One Health

People, Animals, and the Environment

EDITED BY

Ronald M. Atlas and Stanley Maloy

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PREFACE

One Health, the emerging discipline that brings together human, animal, and environmental health, is critical for the future control of infectious diseases. Over the past 30 years, new infectious diseases have been arising at an unprecedented frequency. Many diseases such as *Escherichia coli* O157:H7 infection, Lyme disease, hantavirus pulmonary syndrome, Nipah virus disease, and severe acute respiratory syndrome (SARS) were unknown before 1982. Other diseases that seemed to be dying out are now reemerging, including rabies and food-borne diseases. Some diseases like West Nile fever have leaped across oceans and spread across continents. Antibiotic resistance is increasing at an alarming rate. Where are the new diseases coming from? Why is the incidence of these diseases increasing? What can we do to respond to these health threats that seemingly arise suddenly? The answers to these questions lie in the One Health approach for achieving harmonized strategies for disease detection and prevention.

The vast majority of emerging infectious diseases in humans are zoonoses. The factors responsible for many of these diseases in humans often share common themes: environmental disruption by humans, exposure of microbes to a different niche that selects for new virulence traits and facilitates transmission to animals, and genetic changes that permit subsequent transmission to humans. In retrospect, this sequence is not surprising. Microbial evolution occurs rapidly. The increase in the human population has prompted the encroachment of humans into new environments, disrupting the ecology of these habitats and bringing humans and domestic animals into contact with wildlife. Exposure to wildlife facilitates the transmission of new diseases that were previously contained within localized niches.

This process is not unidirectional. Devastating infectious diseases in animals often result from human disruption of habitat. Examples include toxoplasmosis in marine mammals, leptospirosis in river otters, white-nose bat syndrome, and many other diseases that impact threatened species and reduce biodiversity.

Furthermore, as clearly demonstrated by the international spread of SARS and influenza and the impact of chytridiomycosis on amphibian populations worldwide, the emergence and re-emergence of infectious diseases are global problems. Extensive international travel and trade networks make it possible for pathogens to move from anywhere in the world to dense population centers within days.

This interdependence between human health, animal health, and environmental health underpins the concept of “One Health.” Solutions to the growing problems with infectious disease demand collaboration between experts in many disciplines, including human medicine, animal medicine, and environmental sciences. However, there remain many barriers to implementation of an interdisciplinary One Health approach. Education of physicians, veterinarians, and environmental scientists is typically done as a focused discipline with little emphasis on the other domains. Most funding sources are directed specifically at human medicine, animal medicine, or environmental science, rather than the interfaces among these domains. Further, there is often ineffective communication between governmental agencies responsible for each of these domains within and between countries. Now, however, driven by the tremendous health and economic impact of infectious disease, the barriers are beginning to break down.

One Health is a paradigm shift in how we respond to the threat of emerging infectious diseases. The traditional approach has been to identify a sick person or animal, identify the pathogen, and apply a therapy to reduce the symptoms of disease. In contrast, the One Health approach focuses on surveillance of the environment, animals, and humans to predict an outbreak of disease *before* it happens, then to bring together environmental scientists, animal experts, and human physicians to develop upstream interventions that prevent the transmission of disease. This approach was not feasible before the development of computational approaches to analyze the large, complex data sets required to compile information from around the globe, evaluate the data, and pinpoint potential problems. In addition to reports from physicians and veterinarians, the data-gathering required for effective surveillance also includes social networking tools and new rapid laboratory approaches for DNA sequence analysis. Thus, although the close relationship between the environment, animals, and humans has been recognized for ages, the One Health initiative provides practical solutions that have broad implications. Interestingly, the greatest acceptance of One Health is seen in the developing world, where it is having significant impacts on control of infectious diseases.

This book presents core concepts, compelling evidence, successful applications, and the remaining challenges of One Health approaches to thwarting the threat of emerging infectious disease. The scientific insights described are timeless, and the potential solutions are timely. The One Health approach is simply too important to ignore.

