioisis. Despite the gaps in surveillance, general patterns of vector-borne disease across the United States

indicate disease emergence, with increased burden and expanding geographic distribution with each new year. Given the dynamic and interwoven linkages among human, animal, and environmental health, using a One Health approach is critical to preventing and controlling zoonotic vector-borne diseases. These diseases have complex life cycles which are highly dependent on the availability of suitable environmental conditions and presence of both competent vector(s) and animal host(s) (see example of complex life cycle proposed for Heartland virus, Figure 1). The ecological interactions between vector-borne diseases and their biotic and abiotic environment drives their potential for emergence and are impacted by factors such as urbanization, land use change, climatic changes, and human and wildlife population dynamics.

Table 2. Endemic vector-borne diseases with primarily zoonotic transmission notifiable through National Notifiable Disease Surveillance System (NNDSS).

Disease	Primary Vector
Anaplasmosis	Tick
Babesiosis	Tick
Ehrlichiosis	Tick
Lyme disease	Tick
Powassan virus disease	Tick
Spotted fever rickettsiosis*	Tick
Tularemia	Tick, Deer fly
Plague	Flea
Eastern equine encephalitis virus disease	Mosquito
Jamestown Canyon virus disease	Mosquito
La Crosse virus disease	Mosquito
St. Louis encephalitis virus disease	Mosquito

*Includes Rocky Mountain spotted fever and *R. parkeri* infections

This list is limited to diseases endemic in the U.S. that are primarily transmitted through cycles of animal-vector-human with human-vector-human transmission less often. (CDC 2019b)
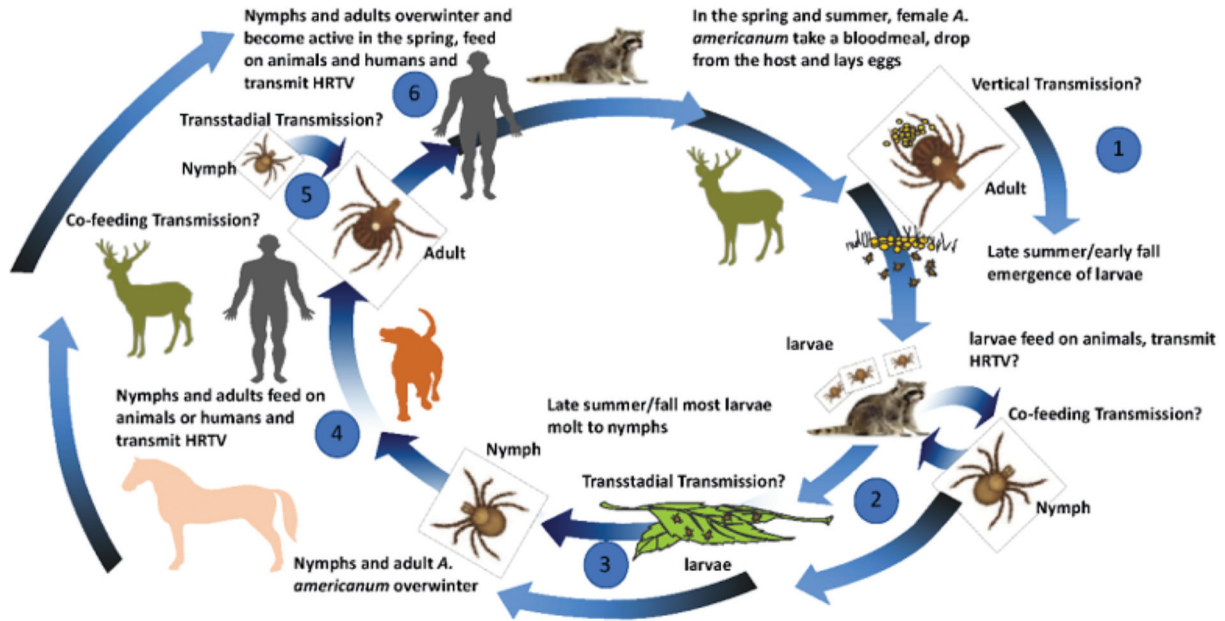
Figure 1. Proposed transmission model for Heartland virus borrowed from Brault et al. 2018. This proposed lifecycle illustrates the complexity of vector-borne diseases and their interaction with humans, domestic animals, wildlife, and their environment. Specifically, this lifecycle highlights the tick vector (*Amblyomma americanum*) over a 2-year period (Brault et al. 2018).

Climate is one of the factors that influence the distribution of vector-borne diseases. The geographic and seasonal distribution of vector populations, and the diseases they can carry, depends not only on climate but also on land use, socioeconomic and cultural factors, pest control, access to health care, and human responses to disease risk, among other factors. Daily, seasonal, or year-to-year climate variability can sometimes result in vector/pathogen adaptation and shifts or expansions in their geographic ranges. Such shifts can alter disease incidence depending on vector-host interaction, host immunity, and pathogen evolution. A changing climate's impact on the geographical distribution and burden of vector-borne diseases in other countries where these diseases are already found can also impact the United States, especially as a result of increasing trade with, and travel to, tropical and subtropical areas. Whether a changing climate will increase the chances of domestically acquiring vector-borne diseases is uncertain due to domestic vector-control efforts and lifestyle and behavioral factors, such as time spent indoors, that reduce human-insect contact.

The current presence of tick, fleas, mosquitoes, and other arthropod species in the United States with the potential to serve as competent vectors for foreign and non-native diseases creates a risk to human and animal health. There must be a successful establishment of both the pathogen and a competent vector for vector-borne disease to become endemic. This hypothesized risk became reality with the introduction and establishment of West Nile virus. Because of suitable native wildlife and mosquito populations in the United States, West Nile virus is now an endemic disease and the most commonly reported mosquito-borne infection associated with zoonotic transmission (McDonald et al. 2021).

The United States is exceptionally vulnerable to emerging vector-borne disease in areas where suitable arthropod vectors are already established and maintained in the environment. Modeling of potential pathways for introduction has been done for diseases such as Rift Valley fever (Golnar, Kading, and Hamer 2018). However, West Nile virus establishment outlines one successful path for a vector-borne disease from introduction to endemism.

The introduction of the Asian longhorned tick (*Haemophysalis longicornis*) in 2017 to the east coast of the United States and the tick's continuous westward range expansion, as well as affinity for livestock illustrates the ease of which a foreign vector can quickly establish endemic status (Rainey et al. 2018). In Asia, this tick has been found infected with pathogens similar to those causing human disease in the United States, such as *Anaplasma, Babesia, Rickettsia,* and *Borrelia* (Kang et al. 2016). The Asian longhorned tick could, therefore, play a potentially significant role in the expansion of an existing zoonotic vector-borne disease or emergence of a new disease in the United States, presenting

an additional threat for both human, livestock, and wildlife health.

We have become acutely aware while living through the COVID-19 pandemic that diseases don't respect political borders, and the same is true of the vectors and wildlife hosts that are responsible for their transmission. The United States is now confronting ongoing threats to the health of human, domestic animals, and wildlife from vector-borne diseases, specifically associated with substantial increases in the burden of endemic diseases, importation of pathogens through travel and trade, increases in newly discovered diseases of which little is known, and establishment of foreign arthropod vectors (Petersen et al. 2019). To further prepare and reduce the impact of these diseases on human and animal health we must take a multifaceted, One Health approach.

With few exceptions, zoonotic vector-borne diseases in the United States of greatest concern for public health have minimal overlap with those of primary concern for livestock. Although, currently, we have fewer zoonotic vector-borne diseases impacting livestock compared to other countries, we should not assume this will be the case in the future. Advancements are needed to increase timely reporting and accurate disease surveillance among people and animals. Future efforts are needed to support improved diagnostic capacity and pathogen detection, innovative and effective prevention and control methods, and advancements in development of therapeutics and vaccines. Building partnerships across human, animal, and environmental sectors, including both governmental and non-governmental partners, are crucial in prevention and control of zoonotic vector-borne diseases.

Waterborne Diseases

"Water Quality is Health. Our global health, that is the biohealth of the planet is at risk like no other time in history. Water quality is degrading and it is a complex wicked problem that requires better knowledge on sources, impacts and risks. The status of water quality data is dismal, but we now have the tools to tackle this problem." Joan B. Rose

Introduction:
One Health One Water

Waterborne diseases are global concern tied to fecal pollution of water systems and disruption of aquatic ecosystems. Water quality is degrading worldwide. Water quality issues include pollution of rivers, lakes and marine coastlines, groundwater, and water at the tap. Pollutants are attributed to the acceleration of the human population, the number of agricultural-based animals, and deterioration of our delivery systems. In addition, there are hundreds of microbial hazards including zoonotic pathogens, antibiotic resistance, and toxic algal blooms.

A growing concept in managing water resources and water quality is "One Water" where the complete water cycle including human-derived and climate-accelerated discharges are considered as one system (Figure 2) and is tied to One Health via the various exposure pathways impacting waterborne disease. A One Water/One Health approach would formalize the assessment, restoration, and protection of source water, return waters, and stormwaters thus ultimately improving biohealth of the planet.

The health of both animals and humans are of concern. It is well understood that infections in domesticated animals (particularly those diseases in which the infectious agent ends up in manure) can influence human health and the long list of zoonotic pathogens which can be waterborne are a growing issue. The FAO reports that animal manure and agricultural sources are now the number one cause of pollution (Mateo-Sagasta et al. 2008). All ecosystem services, drinking, recreation, fisheries, and irrigation are at risk.

Quantifying the Risk and Burden of U.S. Waterborne Diseases

Waterborne diseases are generally assessed in two primary categories—disease acquired through drinking water

Figure 2. The One Water and One Health System.

and disease transmitted via exposure to recreational waters. Outbreaks associated with one or more individuals with a common exposure are documented at the state and reported to the Centers for Disease Control and Prevention, but these outbreaks are considered just the tip of the iceberg because of an underestimation along the healthcare supply chain. The major burden of waterborne diseases are estimates of the illnesses that could be associated with exposure to contaminated water.

There are more than 150 disease agents which cause not only waterborne diarrheal illness, but also cardiovascular disease, kidney failure, cancer, reactive arthritis, paralytic disease, and pneumonia to mention a few (Haas, Rose, and Gerba 2014; Rose and Jimenez 2019). The major bacteria, protozoa, and viruses are shown in Tables 3, 4 and 5. Most of

these are enteric pathogens are transmitted by the fecal-oral route where the microbe is excreted in the feces of an infected individual (human or animal) and the exposure to the next susceptible individual is via ingestion. These pathogens are spread efficiently through contaminated water and a key characteristic of these pathogens is their high concentrations found in sewage.

Outbreak data for drinking and recreational waters (for untreated ambient waters) over the last 10 years was compiled, where data were available (2005-2017; CDC NORS). A total of 253 drinking water outbreaks and 179 recreational outbreaks in natural waters were documented. Table 4 outlines waterborne disease outbreaks from 2005 to 2017.

There was no major decrease in the numbers of outbreaks over this period. Similar pathogens were found with the ex-

Table 3. Selected bacteria of importance transmitted through water

Family, Genus, Species	Disease	Route of Transmission and Source
Spirochetes Gram-negative helical bacteria *Leptospiraceae* *Leptospira interrogans**	Leptospirosis High fever, headache, bleeding, muscle pain, chills, red eyes, and vomiting are some symptoms. Without treatment, leptospirosis can lead to kidney and liver damage and even death. Antibiotics clear the infection.	Recreational Contamination via animal urine
Microaerophilic, helical gram-negative bacteria *Campylobacter jejuni**	Gastroenteritis also associated with Guillain-Barré syndrome and reactive arthritis	Water, food (fecal contamination from humans and animals) often associated with non-disinfected ground waters.
Gram-negative aerobic rods and cocci Pseudomonodaceae *Pseudomonas aeruginosa* Legionellaceae *Legionella pneumophilia*	Wound/burn infections, urinary tract infections Pneumonia (Legionnaire's disease)	Water aerosols Recreational, hot tubs Aerosols from built water systems (premise plumbing, cooling towers, fountains)
Facultative anaerobic Gramnegative rods Enterobacteriaceae *Escherichia coli** *Shigella dysenteriae* *Salmonella typhi; other Salmonella species** *Yersinia enterocolitica**	Diarrhea, kidney infections (0157 H7) Dysentery Typhoid fever, diarrhea, reactive arthritis Diarrhea	Fecal contamination of water and food Associated with non-disinfected recreational and drinking waters.
Vibronaceae *Vibrio cholera* *V. parahaemolyticus* *V. vulnificus*	Cholera Gastroenteritis Septicemia	Water, food fecal contamination Shellfish Recreational exposure via skin, marine waters, found post flood in coastal systems.

*These pathogens are zoonotic

Table 4. Waterborne outbreaks in drinking waters and in recreational waters in the United States, 2005 to 2017

	Drinking Water		Recreational Water (untreated ambient waters)	
Years	Etiological Agents (#s of outbreaks)	Number of outbreaks (cases) % groundwater sources/springs	Etiological Agents (#s of outbreaks)	Number of outbreaks (cases)
2015-2017	*Campylobacter* (2) *E.coli* (3) includes 0157H& *Legionella* (75) *Shigella* (1) *Giardia* (1) Norovirus (6)	90 (951)	*Campylobacter* (3) Cyanotoxins (2) *E.coli* 0157 H7 & others (2) *Salmonella* (1) *Shigella* (5) *Cryptosporidium* (8) *Giardia* (1) Schistosomes (3) Viruses (6)	34 (1068)
2013-2014	*E. coli* (1) *Cyanobacteria* (2) *Cryptosporidium* (5) *Giardia* (3) *Legionella* (25) Viruses (3)	42 (1006) 26.2% groundwater/springs	*E.coli* 0157 H7 & others (4) *Leptospira* (1) *Shigella* (3) *Cryptosporidium* (1) Viruses (8)	16 (2580)
2011-2012	*Campylobacter/ Shigella* (2) *Giardia* (2) *Legionella* (21) Viruses (2)	32 (431 cases) 34.4% groundwater/ springs	*Cyanobacteria* (2) *E.coli* 0157 H7 & 0111 (6) *Shigella* (2) *Cryptosporidium* (1) *Giardia* (3) Schistosomes (4) Viruses (3)	21 (479)
2009-2010*	*E.coli* 0157 H7 (2) *Campylobacter* (6) *Cryptosporidium* (2) *Giardia* (3) *Legionella* (19) Viruses (2)	33 (1040) 63.6% groundwater/ springs	*Campylobacter* (1) *Cyanobacteria* (11) *E.coli* 0157 H7 (3) *Shigella* (1) *Cryptosporidium* (3) Schistosomes (2) Viruses (2)	24 (296)
2007-2008	*E.coli* 0157 H7 (1) *Campylobacter* (4) *Cyclospora* (1) *Giardia* (2) *Legionella* (12) Viruses (3)	36 (4128) 52.8% groundwater	*E.coli* 0157 H7 (1) *Shigella* (5) *Cryptosporidium* (8) *Giardia* (3) *Naegleria* (8) Schistosomes (4) Viruses (13)	64
2005-2006	*E. coli* 0157 H7 and 0145 (1) *Campylobacter* (2) *Cryptosporidium* (1) *Giardia* (1) *Legionella* (10) Viruses (4)	20 (620) 40% groundwater/ springs	*E.coli* 0157 H7 (3) *Leptospira* (2) *Shigella* (3) *Cryptosporidium* (3) *Naegleria* (1) Viruses (3)	20

*11 more outbreaks associated with drinking non-potable water sources

ception of *Leptospira*, *Naegleria*, and *Schistosoma* being unique to recreational waters and *Legionella* being unique to drinking water. Groundwater was a key risk associated with drinking water outbreaks and was the source of 26.2% to 63.6% of the outbreaks averaging 43.4%.

The burden of waterborne disease was evaluated for 17 pathogens including *Escherichia coli*, *Campylobacter*, *Legionella*, *Pseudomonas*, *Salmonella*, *Shigella*, *Vibrio* spp, *Cryptosporidium*, *Giardia*, and norovirus (Collier et al. 2021). This study suggests that 1 in 44 individuals suffer from a waterborne illness in the United States per year and that this results in 601,000 emergency room visits, 118,000 hospitalizations, and 6,630 deaths. Others have suggested that this is a woeful underestimation and approximately 90 million recreational waterborne illnesses occur from exposure to untreated waters costing as much as $2.9 billion per year (DeFlorioBarker et al. 2018).

Key Zoonotic Pathogens

Many of the bacterial and protozoan pathogens are zoonotic as indicated in Tables 3 and 4. The key bacteria include *Campylobacter*, *E. coli* serotypes, *Salmonella*, and *Leptospira*.

Campylobacter, *E. coli* serotypes, and *Salmonella* are all enteric pathogens, with poultry and cattle manure the major sources of the animal fecal contamination. These bacteria are often found together, and rainfall has been linked to their spread. One iconic outbreak was manure contamination of the drinking water well in Walkerton Ontario, Canada, a rural small community, where both *E.coli* O157:H7 and *Campylobacter* were associated with a rain event and failure to disinfect the drinking water (Hrudy and Hrudy, 2014). These pathogens cause more serious illnesses, deaths in young children, kidney failure, and long-term reactive arthritis.

Cryptosporidium and *Giardia* are the most important zoonotic protozoan pathogens and are often associated with exposure to contaminated water. *Cryptosporidium* is associated primarily with cattle, particularly calves, whereas *Giardia* is found in a wide array of wildlife and domestic animals. Infected individuals excrete highly disinfectant-resistant oocysts in high concentrations in feces. They have caused multiple high-profile outbreaks including the *Cryptosporidium* outbreak in Milwaukee after high intensity rain caused both overflows of cattle wastes and human sewage into the water supply. Both the human and zoonotic species were found (Zhou et al. 2003). In a less known outbreak, 20 of 33 firefighters had gastroenteritis after controlling a barn fire housing 240 week-old calves using a swimming pond on the farm to put out the fire. Testing showed that the firefighters were infected with *Cryptosporidium* from the contaminated pond (CDC 2012). These two examples show large- and small-scale agriculture-associated risks.

Leptospirosis may be one of the most neglected and widespread zoonotic infections with three main transmissions routes including water-based due to swimming or bathing in contaminated water, exposure to environments contaminated by rodents, and livestock/pets (Goarant et al. 2019). The bacteria are found in a large number of different types of domestic and wild animals, including rats and mice, which harbor the bacterium in their kidneys and release it through their urine (Calderon et al. 2014; Ko et al. 2009). Humans acquire the bacteria via exposure to broken skin or mucus membranes. Wildlife has been found to be a source of interspecies transmission in the United States (Grimm et al. 2019). In areas with poor hygiene the transmission was related with rats and other rodents and the rainy season/flooding.

Emerging Threat—Harmful Algal Blooms

Excess nutrients in the natural waters around the United States and the world are associated with harmful algal blooms (HABs). These excess nutrients (nitrogen and phosphorus) are often the result of runoff from over fertilized farmland and yards and leaching from septic systems. These excess nutrients overfeed toxic algae called cyanobacteria (also known as blue-green algae) in freshwater systems. Dinoflagellates and diatoms can cause HABs in marine and brackish waters. HABs can produce toxins, dependent on the species, as well as harm aquatic environments by blocking sunlight, using up the available oxygen, or blocking the gills of fish. The toxins from the HABs can cause dermatologic, gastrointestinal, respiratory, and neurologic signs and symptoms and have been occasionally associated with deaths in pets, livestock, and wildlife.

Major impacts to drinking water systems are now emerging. In 2014 the Toledo, Ohio water plant issued a "Do Not Drink" order due to a massive toxic bloom in Lake Erie, the source of the drinking water. Approximately a half million people served by the water system in Michigan and Ohio were affected when toxins were detected in the finished water. A similar event in Salem, Oregon occurred in 2018 when toxins were detected at a level that exceeded EPA's drinking water advisory levels for vulnerable populations, such as infants.

The economic impact of HABs has not been well quantified but an analysis of the impacts of eutrophication of U.S. freshwaters estimated a combined cost of about $2.2 billion USD annually, with costs related to recreational use alone ranging from $0.37 to $1.16 billion per year (Dodds et al. 2009). In the 2012 National Lakes Assessment, using cyanobacteria cell counts the data reported that "15% of lakes

Table 5.   Selected enteric protozoa transmitted through water

Protozoan	Disease	Route of Transmission and Source
Cryptosporidium*	Severe diarrhea	Both are associated with fecal-oral transmission and recreational as well as drinking waterborne disease.
Giardia*	Diarrhea, chronic fatigue syndrome	

*These pathogens are zoonotic

Table 6.   Selected enteric viruses transmitted through water

Virus	Disease	Route of Transmission and Source
Adenoviruses	Diarrhea, respiratory illness, eye infections	All are associated with fecal-oral transmission and recreational as well as drinking waterborne disease. Also cause shellfish associated disease.
Enteroviruses: includes Coxsackie viruses and Echoviruses	Diarrhea, respiratory illness, myocarditis, eye infections, neurological complications, meningitis.	
Hepatitis A virus	Liver infections	
Hepatitis E. Virus* Genetic similar to the pig HEV	Liver infections	
Norovirus	Vomiting and diarrhea	
Rotaviruses	Often associated with childhood diarrhea	

*This pathogen might be zoonotic

Content source: Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID) National Outbreak Reporting System (NORS) https://wwwn.cdc.gov/norsdashboard/

are in the most disturbed condition (i.e., pose a high risk of exposure to the public); 23% indicate moderately disturbed condition; 61% are in the least disturbed condition; and 1% were not assessed." This was a significant increase (+8.3%) of lakes in the most disturbed category between 2007 and 2012 (USEPA 2016). EPA has issued recommended recreational ambient water quality criteria or swimming advisories, as well as drinking water health advisories, for two cyanobacterial toxins (i.e., microcystins, cylindrospermopsins).

Risks for Agricultural Communities

Agricultural and rural communities are unique in that the populations rely on groundwater, often individual wells (15% of the population) for drinking water and on-site wastewater systems (e.g., septic tanks) for managing human sewage. There is less monitoring and treatment and as mentioned previously untreated groundwater is the source of many waterborne outbreaks. There is an increased risk of contamination of water systems by enteric pathogens and a threat to human health in rural environments. Sources of contamination include agricultural animal waste/manure, animal wastewater, septic tank effluents, and septage.

Dreelin and colleagues (2014) found that *Cryptosporidium* and *Giardia* were more prevalent in rural versus urban environments based on the number of positive samples. Genotyping showed that both the human and animal types of the parasites were found in rural and urban environments, but rural areas had a higher incidence of disease compared to urban areas based on the total number of disease cases. Septic tanks have been correlated with diarrhea in children in Wisconsin and with the increasing appearance of human sewage fecal markers in the watersheds in Michigan (Bordchardt et al. 2013; Verhougstraete et al. 2015).

Zoonotic Potential of Influenza A Viruses of Poultry and Other Avian Species

Sources of Influenza for Poultry and People

Avian influenza (AI) virus (AIV) can become adapted to numerous avian and mammalian host species, but free-flying aquatic birds are the natural hosts. Strains of AIV from aquatic birds have the greatest genetic diversity and can be any of the 16 hemagglutinin ("H") subtypes (Swayne, Suarez, and Sims 2020). The H5 and H7 subtypes are of unique importance for chickens and turkeys because they may be, or mutate to, the deadliest form of AIV, highly pathogenic (HP). HPAI can kill 100% of non-vaccinated chickens or turkeys in a few days. Less virulent forms of AIV (low pathogenicity AIV, LPAIV) can still cause disease resulting in negative economic consequences. To prevent spread, many countries will restrict trade with countries where HPAI is present in poultry (Hall 2004; Swayne, Hill, and Clifford 2017). Backyard poultry are very susceptible to HPAI.

Although the exact route of contact is not always clear, poultry infections with AIV come from wild birds, as has been the case with all the recent HPAI outbreaks in US poultry. Because climate change affects migration routes and waterfowl habitats, there will likely be some change in AIV dissemination patterns over time.

Farm-to-farm spread is associated with personnel and visitors, sharing equipment, and utilizing untreated surface water for the birds. There is some evidence that airborne spread can occur over short distances. Proximity to an infected farm or road where infected birds are transported are risk factors (USDA-APHIS 2015). It is not uncommon for the specific route of infection on a farm to be unknown. If not controlled, LPAIV can become adapted to poultry, then spreads more easily, and the H5 or H7 subtypes can mutate to HPAI, increasing economic devastation.

Prevention and Control of Influenza Infections in Poultry

Prevention and control of AIV is complicated by the diversity of poultry rearing practices worldwide; small-holder farms (including household poultry), industrial (i.e., large-scale integrated) farms, and live poultry markets (LPM). Practices also vary by use (eggs, breeding, or meat). Susceptibility to infection differs among poultry species; turkeys are more susceptible than chickens to infection and disease.

Prevention of AIV infections in poultry relies on farm biosecurity. Specific biosecurity procedures vary among farming systems and available resources. Most industrial farms will have some level of biosecurity in place to protect animal health against all important diseases.

Consolidation of industrial poultry has resulted in more uniform biosecurity practices. Smaller operations, including small-holders, and LPMs generally have minimal biosecurity in place. In the United States, educational programs for farmers on disease prevention are available through poultry companies, industry associations, states, and the USDA (e.g., "Biosecurity for the Birds" program). Because biosecurity is expensive and reduces efficiency by restricting access to premises and disrupting workflow with disinfection procedures, compliance can vary.

LPMs can't restrict access and have a constant influx of new animals, therefore often serve as reservoirs for AIV in poultry (Chung et al. 2022; Jagne et al. 2021).

In the United States, active surveillance programs are a key component of prevention and control. Spread can be prevented when infected animals are identified quickly. Poultry reared in industrial settings and LPMs are tested regularly through standardized programs (e.g., National Poultry Improvement Plan). Small-holder poultry are tested if animals show disease signs consistent with AIV.

Quarantines are immediately placed on infected flocks, which are often depopulated to prevent spread. Epidemiological studies are conducted to find any common traffic between the infected premises and other poultry. Control zones are also established where permits and/or testing are needed to move poultry and poultry products. Vaccines are available for AIV in poultry; however, they are expensive to administer and may take time to produce if suitable vaccines are not available in a veterinary vaccine bank. Historically, vaccination for AIV has been limited in the US because of the cost and the perceived potential for negative impact on trade. World Organization for Animal Health (WOAH) Code does not support vaccination as a non-tariff trade barrier if accompanied by adequate surveillance for AIV.

Influenza A in Poultry: Current Situation

The incidence of avian influenza in poultry varies through-

out the world (Swayne et al. 2020). In the United States and other high-income countries, infection in industrial poultry is uncommon, and occurs primarily as LPAI in an individual flock or small region, and occasionally as outbreaks of HPAI. Some HPAI outbreaks can spread extensively before being brought under control by eradication. HPAI and most LPAI are eradicated by stamping-out programs in highincome countries. Incidence of LPAI, especially the H9N2 subtype is common in all sectors of low-income countries in Africa, Asia, and Middle East, and H5N2 LPAI is in industrial poultry of Mexico. HPAI has become endemic in some low income and transition countries. For example, H7N3 HPAI is endemic in central Mexico in industrial poultry, H7N9 HPAI is in LPMs of China, and H5Nx HPAI is in the poultry of China, Egypt, Vietnam, Indonesia, Cambodia, Nigeria, and Bangladesh. In 2022, the USA is experiencing a large outbreak of H5N1 HPAI on 532 premises in 42 states (242 commercial and 290 backyard flocks) which affected 47 million domestic birds and over 2900 wild birds as of October 2022. The virus was introduced from Europe via migratory aquatic birds.

In low-income and transition countries, vaccination is commonly used against H9N2 LPAI as a management tool (Swayne and Kapczynski, 2017; Swayne and Sims2021). Some countries have implemented vaccination against HPAI,

once it became endemic, as a supplemental management tool in addition to stamping-out strategies. Vaccination increases resistance to infection, decreases virus replication and shedding when infection occurs, reduces virus transmission, and maintains food security and livelihoods, mainly for the rural poor. However, vaccination cannot replace basic biosecurity as an exposure prevention strategy and special surveillance and diagnostic methods are needed to identify infections in vaccinated populations.