Ronald M. Atlas and Stanley Maloy
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One Health: What Is It and Why Is It Important?

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Chapter 1

Combating the Triple Threat: The Need for a One Health Approach

***Lonnie J. King*[1]**

INTRODUCTION

We live in a world that is rapidly changing, complex, and progressively more interconnected. The convergence of people, animals, and their products embedded in a threatened environment has resulted in an unprecedented 21st-century mixing bowl. This convergence has created a new dynamic, one in which the health of three domains—animals, people, and the environment—is now profoundly and inextricably linked and elaborately woven together.

One way to think about this interconnectivity is to picture the domains of people, animals, and the environment as a group of interconnected circles (Fig. 1) that push and pull on one another and create profound forces through their interactions. The interaction of these forces is similar to the dynamics of Newton's third law of motion, which simply states that for every action there is an equal and opposite reaction. Thus, our actions and interventions in any of the three domains have an impact on the other domains. In today's world, these forces have mostly resulted in negative impacts on the health of all three. In addition, with the growing global populations of people and animals, human-animal interfaces are accelerating, expanding, and becoming increasingly consequential. The ultimate result is a threat to the health and well-being of people, animals, and the environment, where problems in one domain are causing greater challenges and problems in the others and have created the biological equivalent of the third law of motion.

To effectively address the connected and changing health challenges of today and tomorrow, we must alter our mindset and consider health through more of an ecological, holistic, and systems-based approach. There is a growing acceptance and revival of the concept of "One Health" to better understand and more appropriately address our contemporary challenges and the threats to the health of people, animals, and the environment. The essence of One Health is a collaborative, integrated, and multidisciplinary approach to improve health in all three domains rather than restrict our views and interventions to any single domain.

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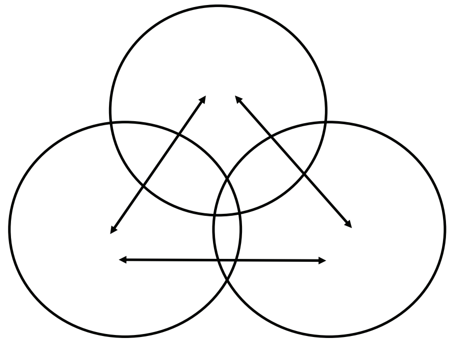

Figure 1. The domains and forces of One Health.
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BACKGROUND

While noninfectious diseases, chronic diseases, and environmental degradation are of growing importance to our health, central to the concept of One Health is understanding and controlling the infectious diseases that have helped shape the course of human history. The conditions that promote and favor the emergence and reemergence of infectious diseases are well established and have become even more entrenched as the 21st century evolves. These conditions were identified and described by an Institute of Medicine report in 2003 that referred to a new convergence model and factors producing a “perfect microbial storm” (1).

The perfect microbial storm has been created due to the following factors: adaptation of microbes; global travel, trade, and transportation; host susceptibility; climate change; economic development and land use; human demographics and behavior; poverty; social inequity; breakdown of public and animal health infrastructures; and war and the intent to do harm (1). Most of these factors are anthropogenic and have produced a new milieu and ingredients for a global mixing bowl, in which microbes have greater opportunities to establish new niches, cross species lines, be transported globally, become resistant, and very quickly create new exposures and challenges in the populations of people and animals and in the environment. Microbes can be transported directly among hosts, indirectly through food and water, or through vectors such as mosquitoes and ticks, and they may survive as environmental contaminants or microbial populations where they are maintained in nature outside of living hosts.

The result has been the creation of a new era of emerging and reemerging diseases that has been characterized especially by new zoonotic diseases. Over the last 3 decades, approximately 75% of new emerging human diseases have been zoonotic and many have come from and/or through wildlife (2). These diseases are also being found in new geographic locations. For example, in 2003 just in the United States, West Nile virus, monkeypox, and severe acute respiratory syndrome (SARS) infections were all found concurrently, and none of these diseases had ever previously been found in the Western Hemisphere.

The factors that created the perfect microbial storm are still in place and have largely been unabated. Thus, the era of emerging infections and new zoonoses is likely to continue. In a recent foresight study, scientists predicted that there will be two to four new emerging diseases every year. The highest probability for emergence will be associated with RNA viruses, especially those found at the human-animal interface (3). We are reminded that the current HIV/AIDS epidemic, which has resulted in more than 40 million human cases worldwide, had its origin in a chimpanzee retrovirus that jumped species and then adapted itself to human-to-human transmission. Exotic animals and bush meat are now popular and represent significant products in global trade and new threats to both human and animal health.

Our complex and interrelated global health threats are, unfortunately, also caused by complex and interrelated issues and problems, and thus lack simple solutions. The concept of "wicked problems" comes from the world of business but also aptly describes our health threats. Wicked problems are characterized by complexity, uniqueness, enigma, the lack of simple solutions, and the failure of past solutions to address them, and they are often symptomatic of other problems. Wickedness does not refer to the difficulty of the problem, but rather to its inability to be solved by standard approaches used in the past (4). For example, in the future the prevention of many diseases such as food-borne illnesses will come from new strategies and interventions focused on the animal or environmental domains emphasizing prevention, as opposed to the narrow focus of the past, which targeted people suffering from such illnesses and thus limited the response to the human domain.

The former director of the World Health Organization, Gro Harlem Brundtland, once said, "In a modern world, bacteria and viruses travel almost as fast as money. With globalization a single microbial sea washes over all human kind. There are no health sanctuaries" (address to Davos World Economic Forum, January 29, 2001). That sea also washes over all other species, and the microbial world has new opportunities for transmission, new niches and species to infect, and new geographical sites in which to become established. Thus we are, indeed, part of one large, interconnected, global village, where one country's problem can be another country's problem in a matter of hours.

HUMAN DOMAIN

The world population currently has a growth rate of 1.2% per year, and the next century will represent a period of exponential growth. The global population now exceeds 7 billion people and is estimated to increase to over 9 billion by the middle of this century. It is estimated that 90% of the global population growth will take place in the developing world and the world's fastest growth will actually take place in periurban settings that are now a part of almost all large cities in developing countries (5). Today almost 1 billion people inhabit these sites. Global slums are creating unprecedented conditions where new emerging and reemerging diseases are highly probable outcomes. There is further concern that developing countries lack the public and animal health infrastructures needed to quickly detect an emerging health threat or to effectively respond to or control such threats. In an interconnected world, this reality makes the entire world riskier and more vulnerable.

At the same time, we are now witnessing an era characterized by the phenomenal relocation, migration, and movement of people worldwide. The global economy is a key driver causing people to shift from rural settings to urban centers. Furthermore, new diasporas are being created as populations relocate globally due to the changing economy and job availability, and large populations of refugees are being created due to social and political unrest. In addition to this unique human relocation phenomenon, people are also traveling more. Today more than 1 billion people cross international borders each year. Not only are people on the move, but animals, vectors, food, and other commerce are also on the move and microbes are given unprecedented opportunities to migrate rapidly.

The world is literally in motion and on the move. Geographers refer to the world as "collapsed space." Our global travel, trade, commerce, and human movements have literally merged space, resulting in the acceleration and increase in interactions of people, animals, and animal products with potential exposure to microbes capable of crossing species lines. To add further to this risk, people are invading new territories and changing habitats and a substantial part of the world's surface has been inexorably altered, threatening the environment and its sustainability.

Finally, there are growing segments of our human population that have acquired vulnerabilities to certain diseases. In the United States, and indeed worldwide, there is an increase in the global cohort of people classified as seniors. In the United States, the baby boomers are approaching retirement and may represent a large population that could collectively experience a potential reduced immunity with age. We now have growing populations of immunocompromised individuals, including cancer patients, organ transplant patients, and HIV/AIDS patients, who are part of a growing cohort with greater susceptibility to infectious diseases.