Human Infection with Influenza from Poultry

Multiple genes from H1, H2, and H3 human influenza A viruses originated from AIV of aquatic birds long ago and were initially pandemic and later endemic. Human influenza A pandemics were reported in 1918 (H1N1), 1957 (H2N2), 1968 (H3N2) and 2009 (pH1N1). However, the pathway to becoming a pandemic strain is complex, involving influenza A virus genes transmitted across birds, mammals, and humans and is not fully understood. Sporadically, direct AIV infection of humans has occurred, resulting in high fatality rates with some viruses (Table 7) (Cox, Trock, and Uyeki 2017). Two AIV lineages (genetically related strains) are

Table 7. Confirmed human clinical cases of infection with AI viruses (data for 1978-2021). Cases reviewed in Cox et al. 2017; Swayne et al. 2020; Swayne, Suarez, and Sims 2013

Year(s)	Subtype(s)	Lineage	Pathotype	Location	Cases	Deaths
1978–79	H7N7	North American wild bird	LP	USA	3	0
1996	H7N7	Eurasian wild bird	LP	United Kingdom	1	0
1997–2021	H5N6, H5N8	Goose/Guangdong/1996	HP	Asia, Africa, Canada[1]	948	92
1998–2021	H9N2	Eurasian (G1, Y280)	LP	China, Hong Kong, Bangladesh	82	1
02-03, 2016	H7N2	North American live bird market	LP	USA	3	0
2003	H7N7	Eurasian wild bird	HP	Netherlands	89	1
2004	H7N3	North American wild bird	HP	Canada	2	0
2004	H10N7	Eurasian	LP	Egypt	2	0
2006	H7N3	Eurasian wild bird	LP	United Kingdom	1	0
2007	H7N2	Eurasian wild bird	LP	United Kingdom	4	0
2013–2021	H7N9	Anhui/2013 lineage	HP and LP	China[2]	1625	23
2010	H10N7	Australian	LP	Australia	5	0
2013	H6N1	Eurasian wild bird	LP	Taiwan	1	0
2013	H10N8	Eurasian	LP	China	3	2
				Total	2769	119

[1] Human emerging respiratory pathogens bulletin: Issue 57, September 2021 - Canada.ca 2 http://www.fao.org/ag/againfo/pro grammes/en/empres/h7n9/situation_update.html

[2] http://www.fao.org/ag/againfo/programmes/en/empres/h7n9/situation_update.html

responsible for most documented human infections. Human infection with AIV is very rare in the United States.

Human infections are primarily associated with exposure to infected poultry in LPMs or during stamping-out activities of HPAI outbreaks. Epidemiological studies have not linked AI human infection to food consumption (Cox, Trock, and Uyeki 2017). Airborne AIV has been recovered from samples in LPMs in Asia (Zhou et al. 2016). Experimental studies on the slaughter process with asymptomatic infected chickens and ducks have isolated HPAI from air samples and demonstrated transmission to ferrets (animal model for human transmission and infection) housed within the same air space (Bertran et al. 2017; Bertran, Clark, and Swayne 2018). Human AIV infections from direct exposure to wild aquatic birds are rare. However, antibodies to strains associated with wild birds have been found in asymptomatic duck hunters and wildlife professionals (Gill et al. 2006).

In the United States and other high-income countries, HPAI-infected poultry are prohibited from entry into the human food supply. Infected poultry are depopulated, and their carcasses sanitarily destroyed. Furthermore, AIV infections in humans have not been a food safety issue, as the virus is inactivated by pasteurization and cooking (Swayne and Beck 2004; Thomas and Swayne 2007). LPAIV have even lower risk of human food safety risk as the virus is not contained within the meat or internal contents of eggs (Lu et al. 2004; Swayne and Beck 2005).

Swine Influenza A Viruses and Pandemic Preparedness

People and Pigs Exchange Influenza Viruses

Influenza A viruses (IAV) are the causative agents of one of the most important viral respiratory diseases in pigs and humans. Additionally, swine IAV are an ongoing zoonotic risk to humans. Human and swine IAV are linked by sporadic incursions of human IAV to swine and swine IAV to humans. This bidirectional transmission greatly influenced the evolutionary history of IAV in both species and led to the first human pandemic of the twenty-first century in 2009. A One Health zoonotic disease prioritization workshop in the USA ranked animal IAV the number one priority (CDC 2017). IAV in swine is a primary example of a One Health challenge for human and animal health, requiring response to zoonotic human infections by swine IAV (called variants); strategies to minimize swine infections by human seasonal IAV; and integrated pandemic prevention plans (Kasowski, Garten, and Bridges 2011). Public health documented zoonotic infection of people with swine IAV for the past several decades, which generally resulted in an influenza-like illness similar to human seasonal IAV with limited onward human-to-human transmission. The most dramatic exception to this was the 2009 H1N1 pandemic (H1N1pdm09) with sustained global transmission (Garten et al. 2009; Smith et al. 2009).

Figure 3. Human seasonal influenza viruses repeatedly make incursions into pig populations around the world. These human to swine spillover events can lead to regionally unique subtype lineages that continue to evolve away from the human precursor with sustained transmission in swine. Major introductions that continue to circulate in swine are indicated by subtype and continent of first detection along the timeline.

Novel IAV that are detected in humans are concerning, but those with little immunity in the human population and capable of human-to-human transmission are of particular concern.

Swine Influenzas Are Highly Diverse

The endemic transmission and spread of genetically and antigenically distinct IAVs in swine are a primary challenge to minimizing the emergence of IAVs with pandemic potential. Subtypes of H1N1, H1N2, and H3N2 are endemic in swine around the world. Despite only three circulating subtypes, the genes encoding the surface glycoproteins that define subtype, hemagglutinin (HA) and neuraminidase (NA), exhibit tremendous diversity. Much of the observed diversity is the result of two-way transmission between swine and humans (Figure 3), followed by evolution within swine host populations, and viral diffusion through live animal transport and trade (Nelson et al. 2012; Rajao et al. 2018). There are significant numbers of weaned pigs transported between the United States and Canada, a source of domestic swine IAV dispersal (Nelson et al. 2015). Similar dynamics around the world contributed to the generation of numerous genetically and antigenically distinct lineages co-circulating in swine. The repercussions of these evolutionary events were starkly demonstrated with the swine-origin pandemic in 2009 and the subsequent impact of continued human seasonal H1N1-pdm09 and H3N2 spillovers into pig populations (Anderson et al. 2021).

Influenza Disease and Control in Swine

Swine IAV in the United States has seasonal peaks similar to the human influenza season. Control of IAV in swine populations through vaccine programs may reduce zoonotic transmission, particularly targeted to peak seasonal levels or at high-risk human-swine interfaces. A high incidence of influenza in sow farms is likely due to immune variability in populations of mixed ages. Producers primarily use influenza vaccines in sows to protect the gestating dam and her suckling piglets and vaccine may also be used in growing pigs. Vaccines in the United States are either fully licensed commercial products or can be formulated with custom farm-based strains. However, the number of strains required to immunize against all antigenically distinct circulating IAV strains makes the production of efficacious vaccines difficult (Bolton et al. 2019; Rajao et al. 2018).

IAV in swine is not a regulated disease. The USDA pro-

vides funding to support monitoring and reporting of clinical respiratory submissions tested at veterinary diagnostic laboratories that are part of the National Animal Health Laboratory Network, however, the majority of data provided to the USDA are anonymous, leaving monitoring and control largely driven by private producers and veterinarians. These clinical submissions are often part of monthly veterinary monitoring used by production systems to inform downstream pig movement or gilt replacement practices. If IAV is detected, the diagnostician and veterinarian compare the HA and NA sequences to current vaccine viruses to inform vaccine selection or strain updates. Consequently, a surveillance program that monitors trends in the genetic diversity of IAV in swine (Arendsee et al. 2021; Zeller et al 2018) with antigenic characterization of representative strains will allow for the early detection of new introductions or of antigenically drifted strains for updating vaccine viruses for improved vaccine efficacy.

Swine Influenza as a Zoonotic Risk for Humans

Highly variable swine IAV pose a recurrent threat to human health and challenge the development of integrated pandemic preparedness plans. High genetic and antigenic diversity along with human and swine interactions are important in the context of variant IAV infections in humans. However, substantial proportions of variant detections in the United States are not associated with adults with occupational exposure to swine. Dramatic increases in reports of human variant IAV infections began with H3N2 viruses associated with adolescents and animal exhibits in 2012 (Epperson et al. 2013). Since then, variant viruses are regularly detected in the USA and periodically in other countries with detection capacity (WHO 2021). The risk of variant infection is likely dependent on animal production systems, animal-human interfaces (e.g., live animal markets, exhibition practices), and the ecology of the virus (Karesh et al. 2012). Children are likely less immune to contemporary swine strains than adults, based on the greater antigenic divergence between dominant swine strains and recent human seasonal vaccine strains (Souza et al. 2021). However, adults also make up a consistent proportion of variant cases and are more mobile with greater contact points outside of the household and outside of the community, and thus likely to play a significant role in expansion of a novel viral epidemic or pandemic.

A One Health perspective for influenza pandemic preparedness requires continued surveillance and assessment of contemporary swine IAV. The level of surveillance in swine increased globally in the years following the emergence of the H1N1pdm09 but has decreased in recent years. These

data revealed the presence of swine IAV in regions not previously known to have endemic IAV and the presence of novel gene lineages not previously recognized in swine (Anderson et al. 2021). Surveillance activity in swine remains high in the United States, but contemporary surveillance efforts and genetic sequence data are sparse globally. Despite these limitations, approximately 30 phylogenetic clades of H1 and H3 genes were detected worldwide in the past 3 years in swine (Anderson et al. 2021).

Pandemic Preparedness for Animal Influenza

The determination of zoonotic risk of animal origin IAV occurs biannually at the WHO technical consultation on the composition of influenza virus vaccines. The detection frequency of genetic clades of swine IAV are quantified in 6-month periods, representative swine IAV are antigenically characterized, and these data are presented in conjunction with human seasonal influenza activity data. If variant cases are identified from swine IAV lineages, their antigenic novelty is tested against human seasonal vaccine antisera, pre-pandemic candidate vaccine virus (CVV) antisera, and pooled sera from influenza vaccinated humans. If variant cases are significantly drifted from previously recommended CVVs or current human seasonal vaccine strains and human antibody immunity is lacking, the variant strain may

be considered for development as a new CVV (Robertson et al. 2011). Prior to the H1N1pdm09, CVVs were exclusively of avian origin, but multiple viruses of swine origin were more recently selected. Despite these efforts, human vaccine preparedness for swine IAV is difficult without the ability to create CVVs for each swine genetic clade or predict which of the 30 current clades may cause a pandemic.

Repeated introduction of human seasonal viruses into pigs, including the H1N1pdm09 lineage, potentiates reassortment and diversification of HA and NA in endemic swine lineages. This diversity has important implications for both swine health, the global public health community, and control of IAV using vaccines. Only one-third of the distinct genetic clades detected in swine globally currently contain a CVV or a virus selected for human seasonal vaccines. Additionally, many of these viruses are distantly related and/or demonstrate antigenic differences from vaccine antisera. Since human and swine IAV evolution are inherently entwined, a system to regularly and rapidly prioritize and evaluate evolving swine IAV in the context of human risk should be part of a pandemic preparedness plan. Surveillance in swine must continue to be a priority for animal and public health, with priority given to geographic areas with high levels of swine IAV diversity, rapid evolution, production practices that support viral transmission and migration, as well as specific animal-human interfaces that promote greater contact between pigs and people.

Antimicrobial Resistant Zoonotic Pathogens

Introduction

We live in a global village and today, more than ever, we realize that microbes (bacteria, archaea, fungi, protozoa, algae, and viruses) do not respect any geographical boundaries, and international travel has enabled the rapid spread of many zoonotic pathogens. There is another ongoing silent pandemic that can only be addressed through a One Health approach: antimicrobial resistance (AMR) (Strathdee, Davies, and Marcelin 2020). Human, animal, plant (specifically crops), and environmental health are interconnected such that a collaborative, multisectoral, and transdisciplinary approach–working at the local, regional, national, and global levels–is imperative if we want to curtail AMR (PACCARB 2021b, UK-SIN 2018). One Health provides a framework for understanding the complexity of highly integrated etiologies surrounding AMR. A One Health approach requires full engagement with disciplines beyond human and veterinary medicine and environmental science. In the case of AMR, we also need, for example, economists, anthropologists, agronomists, hydrologists, epidemiologists, social scientists, and manure management specialists. A multidisciplinary One Health approach will break down the inherent barriers that surround our disciplines, our funding mechanisms, our practices, and our educational curricula. Moreover, One Health can assist in showcasing the benefits of collaboration, the sharing of surveillance data, conducting joint analyses, and disseminating information on follow-up AMR action items. One Health has been heralded as a necessity to address zoonotic diseases and is especially relevant to addressing AMR, which is often referred to as the quintessential One Health issue. AMR is the ability of a microorganism to stop an antimicrobial (such as antibiotics, antivirals, antifungals, antimalarials, and anthelmintics) from working against it (e.g., bacteria often become resistant naturally through the acquisition of transmissible genetic elements, such as plasmids, that carry several resistance genes.). The use and misuse of antimicrobial drugs in humans, animals, and plants across the globe have all contributed to the emergence of AMR in bacteria, thereby reducing the effectiveness of antimicrobial drugs for treating diseases. The antibiotics used to treat infections may be the same or similar in humans, animals, and plants; the manufacture, use, and disposal of antibiotics in all settings can potentially drive the emergence of resistance. When antibioticresistant bacteria arise, they may spread among humans, animals, and the environment. A One Health approach recognizes the interconnectedness between the health of people, animals, plants, and the environment and encourages a collaborative response to the threat of antibiotic resistance (USDHHS 2020).

The Silent Pandemic

The use of antibiotics has been rising across the globe, as exemplified in the 2000-2015 report from 76 countries stating that antibiotic consumption had increased 39% (Klein et al. 2018). These findings emphasize the need for global surveillance of antibiotic use in humans, animals, and plants to support policies that embrace antimicrobial stewardship while providing access to these life-saving drugs.

The CDC Antibiotic Resistance Threats Report – (CDC 2019a) indicates that antibiotic-resistant bacteria and fungi cause more than 2.8 million infections and 35,000 deaths in the United States each year. In 2019 the World Health Organization's Interagency Coordination Group (IACG) on Antimicrobial Resistance released a report (WHO IACG 2019) warning that drug-resistant diseases could cause 10 million deaths each year by 2050 and damage to the economy as catastrophic as the 2008-2009 global financial crisis if no further action is taken. By 2030, antimicrobial resistance could force up to 24 million people into extreme poverty. In 2019, a global survey estimated that 4.95 million people died from illnesses in which bacterial AMR played a part, of those, 1.27 million deaths were the direct result of AMR (ARC 2022).

The WHO-IACG recommendations recognize that antimicrobials are critical to safeguard food production, safety, and global trade, as well as human and animal health, and it clearly promotes responsible use of antimicrobials across sectors. The report also highlights the need for coordinated and intensive efforts to overcome antimicrobial resistance: a major barrier to the achievement of many of the United Nations' Sustainable Development Goals (United Nations 2021), including secure and safe food, sustainable farming systems, and clean water and sanitation.

Addressing antimicrobial practices in crops must not be overlooked because traditionally antimicrobials are applied to crops preventatively, at pre-bloom or at bloom (PACCARB 2021a). This practice is different from those in human and animal health where antimicrobials are generally given

following the diagnosis of an infection. There is a growing concern with emerging resistance in fungi that is likely related to the increased use of fungicides for crops and plants around the world. Antimicrobial stewardship is needed across the entire One Health spectrum: human health, animal health, crop health, and environmental health. Overall, this will necessitate effective collaborative education and practice in which students and professionals from human, animal, plant, and environmental health disciplines learn about, from, and with each other, as well as work together to achieve greater One Health outcomes (PSCCSRB 2021b, NASEM 2020) (See Figure 4).

Collaborative Actions

In addressing AMR, it is paramount that production agriculture and food security be sustained and that means keep-ing our livestock healthy. The FDA, through a collaboration started in 2013 involving the public as well as the public health, animal health, and animal agriculture communities, developed and implemented a feasible strategy to assure that public health is protected and that the health needs of animals are addressed. The strategy led to a successful transition of the use of medically important antimicrobials that are used in the feed or drinking water of food-producing animals to veterinary oversight, and the elimination of the use of these products for production purposes (e.g., growth promotion and increased feed efficiency) by 2017 (USDHHS 2020). Following this action there was a 41% reduction in the sales of antimicrobials and a further enhancement of antibiotic stewardship in veterinary settings (USFDA 2020b) (See Figure 5).

Antimicrobial stewardship is a coordinated strategy for prescribers of antimicrobials that is designed to improve the appropriate use of antimicrobial agents to optimize clinical

Figure 4.   Antibiotic resistance, when germs defeat the antibiotics designed to kill them, can develop and spread across settings. It can affect our progress in health care, food production, and life expectancy. Antibiotic resistance is a OneHealth problem—the health of people is connected to the health of animals and the environment (soil, water). https://www.cdc.gov/drugresistance/pdf/threats-report/AR-EverythingConnected-Settings-Summay-508.pdf
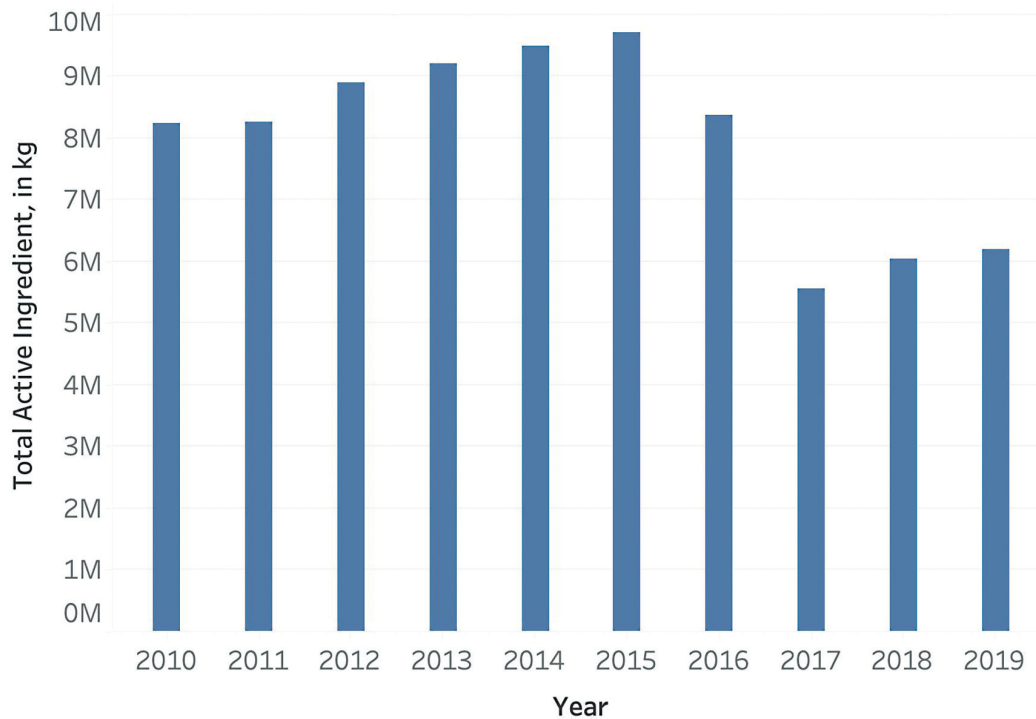
Figure 5. Domestic sales and distribution of medically important antimicrobial drugs approved for use in food-producing animals, actively marketed 2010-2019 (USFDA 202b).

outcomes while minimizing antimicrobial resistance. Many countries have followed suit, but there is still a lot of work remaining to be accomplished. Meanwhile in other countries, especially low-income countries, there is often difficulty in accessing effective antimicrobials to treat diseases in animals and accessing professional veterinary services (Subbiah et al. 2020; WHO 2017; Yam et al. 2019). Moreover, antimicrobial stewardship requires knowledge about the various selection pressures to understand potential risk factors for the development of AMR. Ongoing surveillance and monitoring of AMR and antimicrobial use in human medicine, veterinary medicine, and agriculture is needed at the international level along with open sharing of data (O'Neill 2016; PAHO 20221).

The National Action Plan

Beginning in 2015, the National Action Plan (NAP) was created to help address the AMR problem. The NAP is led by federal agencies and designed to help reduce or prevent AMR. The NAP was built on a One Health platform and has five key strategies with multiple tactics spread across the domains of human, animal, and environmental health (USD-HHS 2020). The key strategies are:

1. Slow the emergence of resistant bacteria and prevent the spread of resistant infections (Stewardship)
2. Strengthen national one health surveillance efforts to combat resistance (Surveillance)
3. Advance development and use of rapid and innovative diagnostic tests for identification and characterization of resistant bacteria (Diagnostics)
4. Accelerate basic and applied research and development for new antibiotics, other therapeutics, vaccines; and alternatives to antibiotics (R&D)
5. Improve international collaboration and capacities for antibiotic-resistance prevention, surveillance, control and antibiotic research and development (Global Collaboration)

There was significant progress in completing many key actions associated with the 2015–2020 NAP. A new NAP (2020–2025) was developed and is being implemented today and still uses the five overarching goals of the earlier plan.

Another important organization emerged in 2018 that emphasized AMR in One Health settings with a special focus in agriculture. The National Institute of Antimicrobial Resistance, Research, and Education (NIAMRRE) is a novel public-private partnership that drives cross-sector engagement and coordinated action to combat the global threat of AMR across humans, animals, and the environment. NIAMRRE
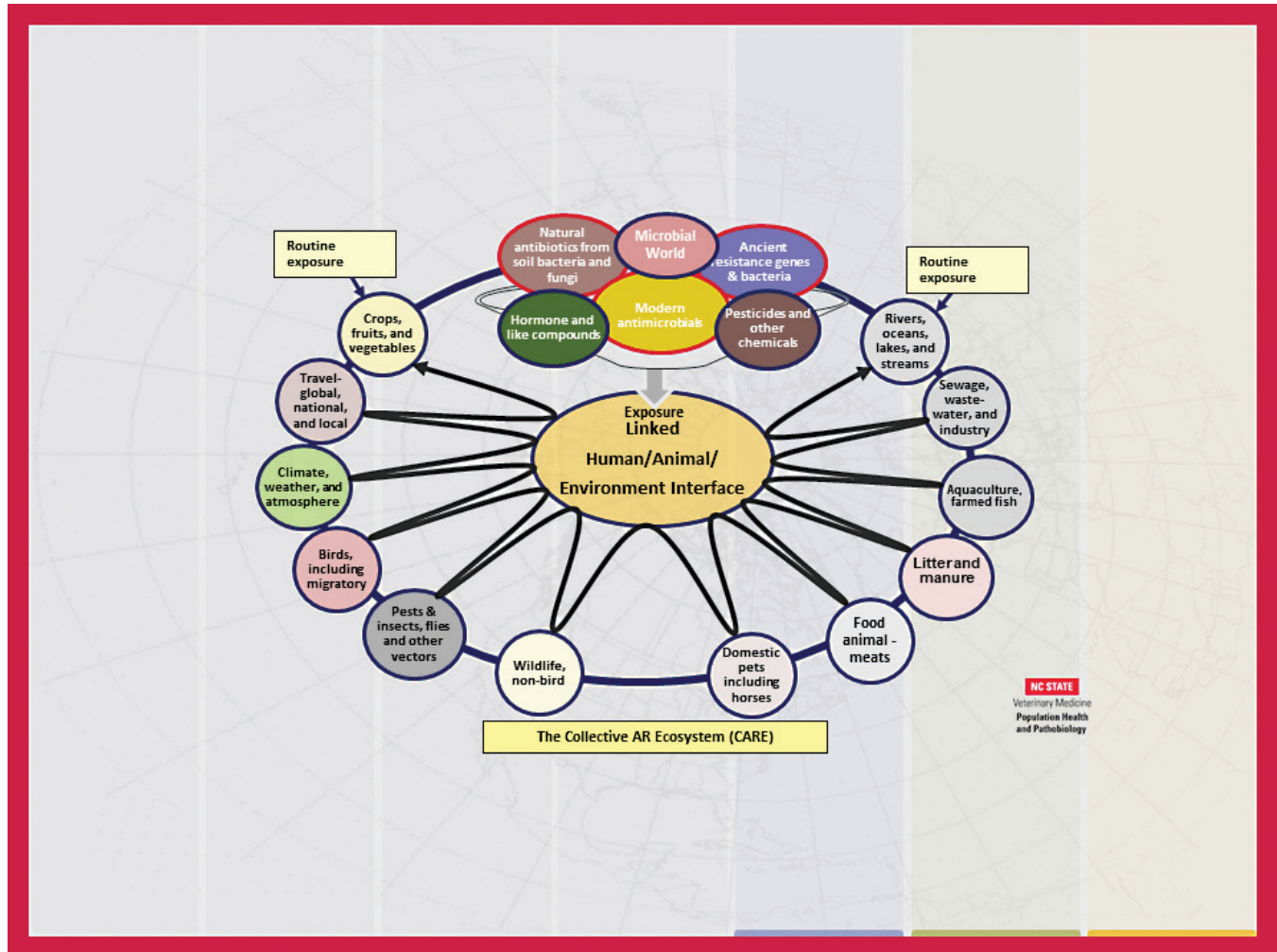
Figure 6.   The collective antibiotic resistance ecosystem (CARE). Source - Paula J. Fedorka Cray, MS, MAS, Ph.D., Professor and Head, Department of Population Health and Pathobiology, College of Veterinary Medicine, North Carolina State University.

helps address prioritized gaps in knowledge related to antimicrobial use, stewardship, and resistance, and advances the NAP (NIAMRRE 2018).

Movements of Pathogens and Genetic Materials Across the One Health Domains

Zoonotic bacteria such as *Salmonella*, *Escherichia coli* (E. coli) and Shiga toxin producing *E. coli* (STEC), *Campylobacter*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Listeria* monocytogenes and *Brucella* are important whenever we discuss AMR, specifically, the role of food animal production in public health (EFSA 2018; EFSA 2019, Friedrich 2019; Leon-Felix et al. 2021; WHO 2017). It is vital that we have access to scientifically sound data relating antimicrobial use and resistance to understand the drivers of resistance and assess the impact of interventions designed to slow the development and spread of resistance (Bright-Pont 2020; Holmes et al. 2016.). Moreover, we need to better understand the role of the environment as a source of antibiotic resistance genes (i.e., resistome) for various pathogenic bacteria. Consider the fact that a concentration of antibiotic that kills or inhibits growth of some bacteria will be selective at the community level. This leads us to examine what is being released into the environment and what is the degradation

process of the various antibiotics and their metabolites that are coming from, for example, municipal sewage treatment plants, pharmaceutical manufacturing sites, or animal-agricultural watersheds (Bengtsson and Joakim Larson 2015; CGIAR 2021, Haack et al. 2016) (see Figure 6). The U.S. National Action Plan for Combating Antibiotic-Resistant Bacteria now includes goals and priorities that embrace the microbiome's role in resistance development (USDHHS 2020).

New Technology and Data Sharing

The good news is that we continue to advance genomic technologies in our clinical laboratories and develop sharable data networks. For example, whole genome sequencing (WGS) can provide genetic evidence of a phylogenetic cluster that links food, environment, and clinical isolates (Allard et al 2020; US FDA 2020a). The National Antimicrobial Resistance Monitoring System (NARMS) has adopted this new genomic approach and sharing the data takes advantage of WGS to provide predicted resistance information in a timely manner (US FDA 2020a). Genotypic resistance is determined by assessing whether genetic sequences in bacterial samples match any genetic sequence(s) associated with resistant organisms, while phenotypic resistance assesses the growth of microorganisms in the presence of antimicrobials. Only by sharing and communicating across a One Health network can more pathogens be identified and characterized sooner, thereby reducing the burden of diseases impacted by antimicrobial resistance.

Alternatives to Antibiotics

Further, groups like the Consultative Group for International Agricultural Research (CGIAR) have embraced a One Health approach, and they will test interventions that enable farmers to improve livestock and fish health via improved nutrition, vaccination, biosecurity, and diagnosis to guide treatment (CGIAR 2021). The development of vaccines, phage therapies, and nanoantibiotics to prevent disease in both humans and animals can reduce the need for antibiotics and is an active area of research at the global level (Cross et al. 2019; World Bank 2017). Phage therapy involves the use of viruses, harmless to people, to attack bacteria causing infections and nanontibiotics are new tools where nanoparticles help deliver higher doses of antibiotics, prolong their release, and create an inhibitory effect on bacterial growth. Concurrently, CGIAR will work with governments to improve antimicrobial stewardship and coordination across sectors through implementation-based research on surveillance, veterinary service provision, and regulatory monitoring and enforcement, while also strengthening public sector capacity and developing policies for antimicrobial use in fish and livestock systems (CGIAR 2021). Recognizing that the interpretation of antimicrobial metrics, without detailed knowledge of the production system(s) from which the metric is derived, has pitfalls, necessitates that we need to try an increase the use and interoperability of data systems to support antimicrobial stewardship across the globe (EFSA 2017; Holmes et al. 2016).

While our current attention is focused on the COVID-19 pandemic, the silent pandemic of AMR is getting worse. COVID-19 is acute and urgent, and AMR is more of a "slowly burning" pandemic but just as serious and also a threat to our global health and security. The CDC, in their 2022 *Special Report: COVID-19 U.S. Impact on Antimicrobial Resistance* stated that the pandemic resulted in more resistant infections, increased antibiotic use, and less data and prevention actions (CDC 2022a). Without effective and sustained actions to address AMR across all One Health sectors, it is possible we will enter a post-antibiotic world much costlier than COVID-19 and profoundly changing human and animal health for years to come.