One of the key factors determining health is poverty. Poor health is both a cause of and a result of poverty. Often people are trapped in poverty for a lifetime, and their health and quality of life are also reduced and threatened over an entire lifetime. While poverty takes many tolls, one of the most tragic has been its inexorable link with infectious diseases.

Approximately 1 billion people live on less than $2 a day. Worldwide, almost two-thirds of the rural poor and one-third of the urban poor depend on livestock to provide them with essential household income and a source of food and nutrients (6). Poor livestock keepers are found especially in Southeast Asia, Africa, and India. This large global population is threatened by zoonotic diseases because of their close proximity to livestock and dependence on animal products. Zoonotic diseases carry a double impact. They add substantially to disease morbidity, mortality, and loss of productivity of livestock and poultry themselves but may also produce illnesses in their keepers. A recent study by the International Livestock Research Institute highlighted a strong association among poverty, hunger, livestock keeping, and zoonoses (20). Globally, the top 13 zoonotic diseases are responsible for 2.4 billion cases of illness and 2.2 million human deaths per year. Examples of these zoonoses include gastrointestinal parasites, leptospirosis, cysticercosis, bovine tuberculosis, rabies, brucellosis, toxoplasmosis, and Q fever (6). Livestock and poultry production is rapidly increasing in the developing world, where the demand for protein from animal sources is rapidly expanding and the production of livestock and poultry holds the promise of a path out of poverty.

A One Health perspective is essential to reducing the huge economic, social, and health impact of zoonoses in developing countries. These diseases often involve wildlife as well as domestic animals, and almost all of these zoonoses are amenable to agriculture-based interventions, which gives further credence to One Health strategies.

ANIMAL DOMAIN

As the world's human population grows significantly, animal populations are also increasing rapidly. The growth in companion animals and recreational animals such as horses is also on the rise. Exotic animal pets are popular, and the illegal export and movement of these animals is a growing problem both because of human exposure to potentially new zoonotic agents and because of the emergence of novel diseases in new animal species. HIV/AIDS, malaria, and tuberculosis represent the major infectious diseases today. However, all three are likely to have had their origin in animal populations and subsequently adapted and become capable of person-to-person transmission.

A major global trend today is the substantial growth and expansion of food animal populations due to the growing demand for protein from animal sources in human diets. There were more than 24 billion food animals produced last year to help feed more than 7 billion people (6). The Food and Agriculture Organization of the United Nations describes a new agricultural revolution and predicts that there will be a demand for a 50% increase in animal proteins over the next 1 to 2 decades. This remarkable agricultural revolution is based on the relative increase in wealth in many developing countries and the subsequent change in diets toward more animal products (7).

In addition to the need to produce an unprecedented number of food animals, this livestock revolution is driving profound changes in how livestock and poultry are produced, where they are produced, and the environmental consequences of this phenomenon. While literally billions of food animals will need to be produced using more integrated, larger, and specialized production systems, they will be reared and produced to a progressively greater extent in the developing countries of the world. As part of this phenomenon, there will be an expansion of grazing lands and more grain crops will need to be produced to feed these animals. Major issues including environmental sustainability, nutrient management, and an enlarging carbon footprint are growing and emergent challenges.

GLOBAL FOOD SYSTEMS

Inherent in the concept of the great convergence is the creation of an immense and widely distributed global food system. In 2011, U.S. producers and ranchers alone produced almost 93 billion pounds of meat. Food imports and exports represent one of the world's largest trade and commercial markets. Currently the United States imports approximately 15% of its food; however, some products like shrimp and other seafood, fruits, and vegetables are imported to a much higher degree (8). Global food systems are remarkable but also add to the risk of transporting microbes. Microbes can move worldwide faster than their incubation periods, and the threat to both human and animal health is increasing, with food and water as potential vehicles for the dissemination of pathogens.