The Growing Importance of Environmental and Ecological Factors on the Dynamics of Disease

Introduction

Over the past century, two new infectious diseases have emerged every year from natural hosts to humans (Dobson et al. 2020). Such diseases have continued to accelerate in recent decades and most of these have been zoonotic in nature (Jones et al. 2008; Smith et al. 2014). As we know all too well from the recent COVID pandemic, these trends are catastrophic: each year infectious diseases kill at least 9.6 million people (Lozano et al. 2013) and cost around $120 billion in the United States alone (Trust for America's Health 2017). The WHO estimates that there have been over 600 million COVID cases globally with almost 6.5 million deaths as of September 2022. Multiple factors have converged to create a new era of emerging, transmission and reemergence of infectious diseases as the world has become progressively more connected and interdependent. Changes in species biodiversity, environmental and ecological conditions (e.g., habitats, climate) and human population growth have ushered in this new era. Thus, environmental health has now been recognized as a significant domain of the One Health concept.

Defining One Health, Environment and Ecology

The terms environmental and ecological have been used interchangeably and sometimes confusingly; indeed, Einstein is reported to have defined environment as 'everything that isn't me' (O'Riordan 1999). Even so, it is important to define both as well as ecosystem because they are essential to understanding disease emergence, different concepts with different emphases, and importance to One Health: Ecology is the branch of science concerned with the interrelationships of organisms with each other and with their environment; Environment is concerned with context or surroundings (e.g., physical conditions such as habitat and climate or social, cultural or ecological conditions that affect an individual, population or community); and, Ecosystem is a natural unit, ranging in scale from a small pond to the globe, consisting of all animals, plants and microorganisms (biotic) in a given area, interacting with all the nonliving physical and chemical (abiotic) factors of an environment (Alexander and Fairbridge 1999; Levin 2009). The complexity of interactions and multitude of factors are extraordinary, ranging from agricultural encroachment to wetland modification to road construction to coastal degradation to vast expansion of urban environments.

These terms become important when we consider the influential factors or "drivers" of disease (see below) and how ecology, environment and/or ecosystems are involved in the relationships between organisms/pathogens and hosts and among themselves. For example, as species' geographic ranges expand and contract, partly due to increases in human population density, zoonoses arise from exposure to different organisms and/or warmer temperatures (Jones et al 2008; Smith et al. 2014; Stephens et al.2016). Understanding these disciplines is therefore critical to comprehending the risks of disease emergence and transmission.

Mechanisms and Principles of These Factors

Climate change, biodiversity loss, and emerging infectious diseases represent the most significant environmental challenges of our time:

- Global climate change indicates the planet's average surface temperature has risen about 2.12 degrees Fahrenheit (1.18 degrees Celsius) since the late 19th century, a change driven largely by increased carbon dioxide emissions into the atmosphere and other human activities. Most of the warming has occurred in the past 40 years, with the seven most recent years being the warmest; the years 2016 and 2020 are tied for the warmest years on record (https://climate.nasa.gov/evidence/).
- All plant and animal life on this planet has declined 50-68% in last 50 years. At current trajectory, one million species will go extinct by the end of this century (IPBES 2019; Pimm et al. 2014) and modern extinction rates are 1000 time higher than natural extinction rates and future rates are likely to be 10,000 times higher (De Vos et al. 2014).
- Emerging infectious diseases (helminths, bacteria, viruses) have consistently and significantly increased since 1940 (Jones et al. 2013) whilst outbreaks of human diseases, comprising more than 44 million cases occurring in 219 countries, are more diverse and causal mechanisms greater (Smith et al. 2014).
- Principal drivers of global change are habitat transformation, pollution, over-exploitation of natural resources,
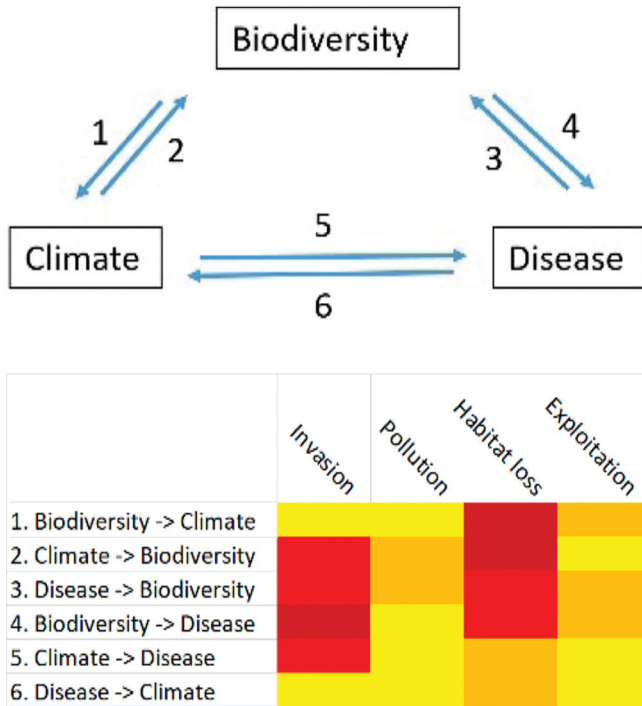
Figure 7.   Climate, biodiversity loss, and disease emergence. Theoretical framework of pairwise interactions (e.g., high incidence- deep red; low incidence- light yellow).

and invasive species.

- These drivers are mediated by changes in the human population size, consumption patterns and socioeconomic factors.

Bivariate interactions (see Figure 7) among these three patterns are well known (e.g., species geographic ranges expand and contract with climate shifts, or zoonoses arise from species decline and warmer temperatures). For example, geographically, on a global scale, changes in climate, biodiversity and disease are congruent ("hot spots"), with high concentrations of vulnerability, in semiarid regions and deltas of Africa and Asia, and river basins of South Asia (Souza, Teixeira, Ostermann 2015).

Drivers

It is the complexity of these interactions, along with synergistic effects and mechanisms of "spillover", that a One Health approach aims to understand, as well as the origins, changes and hotspots of pathogens (Barrett and Bouley 2015; Manlove et al. 2016).

Key to understanding the emergence of new diseases is spillover, the transmission of diseases from wild animal hosts into new populations including humans. A One Health perspective is essential, as it is only when human or domestic animal populations interact with wild animal populations that transmission of zoonotic diseases can occur (Walsh et al. 2020).

Encroachment of humans on wild areas, such as for agriculture, extractive industries including mining and forestry, or to hunt wild animals for food or for sale, are bringing humans into more frequent contact with wild animal populations (Gottdenker et al. 2014). At the same time, anthropogenic forces such as deforestation and climate change are causing local extinctions in some areas and wild species to shift their ranges in others (Algar et al. 2009; Bakkense et al. 2002; Daufresne and Boet 2007). Local extinctions can create a lack of diversity in plants and animals, which can present a greater risk of disease transmission (Heard et al. 2014; Keesing et al. 2020), and range shifts create new combinations of host species and hotspots of potential zoonotic disease transmission (Garcia Peña at al. 2021; Morales-Castilla 2021). Developing accurate, predictive statistical models of spillover and zoonotic disease outbreak risk, that encompass these and other common scenarios, require data on factors that cut-across numerous areas of One Health including ecological (Patz et al. 2004; Schmeller Courchamp, and Killeen 2020; Wilson and Brownstein 2009;), environmental (Daszak et al. 2001; Jones et al. 2013), and socioeconomic (Grace et al. 2012; Molyneux et al. 2011; Wu et al. 2017) factors (Gottdenker et al. 2014, Plowright et al. 2017, Stephens et al. 2021).

Modern 'One Health' Examples

The following examples illustrate the many mechanisms and interactions of animal, human and environmental factors contributing to disease emergence as well as solutions to managing and predicting outbreaks (Patz and Olson 2009).

Lyme disease

Lyme disease is one of the most common vector-borne diseases in the world and the most common in the United States, with an estimated 300,000 cases occurring each year. Lyme disease, caused by the bacterium *Borrelia burgdorferi,* is transmitted by the black legged tick *Ixodes scapularis*. It is a debilitating disease often difficult to diagnose with symptoms including an expanding red rash, fever, headache, lethargy, and repeated episodes of swelling and joint pain that may repeatedly occur for months or years. Meta-analyses reveal that human exposure may occur in grassy and woodland terrain of backyards, neighborhoods, communities, and even golf ranges where wildlife inhabit; higher rates are observed within an area of 500m from home (Firschoff et al 2019; Standaert et al. 1995). The occurrence and ex-

pansion of Lyme disease is a classic 'One Health' case of zoonotics exemplified by interconnectedness and changing distributions of animal (wildlife), environmental (woodland, tall grassland), and human (increasing densities, more rural, "wild" environs) characteristics. A disease such as Lyme also raises greater concern regarding effects from substantial losses of biodiversity because disease transmission tends to decline in areas with higher species richness. The so-called "dilution effect", whereby pathogens spread at lower rates within more diverse ecological communities (Keesing and Ostfeld 2021b) is diminished when populations decline and species go extinct.

West Nile

Another pathogen that illustrates the importance of a One Health perspective is West Nile virus (WNV). In the United States, WNV is now the most common mosquito-borne illness (CDC 2022b). For example, between 2009 and 2018 there were more than 21,000 reported cases (McDonald et al. 2021). This is likely an underestimate. The disease is difficult to track because many cases, at least 74% (Mostashari et al. 2001; Zou et al. 2010), are asymptomatic in humans. However, this does not mean that WNV is inconsequential: in agricultural settings, it produces a form of encephalitis with high (>30%) mortality in horses (e.g., Porter et al. 2003), and many herds must now be vaccinated in the United States and Europe. WNV can also be a conservation concern. Changes in rainfall and temperature due to climate change also have the potential to affect populations of mosquito vectors that drive WNV transmission and increase the potential for outbreaks. For instance, in 2018 Europe experienced the largest outbreak of WNV yet recorded in the region, with more than 2,000 cases (Camp et al. 2020). This outbreak was attributed to a period of unusually high rainfall during the overall fourth warmest year ever recorded (Camp et al. 2020). Climate change and globalization have also accelerated the spread of the disease. Since being introduced to the New World, WNV has become extremely widespread and is now found throughout many parts of South America (Martins et al. 2019) and is endemic in North America as far north as Ontario, Canada (Hadfield et al. 2019). However, bird species richness is negatively correlated with mosquito and human infection rates of West Nile virus (Ezenwa et al. 2006), suggesting that species biodiversity may dampen down human disease risk.

Ebola

Among zoonotic diseases that have caused large outbreaks (>10,000 cases) in modern times, outbreaks of Ebola have been among those with the highest mortality. For example, during the 2014-2016 Zaire ebolavirus outbreak, human-to-human transmission caused at least 11,000 fatalities before it was controlled (Kamorudeen et al. 2020), and other outbreaks of Ebola have had fatality rates of up to 90% (Kuhn 2008). Perhaps in part because of the high mortality, there has been intensive research effort to understand these outbreaks (Kuhn 2008). This has led to the realization that human, animal, and environmental factors of One Health have contributed to the outbreaks. Some of the reported factors include socioeconomic factors such as wild game hunting and consumption (Georges et al. 1999, Leroy et al. 2009), armed conflict (Maurice 2000; Stanturf et al. 2015), inadequate health systems (Shoman, Karafillakis, and Rawaf 2017), poverty (Fallah et al. 2015; Heymann et al. 1999), as well as ecoenvironmental factors such as the transition between wet and dry seasons (Schmidt et al. 2017) and seasonal variation in bat abundance (Amman et al. 2012; Leroy et al. 2009,). Therefore, understanding risk factors for future outbreaks will inevitably require a diverse but unified perspective like that provided by one health.

The 100 Largest Outbreaks

One of the most pressing questions of our time is understanding which diseases and what environmental settings have the greatest potential to generate the next global pandemic. While undoubtedly causing considerable mortality and economic impacts in aggregate (Jones et al. 2008; Murray et al. 2015; Smith et al. 2014), most modern outbreaks are relatively quickly contained and are limited to fewer than 45 cases (Berger et al. 2017; Stephens et al. 2021). Nevertheless, outbreaks that escape control and affect entire regions or even the globe (Dawood et al. 2012; Dong et al. 2020; Ryan et al. 1987,) still occur with alarming frequency. In a study that compiled global data on 4,463 outbreaks of bacterial and viral zoonotic pathogens since the mid-1970s (Figure 8a), Stephens and colleagues (2021) found that the number of large outbreaks with 100 or more cases is either stable or increasing over time. A comparison of pathogens and reported drivers of the 100 largest outbreaks relative to a random sample of the rest (Figure 8b) revealed that large outbreaks were more complex, with more proximate drivers (i.e., factors reported to contribute to the start on an outbreak, outbreak spread, or to hamper control efforts) compared to random outbreaks. This implies that a One Health approach leveraging perspectives from multiple disciplines may be useful. It was also observed that the largest outbreaks were disproportionately caused by eco-environmental drivers including contamination of water systems, extreme weather patterns, and changes in the population density of insect vectors such as mosquitoes.
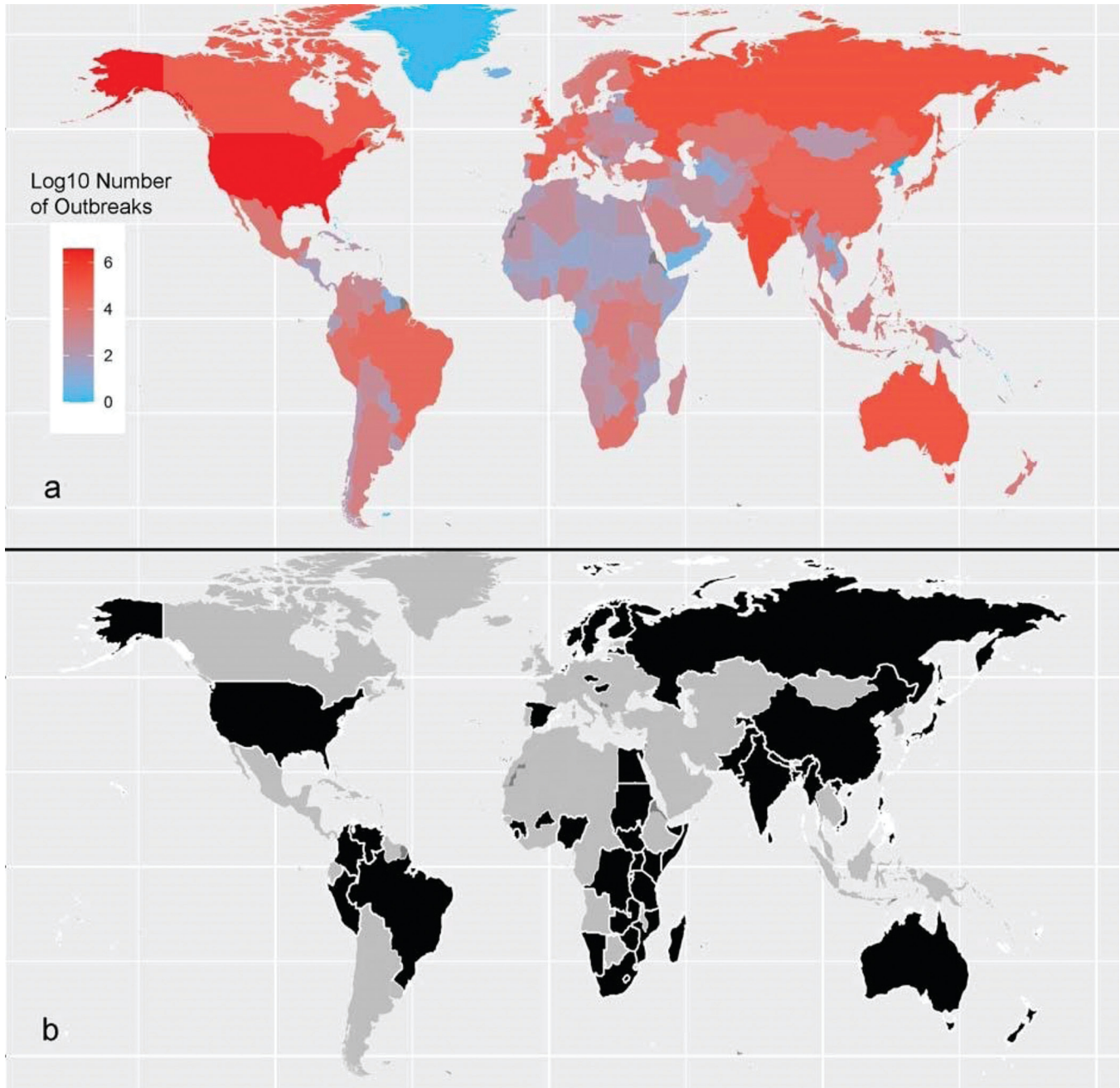
Figure 8 a,b. Global distribution of zoonotic outbreaks (from Stephens et al. 2021). Locations of 4463 potentially zoonotic outbreaks in a global data set (a) and countries that had at least one of the 100 largest outbreaks (b), in terms of number of cases (each with thousands to hundreds of thousands of cases). Countries in gray lacked outbreaks in each respective data set. Outbreaks of zoonotic diseases are a global issue.

The Benefit of Studying the Influence of Environment and Ecology

Because of the growing importance of eco-environmental factors, new knowledge and understanding will greatly advance our ability to ameliorate or prevent diseases or negative impacts on health. Motivated by modern weather forecasting, Han and Drake (2016) developed a three-pronged approach for prediction of infectious disease that includes monitoring, warning, and reactive responses. Each system involves observational and funding agencies, forecasting analytics (disease risk mapping, data mining, statistical modeling), and requisite organismal, human and environmental data. Adopting such an approach with fast-paced precision and coordination of national and global agencies, 'smart surveillance' of emerging infectious diseases in hotspots of lower latitudes of tropical Africa, Latin America and Asia will curtail emergence before it occurs (Jones et al 2008). Further, the cost savings of preventing future pandemics before they happen, focusing on monitoring wildlife, reduction of spillovers, early detection programs, deducing deforestation, and ending wild meat trade, will save trillions of dollars and countless lives; cost estimates for preventive measures may be as small at 2% of the current COVID-19 pandemic over a 10-year period (Dobson et al. 2020).

Future

An important development for the future and successes of One Health is to broaden our educational and research cultures to integrate animal, human and environmental approaches. This will not be easy, particularly at a time when we are flooded with information, fast-moving social networking, hesitancy and denial of science as well as language barriers amongst necessary bodies of information required for advanced training (Rabinowitz et al 2018: see Figure 9).

To date, One Health has largely been the domain of veterinary medicine (Gibbs 2014), excluding ecological and environmental approaches (Barrett and Bouley 2015), though many veterinary schools have developed outstanding programs and the diversity and integration of research has improved (Manlove et al. 2016). We need to advance more well-rounded curricula of planetary concerns in addition to emerging diseases and zoonoses (Rabinowitz et al. 2018). With human population numbers increasing to 9 billion by 2050, we need to expand One Health to truly integrate climate and habitat changes, wildlife conservation, food security, and modern agricultural practices. Advances will be made by developing core competencies in one health (i.e., integration of animal, human and environmental sciences), elucidating changes in terminologies of relevant areas that reflect connectedness (e.g., land use and disease exposure),
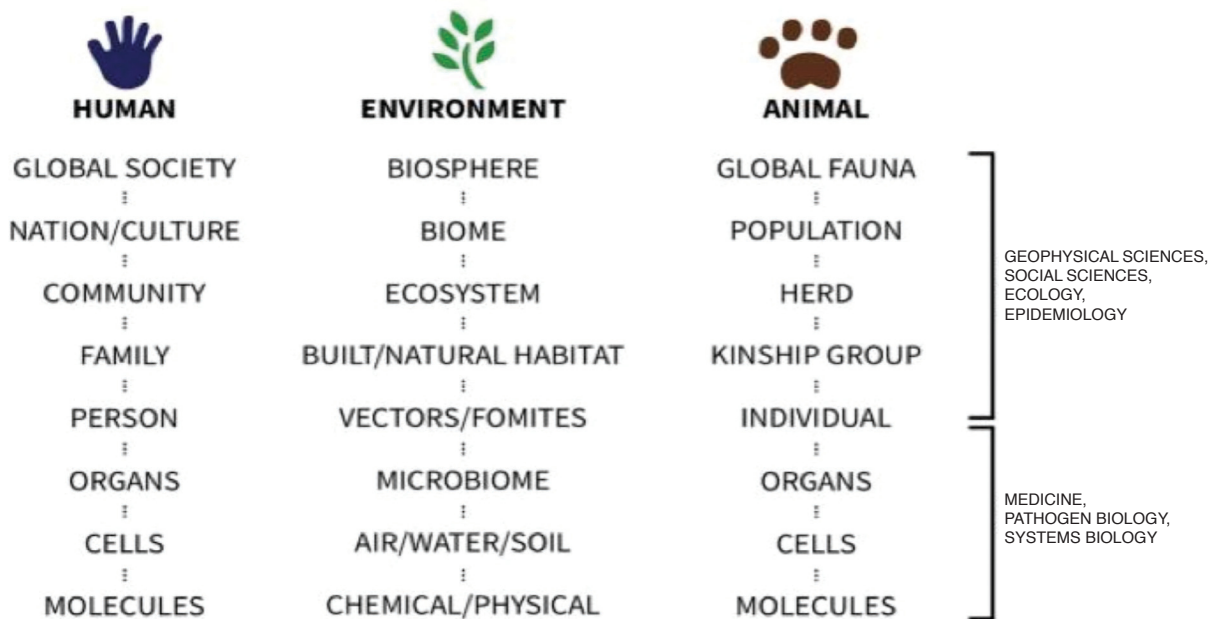

Figure 9.   One Health is a complex topic. While there is consensus for expanding scope of One Health, this is difficult because of the measures, concepts, terms and overall different scientific approaches span across human, environmental, animal fields of study.

and continuing to focus on applied and practical training particularly in clinical veterinary, agricultural and public health settings (Togami et al. 2018); indeed, the majority of existing One Health programs lack any ecological or environmental understanding (see also Lerner and Berg 2017). There are encouraging actions on the horizon to improve this situation. The WOAH, FAO, WHO, and, the Environmental Program of the United Nations have formed a quadrilateral agreement and action team, termed the One Health High-Level Expert Panel (OHHLEP), that has incorporated more environmental/ecological scientists in its membership and planning and has also proposed an expansion of the definition of One Health to be more inclusive of environmental/ecological perspectives and issues.

Given the increasing rate of emerging novel diseases, One Health is a necessary paradigm for prevention and earlier and more effective interventions that will save tremendous capital in human lives and dollars and in the end preserve the health and sustainability of our planet.

Special Opportunity for Synergy Among Animal Agriculture, Human Health, and the Environment – a One Health Approach

Introduction

Disease models suggest that the next pandemic is likely to originate from animals. More specifically, experts believe that "hot spots" can be identified to receive priority attention and focus in implementing mitigation strategies. For instance, the interface between wildlife and people at sites of environmental disruptions are especially high risk for zoonotic transmission. However, it is also feasible that the next pandemic could originate from food animals involving a highly virulent influenza virus or even an antibiotic-resistant pathogen. This threat extends well beyond zoonotic spillover to humans; it has potential to profoundly impact the worldwide volume of food animal production.

With the global population expected to grow to between 9-10 billion people by the middle of this century, the commensurate increase in demand for food production will be exceptionally challenging to meet—producers will need to double production in just the next few decades. It is estimated that almost 90% of the global population growth will occur in low-and-middle income countries (LMIC), particularly those in Africa and Southeast Asia. As populations in those regions make economic gains, they have traditionally demanded more protein in their diets from animal sources. Thus, the global population of food animals will need to increase by approximately 20 billion animals to meet this imminent demand, especially in regions experiencing the greatest human population growth.

In recent decades, the production of food animals has become significantly more efficient due to advances in genetics, nutrition, production practices, and disease prevention. Despite these positive developments, the public and policymakers have often focused on adverse effects of modern production systems. This unfortunate divide will only deepen if zoonotic diseases continue to be associated with food animal populations. Fortunately, adopting the holistic and integrated One Health framework could help to address the complex and socially vexing problems facing animal agriculture, because the approach recognizes that the health of people, animals, plants, and the environment are so closely related that improvements in any one of those domains can spur progress in the others.

Animal Agriculture: Transitions and New Challenges

Agriculture has made numerous transitions in the past to meet demands for food, improve efficiencies, and enhance nutritional quality. However, the industry now faces challenges due to intricate and rapidly changing factors that have yielded a global food animal population that is more vulnerable to the heightened risks of disease transmission and environmental degradation. Contemporary issues such as intensified production systems, use of antibiotics, animal welfare, globalization of trade and food systems, sustainability, food security, and impacts of climate change have coalesced to create flashpoints and a problematic business environment. In addition, these drivers have also generated conditions that are conducive to the occurrence and spread of zoonotic diseases, some with pandemic potential.

The need to produce greater volumes of food—and do so more cheaply—to serve rapidly expanding human populations has led to changing production practices across agriculture. This has resulted in trends toward larger farms and ranches, intensification, global trade, vertical integration, antibiotic use, and concerns about animal welfare, and environmental degradation. Consequently, tension has emerged between animal production practices and public health, resulting in greater scrutiny, criticism, and blame directed from consumers and policymakers toward the animal agriculture industry. Particularly contentious issues concern antibiotic use in animal production and the spillover of resistant organisms into human populations. This tension has been amplified in countries with higher incomes that can pay for foods with special characteristics, grown under special conditions, or differentiated by social values. In addition to the concern of antimicrobial resistance, animal agriculture practices with increased density, mobility, and global connectivity are contributing to an evolving and riskier global disease ecology.

The next transition for food animal agriculture will inevitably be shaped by a broad range of unprecedented factors, including greater consumer demands and criticisms, the increasing influence of food retailers, changing global demands, and the industry's shift from a culture of fierce independence to one of collaboration and recognition of its new interdependence. Animal agriculture should not become defensive and remain independently isolated. Rather, the in-

dustry should be part of a coalition and collaborative with integrated intersectoral teams that work together to help address their shared challenges. The next step is to join forces with other professions and experts toward collective action, a focus on mutual interests, and the design of new strategies to protect and promote human and environmental health while improving and ensuring greater animal health and welfare. While not always appreciated by public health and some consumer groups, this transition must also be implemented as part of a profitable business model for agriculture.

It is critical that this next transition be based on the essential tenets of One Health, because past solutions and thinking will no longer be effective in confronting today's challenges. This approach should envision animal production as a holistic and integrated enterprise, by developing and implementing strategies to expand sustainable, healthier systems for the animal populations that concomitantly improve human and environmental health. Although the One Health framework to accomplish this is already available, it has not been fully embraced by agriculture: this has been a missed opportunity. However, adopting this approach to concurrently improve human, animal, and environmental health is an invaluable opportunity to give the industry a much-needed reset. This shift in thinking should be considered as just another transition, which has been a common denominator of past successes. Importantly, a transition in intensive animal agriculture is already beginning, as evidenced by advances in biosecurity to prevent infection and reduce the need for antibiotics. Further examples are the shift away from caged-layers to cage-free egg production, the movement toward elimination of gestation crates for sows, and the transition from veal calf stalls to group housing.

Benefits of Animal Health to Public Health: Envisioning a Health Continuum

Although not often fully appreciated, good animal health can also benefit the health of humans and our ecosystems. Therefore, the health of animals and health of people should be considered as a continuum, not as separate and disconnected entities. Good animal health is intertwined with good public health, as well as contributing to issues such as food safety and security. Examples of the broader impacts of improving animal health come from successful programs to eliminate and control diseases among U.S. poultry and livestock that are still found in much of the world, such as foot and mouth disease, pseudorabies, classical swine fever, Exotic Newcastle Disease, Pullorum Disease, and Fowl Typhoid. The eradication and control of those diseases has helped to improve production, reduce costs, and reduce ani-

mal suffering, while also generating both public health and economic benefits to the U.S. population. For instance, the U.S. food supply has progressively become safer and relatively cheaper for U.S. consumers. There are also specific mutual benefits and value-added dimensions in eliminating zoonotic pathogens. For instance, programs such as the successful eradication efforts to rid U.S. livestock of brucellosis and bovine tuberculosis have not only benefited the health and wellbeing of food animals but have also eliminated human exposures and infections from these zoonotic threats. Similarly, the eradication of canine rabies from the U.S. succeeded by implementing an effective vaccination program in collaboration with veterinary practitioners; this achievement directly benefited human health as well.

In considering the concept of this continuum, there is also an important group of biologic agents, termed select agents, that are relevant and could threaten human, animal, and plant health and be used as potential bioweapons by terrorists. In reviewing Select Agents, Category A or highpriority agents, 80% of these pathogens that could be used by bioterrorists are zoonotic (Ryan 2008). The Department of Health and Human Services and the United States Department of Agriculture are both responsible for regulating this group of pathogens and potential diseases. Although these departments have separate lists of select agents to regulate, there is also an overlapping group of concern to both. For example, the CDC's highest priority select agents and diseases include anthrax, botulism, plague, tularemia, viral hemorrhagic fevers, and smallpox. All of these are zoonotic except smallpox. The intentional introduction of any of most of these pathogens could have a significant economic impact on agricultural markets, exports and cause food shortages. Such outbreaks could also have severe morbidity and mortality results in people, psychologic impacts and threaten our national security. This reality reinforces the need for agriculture to be closely aligned with One Health activities and the need for integrated surveillance efforts and the coordination and collaboration of diagnostic systems, research and disease prevention, detection and response. An additional benefit is that animals can provide an early warning to people if clinical signs are detected in animals before the emergence of human illness.