As in people, animal diseases are also emerging and reemerging. Global agricultural businesses are increasingly concerned about the exposure, vulnerabilities, and biosecurity of their supply chains, products, and animals. Diseases such as influenza, foot-and-mouth disease, bovine spongiform encephalopathy, and African swine fever have emerged and produced major outbreaks with huge economic losses as well as other consequences, including morbidity and mortality of animals; loss of products; costs of control and recovery; loss of global markets; disruptions of supply chains; loss of protein sources; landscape and environmental damages; loss of income and jobs; detrimental impacts on the economic and social well-being and health of rural communities; and potential public health costs, especially for zoonotic diseases. There are further concerns regarding the loss of wildlife populations and biodiversity, animal suffering, human psychological costs, and potential loss of the public's confidence. Recent experiences in the United Kingdom dealing with epidemics of bovine spongiform encephalopathy and foot-and-mouth disease have given us a new appreciation of the consequences of trying to address devastating diseases of livestock and poultry. In addition to the horrific losses to the animal populations themselves, these epidemics altered people's lives and left deep and long-term social, economic, and psychological scars in many individuals and communities. Furthermore, the SARS epidemic, which originated and was amplified by animals in special live-animal markets, resulted in serious losses to tourism, financial markets, and numerous ancillary businesses. Thus, the incursions of such diseases today have much greater consequences than they did previously and go much further and deeper than just the impact on agricultural communities. Looking though a One Health prism is essential to view and truly understand the driving forces and impacts of these diseases but also to offer insights into the use of new interventions and prevention schemes.

Because of the economic and psychological consequences of incursions of exotic diseases in large populations of animals, another concern and vulnerability has emerged: the intentional introduction of pathogens by bioterrorists. Of the current list of select agents, 80% are zoonotic and could be found in animal populations before human cases are found. Certainly there is a growing need to incorporate animal and environmental surveillance as part of a national One Health preparedness and surveillance plan.

Food Safety

The animal health and public health domains are even more connected today through our food systems and form an important interface with growing concerns. The CDC now estimates that there are approximately 48 million food-borne illnesses in the United States every year, resulting in 128,000 hospitalizations and 3,000 deaths annually (9). Although we lack similar global data, a rough extrapolation suggests that there could be as many as 1 billion such illnesses worldwide each year. Without question, the burden of food-borne disease represents a huge health care cost. A number of food-borne diseases such as norovirus and hepatitis are transmitted directly from person to person with food as a common vehicle; however, many food-borne illnesses are zoonotic and are transmitted across domains.

CDC studies have also demonstrated changing patterns of attribution. Plant-derived foods such as leafy greens, tomatoes, and sprouts have been implicated in more and more food-borne disease outbreaks. In the recent past, transmission has been linked to peanut butter, pizza, spinach, ice cream, cookie dough, pet food, melons, mangoes, peppers, and carrot juice. There is also concern about the concept of "stealth" vehicles in transmission. There are numerous food ingredients that are often mixed in with foods, such as spices, that can be vehicles for transmission but are often not considered in outbreak investigations (10).

In addition to the traditional food-borne pathogens such as *Escherichia coli* and *Salmonella*, *Campylobacter*, and *Listeria* spp., new outbreaks often reveal new agents. The FoodNet System, which analyzes outbreaks, has revealed adenoviruses, sapoviruses, picobirnaviruses, and Saffold virus as potential pathogens. To further complicate our understanding of the safety of our food, transmission vehicles can change when microbes are given new opportunities. For example, the Nipah virus, first found as a zoonotic disease outbreak in Malaysia that killed pigs and people associated with them, has recently been found as a contaminant in date palm sap, a food source in Bangladesh. *Pteropus* fruit bats are the asymptomatic carriers. *Trypanosoma cruzi* is the parasite that causes Chagas disease and is usually transmitted to people via reduviid insects, yet it has recently been found in sugar cane juice in Brazil. There is a remarkable spectrum of foods and pathogens involved in food-borne illnesses and this is an ever-changing dynamic. Produce is of growing importance as a vehicle for food-borne pathogens, yet animal reservoirs are often the origin of these infections. One Health gives us the proper lens to view and better understand this linkage and, more importantly, to develop new insights for changing our interventions and prevention strategies. In many instances, ill people are the endpoint of a complicated epidemiological cycle and serve as indicator hosts; however, if we continue to focus exclusively on food-borne illness by responding to human outbreaks and just conducting retrospective analyses, we will miss the true sites of origin of these diseases and we will forgo critical prevention strategies in other domains. To a certain extent, ill people serve as sentinels of a larger ecological problem and, as such, may not be the best focal point for our interventions. One Health is a mindset that is proactive and preventive; it helps to shift our attention "upstream" to the ecological, animal, and environmental sources responsible for these illnesses and, therefore, helps us to identify the most effective points for the initiation of food safety actions.