The growing global problem of food security also highlights the relevance of the animal-human health continuum. The same drivers and factors underlying our new era of emerging zoonotic threats to humans have also increased the vulnerability of animals and plants to multiple disease outbreaks. Producers are especially concerned about transboundary disease threats that can move rapidly across country borders and infect food animal populations worldwide, often resulting in epidemics and pandemics affecting food animals themselves. For instance, China recently lost half of

its hog population due to an outbreak of African swine fever. Food animal epidemics and pandemics can cause starvation, loss of valuable nutrients, and create major public health crises. Even animal diseases that are not zoonotic can have a profound impact on public health, further highlighting the importance of the animal and human health continuum. A current and relevant example is the impact of poultry losses due to HPAI. The poultry industry experienced serious financial losses to production and poultry populations. Such losses from this outbreak due to the disease and/or culling practices can lead to a lack of animal-based protein and other nutrients in the diet of young children in Low- and Middle-Income Countries (LMIC) which can further cause physical and l developmental disabilities.

The transition of animal agriculture to embrace food safety also demonstrates the value of considering public and animal health as a continuum. Producers and farmers learned that their responsibility for food safety did not end at the farm gate, but rather it carried over throughout the entire food chain. Similarly, livestock and poultry producers have further responsibilities well beyond ranches, farms, and production systems. Reducing antimicrobial resistance, improving environmental health, ensuring conservation, and implementing biosecurity—including protection from zoonotic diseases—are all tied to animal agriculture. New production systems informed by the One Health framework could incorporate changes to improve human and environmental health, such as adopting and responding to life cycle assessments (LCA) and climate-smart agriculture systems, that would extend production systems beyond farms and add special value to food animal products.

Building on Recent Success

Recent successes in policy and practice across the agricultural industry can serve as a platform to catalyze further progress. For instance, there have been notable advances in efforts to control antimicrobial resistance (AMR) in recent years. In 2015, the FDA issued new guidance to eliminate the use of medically important antibiotics to promote growth and production efficiency. Subsequently, antibiotic use by animal agriculture in the U.S. was reduced by over 40%, an achievement that was lauded by public health. Simultaneously, the G-7, G-20 and United Nations have identified One Health as the cornerstone to address AMR in people, animals, and the environment. Thus, animal agriculture was incorporated into coherent and integrated national and international plans to improve health across all the domains of One Health. The U.S. National Action Plan to Combat AMR Bacteria acknowledges the importance of agriculture and envisions it as part of a guiding coalition in helping to address the difficult and complex issue of AMR.

The shift to a One Health perspective should be considered as yet another example of innovation to promote and advance agriculture. The agriculture industry has always been innovative and early adopters of technology, as demonstrated by research and development in genetics, nutrition, precision agriculture, vaccines, diagnostics, and animal health management. Recent adoption of climate-smart production systems is proactively helping farmers and producers to address the impacts of climate change by adopting new practices and interventions to prepare for major disruptions in production. This type of One Health strategy could promote environmental and human health as well as the health of our crops, plants, and food animals. However, effective implementation of One Health, particularly in LMICs, depends on having adequate numbers of highly trained food animal veterinarians, both in government agencies and to serve the needs of producers. The WOAH recently emphasize the need to improve veterinary education and the quality of professional veterinary services in LMICs. More broadly, the One Health approach—if widely adopted—would change the narrative about the role of agriculture in disease control and emphasize the positive societal contributions of agriculture beyond food.

A New Era for Zoonoses and Animal Agriculture: The Path Forward

Today's fast-growing and increasingly mobile human and animal populations, coupled with the huge, interconnected global food system, has created an unparalleled 21st century mixing bowl—that is, a novel disease ecology where pathogen exposure and transmission across species is almost guaranteed. There is nowhere in the world from which we are remote and no one from whom we are disconnected. Numerous animal microbes are only a few mutations away from initiating new spillovers and outbreaks infecting humans.

This new era of zoonoses and elevated risks demands new thinking and approaches. Rather than arguing about responsibility and assigning blame, now is the time to bring domestic and global animal agriculture into the fold of the holistic and integrated One Health approach. Strategies implemented within this approach should focus on building effective surveillance systems, developing early detection and response systems, engaging in new dialogues and collaborations across the health and environmental sectors, garnering greater investment in R&D and animal health infrastructures, and enhancing preparedness and response activities. Specifically, animal production should adopt effective biosecurity strategies, promote vaccines, and readily share information. Such new strategies must be compatible and supportive of an ap-

propriate business model that is fair and profitable for producers but not inwardly focused.

Today's complex and difficult problems cannot be solved using fragmented and singledimension approaches developed in the past. The escalating scale and scope of the risks associated with zoonoses has created an urgent need for systems thinking, in which human health and environmental health are situated on a continuum with animal health. Therefore, the animal agriculture industry should commit to take part in a new community health effort under the common principles and practices of a One Health approach, including engagement with intersectoral One Health partners and involvement in the development of national plans to improve human, animal, and environmental health. Without this critical transition, it is likely that old tensions will persist and worsen, and an opportunity to create broad societal benefits will be squandered to the detriment of all, including the food animal industry.

Conclusions and Recommendations

At the entrance of the National Archives Building in Washington DC, two prominent statues sit across from one another. On one side a statue depicts an old philosopher holding a closed book representing our history and looking down the corridors of time. At the base of this statue is etched the adage, "Study the Past". Opposite of the philosopher is another statue depicting a youthful woman holding an open book symbolizing the future which has yet to be written. She gazes in contemplation of things to come and etched at the base of her statue is the phrase, "What's Past is Prologue" reflecting Shakespeare's quotation from the Tempest.

These opposing messages are symbolic of today's perspectives involving emerging infectious diseases including zoonoses. While we study history and now better understand that profound anthropogenic factors are creating a perfect microbial storm and altering our path to the future, our actions are often reactive and ineffective. Even with warning lights blinking red, our priorities and crises fade in the face of competing pressures and the reluctance to change the status quo. Constantly, we have seen epidemics and pandemics evaporate from our collective memories. For each new crisis, it is common to reinvent strategies de novo rather than learn lessons of the past.

Yet as we contemplate the future, Shakespeare's words hold an important meaning. What's past is prologue suggests that what has taken place in the past, especially over the last three decades, sets the stage for tomorrow. However, our experiences and lessons learned are part of preparing for opportunities to come. The future of zoonotic diseases and One Health is an open book yet to be written but with new thinking and collaborative actions, we can mitigate the risks of these diseases.

It is interesting to note, that we seldom see the full Shakespeare quotation which reads, "Whereof what is past is prologue, what to come, in your and my discharge." The second part of the quote is key and suggests that our future is not predetermined, rather, it will be the product of our individual and collective actions "discharged" today. The physician and epidemiologist, Dr. Larry Brilliant stated that outbreaks are inevitable, but pandemics are optional. The difference lies with appropriate and effective actions that must be planned and implemented across the interdependent domains of One Health. Your and my discharge is essential because the stakes are incredibly high. Failure to address persistent zoonotic outbreaks, especially pandemics, can prevent us from effectively achieving global health targets and sustainable development goals relating to food security, poverty, child mortality and development, environmental sustainability, economic growth, and other vital issues.

The preceding chapters in this report help to elucidate the nature of zoonotic diseases, describe the drivers of emerging diseases, highlight the growing societal impacts of these infections, and emphasize both the need for a One health approach and the need to rethink and execute new innovative actions. The following recommendations and some suggested solutions are based on taking action or discharge that can alter things to come and what we write in our chapters of the future pertaining to zoonoses and other infectious diseases.

Recommendations

1. Change the Narrative

A narrative is the capacity to justify and legitimize a cause, in this case One Health, and to build advocacy and a broader coalition. Narratives are sources of power, influence, and drivers of change. SARS-CoV-2 is the third zoonotic coronavirus to spill over into human populations with profound global impacts just since the start of the 21st century. Early estimates suggest that SARS-CoV-2 has become over a $15 trillion pandemic. Recent experiences and significant costs of Ebola, influenza, and SARS are further evidence that zoonotic diseases are critical global threats. The world has been disrupted socially, economically, emotionally and with extreme health consequences. This ongoing outbreak has taught us that such events are central and pertinent to our national security and that zoonotic diseases must be a critical part of pandemic preparedness. Certainly, commissions and studies will follow this pandemic which will offer special opportunities for discussion. As devastating as SARS-CoV-2 has become, other zoonotic disease pandemics could be even worse such as a novel influenza virus or even an antimicrobial resistant (AMR) microbe. It is highly likely that the next pandemic will originate from animals, and we should be proactive in discussing and preparing for this reality. The prevention, early detection and response of an emerging zoonotic disease is exceptionally costeffective. It has been estimated that, based on the present value of prevention over 10 years, that that the cost of prevention would equal just 2% of the cost of living with the disease (calculation for SARS-CoV-2) (Dobson et al. 2020.) Antimicrobial resistance (AMR), a current silent global pandemic, could cost the world 100 trillion dollars and 10 million annual deaths by 2050 if no action is taken (O'Neill Report). The concept of One Health needs to be central to the narratives and discussion, not only of its disease prevention and financial benefits but also its broader social, environmental and health benefits.

Over the last several years, the G-7, G-20, and the United Nations have touted One Health as the necessary platform to address antimicrobial resistant diseases. International public and animal health organizations including the WHO, WOAH, and the FAO have also recognized the benefits of One Health and have combined their efforts to work together using this approach. One Health is an approach that emphasizes prevention and shifting disease detection and intervention closer to the origin of the threat – often focused on domestic and wildlife animal populations, and environmental sites. More and more, there is an understanding that emerging and re-emerging zoonoses are complex events and involve multiple sectors and disciplines. We are living through multiple threats to the health of people, animals, plants, and the environment with potentially huge costs and global disruptions that go well beyond healthcare. Zoonoses hit poor populations especially hard where millions of poor animal keepers rely on their animals for their food and livelihood. Zoonoses are constant and highly consequential threats to global health yet are often neglected in discussions of global health security. There is an acceptance today of the impact of climate change and its effect on infectious diseases, especially the expansion of vector-borne diseases. A new field of climate and health is emerging, and One Health and zoonotic diseases are critical to understanding and dealing with this evolving science and central to this discussion.

We can no longer think of zoonotic diseases as being something found in remote parts of the world and not relevant to our lives. The new acceptance, awareness, and support of zoonoses and One Health must be included in our national security plans and pandemic preparedness programs. The public health and economic impact of a zoonotic global pandemic can rival the societal impact of traditional wars and deserves similar attention and resources. All the conditions and factors that have propelled us to a new era of zoonotic diseases remain in place and have even intensified and accelerated. Thus, we will certainly experience more outbreaks and pandemics, so it only makes sense to proactively plan for this reality in our national and global pandemic preparedness programs.

Potential Actions

- Continue to solidify support for the G-7, G-20, and U.N. in their One Health commitments
- Engage in discussions on climate change and ensure that zoonoses and the One Health platform are central to their future planning and mitigation activities
- Build on the success of the government's National Action Plan for combating antimicrobial resistance and ensure that there are specific goals and actions across the One Health spectrum to prevent AMR and potential emerging zoonoses
- Commit to preventing and ameliorating zoonotic diseases through new pandemic preparedness programs

▪ Encourage and support an updated Global Health Security Agenda that includes a specific One Health Security component

2. Establish One Health Global Surveillance System(s)

There have been investments and improvements in surveillance systems on a global basis; yet they are still limited and even more limited involving the domains of One Health. A One Health Global Surveillance System would include the systematic collection, analysis, interpretation, and dissemination of information concerning people, animals, plants, and the environment. Such information could inform decisions for effective, evidence-based interventions for the prevention and mitigation of diseases. Based on our knowledge that 75% of newly emerged human infections are zoonotic, the ability to identify threats and microbes quickly and accurately in all domains of One Health is essential. Future zoonoses will likely emerge from Low-and Middle-Income Countries (LMIC) with the fastest growing human and animal populations and a desire for more foods from animal sources. However, these are the countries with the most limited capacity to build and implement surveillance systems within and across sectors. The idea that a threat anywhere is a threat everywhere is true but not well appreciated. More and more, zoonoses are emerging from wildlife, foods and vectors which are associated with changes to our trade, the global food system, and ecosystems including contaminated water sources. We understand the importance of the environment and especially water in the dissemination of AMR microbes and their mobile genetic material. Yet, we lack an integrated, interoperable surveillance system connecting the One Health components. The next pandemic will likely be the result of cross-species zoonotic transmission. This suggests that One Health surveillance including wildlife, and ecosystems need to be established as soon as possible to detect such an event. Wildlife harbor large, diverse, and continuous evolving pools of potential pathogenic microbes. The recent finding of SARS-CoV-2 virus in farmed mink, free ranging, white-tailed deer, companion animals, and other animals in the U.S. (Hale et al. 2021) give us concern about pathogens finding new potential reservoirs of infections and becoming maintenance hosts expanding the possibility of new viral variants emerging and making epidemics more difficult to limit and control. In addition to SARS-CoV-2, *Mycobacterium tuberculosis* and methicillinresistant *Staphylococcus aureus* (MRSA) are other examples and represent additional possibilities within the human-animal environment complex and especially where human populations continue to grow and expand. (Messenger, Barnes, and Gray 2014.)

Recent studies suggest that with the identification of risk factors that we might be able to better focus our surveillance efforts. Some researchers have proposed that global "hot spots" may be identified where zoonotic diseases have the highest probability to emerge or re-emerge and become useful sites to conduct One Health surveillance (Carlson et al. 2021). There should be a special emphasis to conduct surveillance at important human-animal interfaces. Several One Health surveillance systems are in place, although still limited in scope and use, they are examples of effective integrated systems upon which to model and scale up much broader systems. NARMS (National Antimicrobial Resistance Monitoring System) and GLASS (Global Antimicrobial Resistance Surveillance and Use System) are examples of One Health systems to identify and track antimicrobial resistant organisms across species. These examples also support the need for strong diagnostic laboratory networks for all relevant to support any surveillance system, especially in LMIC.