ENVIRONMENTAL DOMAIN

Our environment has continued to undergo changes, mostly to the detriment of our various ecosystems. The threat to the health of our environment is largely anthropogenic. While we are concerned about the sustainability of the environment itself, we also understand more clearly that diseases, too, are often a result of environmental disruption and changes.

The increasing incidence of Lyme disease is very much the result of human changes to the environment, especially on the East Coast of the United States. Forests have been reduced and fragmented and development has chased off predators; thus, an expanding population of deer and white-footed mice helped preserve both *Ixodes* ticks and the *Borrelia* organism. The disease consistently spills over into human populations colocated in these new ecological sites. When ecosystems are disrupted along with our natural biodiversity, we often remove the protective effects of multiple species (11).

Some scientists have referred to today's era as part of Earth's sixth mass extinction, with unprecedented loss of plant and animal species largely due to disruptive human activities (12). As a consequence, there is heightened concern that the protective and buffering effect of biodiversity is being lost and microbes could enter directly into people without first infecting other species that are no longer available as hosts.

Habitat disruption and alteration of land use also affect vector populations. An additional concern is climate change and the potential of changing the geographic range of disease vectors. There are more than 3,000 species of mosquitoes, some of which are very efficient and effective disease transmitters. Historians estimate that mosquitoes may be responsible for half the deaths in human history (13). Malaria, yellow fever, and recently a serious dengue epidemic are vector-borne diseases. The animal disease bluetongue, discovered recently and now found across much of Europe, may be a consequence of the expansion of the *Culicoides* (biting midge) vector due to warmer temperatures. In addition, Schmallenberg virus, an emerging disease affecting domestic ruminants in Europe, is a newly found orthobunyavirus and likely transmitted by *Culicoides* vectors. These vectors seemingly have established new geographic niches, possibly due to warmer temperatures. Rift Valley fever has caused both animal and human epidemics in Africa after flooding rains have greatly increased the population of mosquitoes. Cholera, caused by *Vibrio cholerae*, may be associated with typhoons that flood Bangladeshi lowlands and produce a favorable environment for plankton growth and subsequent larger numbers of vibrio organisms that live off the plankton and then infect people. An epidemic outbreak of cholera in Haiti that followed a devastating earthquake appears to have been introduced into the water supplies by an infected aid worker from Asia.

Recent events have demonstrated that fungi are becoming greater global threats to agriculture, forests, and wild animals than was previously understood. Countless amphibians have been killed; some species have become extinct; and some food crops such as wheat, rice, and soybeans have all experienced serious fungal infections. One-third of the world's amphibian population is globally threatened or extinct due to an epidemic of fungal infections (14).

Increased global trade and travel, changing agricultural practices, and perhaps global warming are responsible for the increase in fungal infections and their geographic shift. Two major animal crises—the profound decline in amphibian species and a disease outbreak in North American bats—have given us new cause for concern. *Batrachochytrium dendrobatidis* is a fungus whose spores survive in streams and ponds and is responsible for a tragic loss of biodiversity in Central and North America and Australia. Bat white-nose syndrome is caused by *Geomyces destructans* and has killed approximately 6 million bats in the United States (19). These fungi can persist in the environment and live outside their hosts for years. In addition, cryptococcal meningitis (*Cryptococcus neoformans*) is estimated to cause 1 million human infections annually, especially in immunocompromised populations. *Cryptococcus gattii*, which has spread into western Canada and the northwestern United States from Australasia, is a fungus that has infected people, domestic animals, marine mammals, and forests. This fungus has shifted in both its geographic location and ecologic niche. Scientists have been able to identify only a small percentage of the global fungal species. They are clearly part of the 21st-century convergence of people and animals in a changing environment. There is further speculation that fungi may adapt very well to globalization and now represent another emerging triple threat to health.