The health of all life on earth is connected more intensely and with greater consequence. Surveillance systems focusing only on people and human health when considering the threat of zoonotic infections is akin to putting on blinders and limiting our knowledge of the disease and reducing the implementation of effective prevention and early detection strategies. Another key feature of a One Health disease surveillance strategy is the ability to comprehend situation awareness which is simply the idea of knowing one's environment and its implications for the present and future. This critical function is based on quality information derived from surveillance systems and enables improved decision-making in disease control and treatment. Surveillance data can only be optimized when it is shared readily and quickly to enable others to prepare and respond effectively. As data collection improves, we now have the luxury to use advanced data analytics to better understand zoonoses and eventually to effectively use modeling and forecasting to predict outbreaks and target high risk populations and ecological sites.

Potential Actions

▪ Expand the scope and scale of current One Health surveillance systems and coordinate data sharing between animal and public health experts and organizations through improved interoperability of data systems
▪ Invest in training and securing a permanent LMIC workforce with expertise in diagnostics, epidemiology, surveillance and disease prevention and management
▪ Create a centralized structure and team to mine surveillance and laboratory data using data analytics and disease forecasting to better focus surveillance activities and the trajectory of outbreaks with a special emphasis on emerging zoonoses

3. Spanning Boundaries: Engaging and Converging Expertise and Disciplines Beyond Medicine

In our complex, interconnected and dynamic world, narrow solutions to profound societal challenges are proving to be inadequate. Challenging infectious disease problems are part of the society that generates them, and effective solutions must come from changes in that society. As such, we need to be open to different ways of thinking and focus on new ideas and directions congruent with our changing times. Zoonotic diseases are complex and challenging and solutions to address them demand the integration of diverse domains and areas of expertise. One Health is a holistic, integrated, and multidisciplinary framework that requires collaboration of diverse organizations, disciplines, and professions beyond veterinary and human medicine and hold the promise of addressing the vexing societal challenge of this growing threat to health and our entire way of life. The ability to span boundaries, integrate knowledge from many disciplines, and share ideas and methods can lead to innovative strategies to improve health. Our prologue is characterized by siloed professions, disciplines, and thinking, compartmentalized interests and legacy funding and organization systems that are becoming ineffective in solving today's complex, interconnected health challenges. Only through synergistic approaches that advocate for an intellectual cross-pollination of experts that include all the medical sciences, social and behavioral scientists, engineers, policy makers, ecologists, and agriculturalists can our thinking and actions be transformed. The recent interest and involvement of the social and behavioral sciences in One Health is an example of engaging a new set of professionals. Additionally, the urgency of the climate change crisis is helping to create a new scientific field based on health and climate which will continue to expand the boundaries of studying zoonotic diseases. One Health is only achieved when there is an exchange of mindsets and insights that lead to fundamentally different approaches and pathways to address the challenges of zoonotic diseases. We can no longer rely on organizations that use yesterday's ideas to solve challenging zoonotic problems that cross multiple sectors, populations, and authorities.

Not only do other disciplines and professions need to be involved with supporting One Health, but they also need to collaborate, integrate their knowledge, and create new alternatives to tackle the global challenge of concurrently improving the health of people, animals, and the environment. The recent SARS-CoV-2 pandemic has impacted all facets of society and our lives. Economic, social, and business disruptions go well beyond the significant morbidity and mortality impacts of the disease. New voices are needed, and future solutions must be determined by a broader group of stakeholders and their ideas. Economists and policy makers are an increasingly important group of experts that need to become stronger One Health advocates. To accomplish this, One Health proponents must build a better business case acknowledging the evidence of broader benefits including social, environmental, cultural, biological, health and economic facets. There needs to be an expanded value proposition that proves the advantages of One Health beyond health care and includes a broader and betterinformed audience especially decision makers, political influencers, and funding bodies.

One of the most difficult problems still facing today's complex society is trying to shift our habitual ways of working, organizing, and thinking to meet dynamic and difficult problems. It has been noted that frequently innovative changes and ideas come from the fringes of organizations or completely from outside groups and disciplines. Spanning boundaries can also expand our vision, insights, and innovations to combat zoonoses. Many of the systems and organizations currently underpinning much of the public and animal health infrastructure tend to be siloed, vertically and narrowly organized. In contrast, One Health endeavors are horizontally organized and much broader in scope and integration than those traditional structures. In this way, the

One Health approach reflects the necessary transition toward the tenets of global interdependence and collaboration that defines our times yet is also a major challenge that will determine our destiny. Improved governance is also key to strengthening One Health capacity (Stephen and Stemshorn 2016). Consequently, establishing multisectoral coordination mechanisms at various levels is essential to ensure good governance and effective collaboration in achieving One Health goals (WHO 2019). Multisectoral coordination mechanisms have both leadership and technical coordination functions, and inter-Ministerial teams can be very useful in their leadership, alignment, and advocacy roles.

Convergence science is an emergent concept to meet society's contemporary challenges and needs and is an example of spanning boundaries to create new teams and innovative solutions. It is characterized by the integration of disciplines originally viewed as separate and distinct. Convergence is relative to both research and operational communities. Convergence science integrates knowledge, methods, and expertise to form novel networks and catalyze innovations and discovery. It is especially compelling as an approach to address complex and wicked societal challenges. The adoption of One Health is an example of using a convergent network and method to accelerate discoveries and innovations focusing on preventing and mitigating zoonotic diseases. It

combines distinct knowledge domains that involve medical, ecological, natural, and social factors. Using One Health as a framework opens new vistas and solutions for zoonotic diseases as a model of convergence science.

Potential Actions

- Support and help to expand the activities of the new Quadrilateral One Health High Level Expert Panel and advocate for the addition of behavior and social science experts to serve
- Engage and help influence funders such as the World Bank, philanthropic organizations, finance ministers, policy makers and national leaders to buy into the concept of One Health and programs to combat zoonoses
- Expand and develop a more effective relationship with environmental and ecological experts and ensure their expertise and collaboration in all future planning and implementation of activities
- Embrace the concept of convergence science and merge with their R&D agenda in support of emerging diseases, global health, and One Health
- Encourage the collaboration and inclusion of the agricultural communities and industries in mitigating zoonotic diseases, transboundary diseases and adopting One Health

4. Rebuilding Global Infrastructures, Capacity, and Biosecurity

For the last few decades, there has been a trend for government's worldwide to reduce critical funding and personnel for public and animal health. A major barrier for animal health has been the lack of support to combat the constant threat of zoonoses and emerging infectious diseases. A research study conducted by the International Livestock Research Institute (ILRI) several years ago, estimated that there were approximately 2.4 billion human cases and 2.2 million deaths per year because of infections from 13 global zoonoses. (Grace 2021). These extraordinary findings occurred mostly in Africa and reveal the huge burden on millions of small farmers and livestock keepers. The World Bank projected that an annual investment of approximately \$1.9–3.4 billion would be required to build and operate infrastructures and systems to effectively prevent and control diseases in LMIC ("People, Pathogens and Our Planet: Economics of One Health; World Bank Group, 2012). After the economic, social, and health costs of recent zoonotic disease outbreaks such as Ebola, SARS, H1N1 influenza, West Nile virus and SARS-CoV-2, the World Bank estimate seems like a bargain. Infrastructure improvements include facilities and equipment and program support but also include diagnostic labs, disease specialists and training. These resources are essential to implement key programs in biosecurity and managing animal production but also are needed to deliver vaccinations and treatments. This deficiency extends to research funds to support and enable One Health programs. In the era of emerging and re-emerging diseases, we need to focus beyond zoonoses. Not only are there human epidemics and pandemics but outbreaks can and do occur within our livestock, poultry, and aquaculture populations and within our plants and crops. Major global agricultural non-zoonotic pandemics can result in food insecurity and hunger. While not a traditionally defined zoonoses, such outbreaks on farms and production systems nevertheless can have profound human health effects involving poor nutrition, human growth deficiencies and stunting of children, cognitive deficiencies, and starvation. This is just an added reality further supporting the need to build animal health infrastructures. Investing in animal health infrastructures and personnel should not be considered as another cost or input but rather as a value-added investment to improve animal, public and environmental health. Recently the World Bank approved the establishment of a Financial Intermediary Fund (FIF) for Pandemic Prevention, Preparedness, and Response which includes One Health financing possibilities. This FIF will build on recent World Bank commitments and has the support of the G20. This important step should help fulfill this recommendation and perhaps catalyze further funding at this critical time (World Bank 2022).

Unfortunately, the lack of sufficient funding and support is not limited to LMIC. In the U.S., public and animal health, except for some emergency funding, has been chronically under resourced and both have faced significant workforce shortage and an eroded and reduced capacity. It has been even more difficult to find support for environmental, wildlife and ecosystem needs. In the United States, the control and eradication of several zoonotic diseases including brucellosis, bovine tuberculosis and canine rabies are examples of successful collaborative programs that have benefitted human and animal health for the last several decades. These programs further demonstrate how a One Health strategy and investments in animal health can have a substantial public health advantage. It is time to rebuild infrastructures globally as the most costeffective strategy to prevent and mitigate zoonoses. When considering rebuilding, it should not be an investment to support old systems, thinking and relationships but rather to create innovative and integrated structures commensurate with future threats and our national security. Lastly, building capacity in One Health also must include improvements in human capacity. This involves better training, educational programs, and a focus on building a workforce with the essential competences to be success-

ful. Collaboration, communications, system thinking, team building and participation, working across professions and organizations, and a tolerance for ambiguity and volatility are a few examples of needed competencies.

Potential Actions

- Support the development of a permanent global workforce with a special emphasis on LMIC and inclusion of diverse experts across all domains of One Health and to help unify disparate activities of animal, public, and environmental health, finance, and agriculture
- Join and participate in national Interprofessional Education (IPE) centers to improve the awareness, knowledge sharing, and collaboration across the health professions of zoonoses and One Health and developing similar competencies
- Enhance and expand global learning networks to build essential skills and competencies; these have proven to be cost effective, easy to implement, and capable of expanding the reach and learning capacity of One Health and global programs
- Add value to the World Bank's financing and technical support programs for pandemic prevention, preparedness and response based on their recent approval of a Financial Intermediary Fund (FIF) that may also be used to support AMR and One Health projects

5. Developing Communities of Solutions: The Need for Collective Action and Implementation

Communities of solutions is a concept that goes beyond communities of practice. The later represents a group of people who share a common interests and backgrounds on a specific topic and focus on sharing best practices. A community of solutions is similar but focuses on developing solutions for difficult problems using experts from very diverse backgrounds and expertise to create innovative and even transformational recommendations and actions.

 "What to come, in your and my discharge" is a simple statement reminding us that we can only change the direction of our precarious future by taking effective action. The initial stage of One Health has been the acceptance of the concept and growing organizational involvement. The next stage is key and that pertains to actual implementation strategies. The last few zoonotic pandemics, H1N1 influenza, Ebola, and SARS-CoV-2, have exposed significant limitations for preventing and ameliorating threats to our global heath and poor implementation of actions have been a common find-

ing. Global health governance operates not only in the realm of health but also includes many other collaborative spheres of players. As such, complex and multifaceted problems represent difficult challenges that require the cooperation and involvement of health, finance, business, and civil society. The ability of international organizations to work with the private sector, government officials from different countries, and numerous diverse stakeholders has often proven bureaucratic, slow and with a lack of coherence of specific goals. Our growing set of challenges such as emerging zoonoses, more and more, cannot be handled by established organizations and systems using yesterday's ideas. New communities of solutions offer new pathways based on collaboration and strong leaders with the skills to tackle them. Today's complex problems that involve multiple entities and authorizations often have no one in charge of solutions. New communities using shared leadership models need to be formed to focus on larger societal benefits and not self-interests. Cross-sector, multistakeholder coalitions will characterize new communities of solutions.

Forming communities of solutions is a concept where effective local actions coalesce into larger integrated partnership. The role of the private sector has proven to be a critical factor in success. Forming communities of solutions can be accomplished by building on existing organizations such as community health organizations that help individuals attain optimal health. Working at the community level allows health professionals to develop strong bonds within their communities and tailor services to unique community needs including interventions to prevent and detect zoonoses. Communities should form true action collaboratives where interdependent actions are performed, shared, and synthesized into new tactics by community team members.

The context of people's lives determines their health. That context today is much greater than just human clinical care. Large global public and animal health organizations function best when they can serve as catalysts and supporters of actions. However, the real work should be conducted at the local level with transdisciplinary teams with broader responsibilities to create solutions, in part, based on One Health strategies in addition to its many other healthcare services. Finally, the concept of a community of solutions is composed of individuals who are mutually dependent and mutually accountable. This team is characterized as convergent, resilient with responsibilities beyond a typical community health team and could improve health across all the dimensions of One Health.

The possibility of redefining and expanding the notion of community health to be more One Health oriented and expand options to advance health has great promise. Communities of solutions should include agriculture. Food safety and security, antimicrobial resistance, environmental deg-

radation, and new emerging zoonoses are all central to our future and have community health implications and need agriculturalists to participate in their solutions. The end point of production agriculture is not when animals leave farms and ranches but rather when production of food also involves improving health and well-being across all domains of One Health. Agriculture and public health are closely and intimately connected and need to be viewed as a continuum with multiple sites of solutions and interventions.

Human population health is determined by multiple factors beyond traditional health care and thus should be reimagined as a convergent science and a One Health concept. An original definition of health first proposed by the WHO suggests that health is not defined by the absence of disease but rather is a complete state of physical, mental, and social well-being. As such, factors including environment, genetics, socio-economic, and behavior collectively are more instrumental to determining our health than medical health care. Community health that is redefined with a One Health viewpoint would advance population health in a more integrated and holistic way based on the WHO definition. Community health will succeed in the future if there is true convergence of science, policy, and practice across the domains of One Health (Amusi et al. 2020).

William McNeill's landmark book published in 1976, "Plagues and Peoples" examined the impact of infectious diseases throughout history and concluded that plagues and people are, and remain, inexorably linked. Today in reflection of his observations, his conclusion is even more relevant and telling. Without rethinking and re-imagining the deepest sense of who we are and how we work to solve today's intractable problems, no country will be able to sustain optimal health. Envisioning and forming new organizations and structures based on developing new integrated solutions is fundamental to our future. If not, McNeill's warning that infectious diseases, especially zoonoses, will continue to fundamentally determine human history – and not for the better will continue to be our reality.

Potential Actions

- Redefine and expand existing community health organizations to better prepare for growing threats of emerging infectious diseases, zoonoses, and environmental degradation by using a broader One Health team and adding critical expertise; the creation of One Health officers would be innovative and timely

- Expand the concept and introduction of "Climate-Smart Agriculture" to include greater participation of animal agriculture producers and use this collaboration to be proactive and strategic in mitigating the impacts of climate change on zoonoses and to help establish stronger One Health ties

- Coalesce and strengthen the diverse interest groups involved with biodiversity, wildlife, ecosystems, and conservation to create a resilient and sustainable community that reenforce many common goals and combine compacities to develop innovative solutions and activities

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Index

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