Nature supports many of our human endeavors. Forests help filter our water, bees and birds help pollinate our crops, and our many diverse animal species help serve as filters and buffers for infectious microbes, thus protecting people from exposure to potential pathogens. As we experience warmer temperatures across the globe, there is concern that the ranges and life cycles of vectors may change significantly and alter the exposure of humans to vector-borne and waterborne diseases. Our understanding of these dynamics gives us a new appreciation of the term "ecology of disease." Thus, if our natural world breaks down, our human and animal health can be negatively affected, often in ways we have never experienced.

CONSEQUENCES OF THIS UNPRECEDENTED CONVERGENCE

There is no question that we live in a world that has become riskier and is on a trajectory to become even more so as our space collapses and more and more people and animals converge and exist in ecosystems that are changing and are not sustainable.

As a consequence, microbes, as they have done for eons, are taking advantage—they adapt; move globally; cross species lines; become resistant to antimicrobials; have increasing numbers of hosts, vectors, and products from which to choose; and are able to target populations with greater vulnerabilities. As our microbial swarms gain a greater advantage and influence, their scope, scale, and impact also increase and there is an undeniable and direct correlation to an increased threat to our health.

An added concern is that in many countries, infrastructures to support both human and animal health are not commensurate with the increasing levels of threat. There is a concern that current economic conditions have reduced funds and investment in public and animal health safety nets and that there has been an erosion of some key systems supporting surveillance and rapid detection and response capacities. Finally, there is also a new appreciation that outbreaks of disease go beyond health costs and may lead to significant losses in travel, commerce, supply chains, and potentially public trust and confidence.

A CALL FOR A NEW MODEL TO CONFRONT THIS CHALLENGE

Our growing interconnectedness and the "wicked" nature of our problems have created not only more complex challenges but also the need to rethink and recreate new solutions and strategies to address the triple threat to our health. Inherent in this contemporary condition is the fact that old solutions no longer work as well and new solutions haven't been invented or effectively incorporated.

One Health is a concept that embraces disease ecology. The holistic understanding of ecology and our connectedness gives us new insights into the control and prevention of disease and improvement of our health. However, this mindset is almost counter to our training in medicine, especially clinical medicine, where we seek definitive diagnoses, try to establish an immediate cause-and-effect relationship, and determine and implement the best treatment. Medicine and science have resulted in phenomenal breakthroughs but have also created a bias toward reductionism as we have made new molecular and genomic discoveries. In part, this bias has led us away from holistic and ecological studies and away from a fuller appreciation of the complexities and dynamics of disease processes, especially for zoonoses. One Health gives us a better balance between reductionism and ecological approaches and leads to more effective medical interventions.

One Health is the collaborative effort of multiple disciplines working locally, nationally, and globally to attain optimal health for people, animals, and our environment (15). It is a paradigm that recognizes the interconnectedness of people, animals, and the environment and emphasizes disease prevention. The scale and complexity of health threats demand that scientists, researchers, and others move beyond the confines of their own disciplines, professions, and mindsets and explore new organizational models of team science; a One Health concept embodies this declaration. The scope of One Health is impressive, broad, and growing. Much of the recent focus of One Health has been limited to emerging infectious diseases, yet the concept clearly embraces environmental and ecosystem health, social sciences, ecology, noninfectious and chronic diseases, wildlife, land use, antimicrobial resistance, biodiversity, and much more.

While these components are appreciated within our understanding of the broad dimensions of health, they also add to the complexity of One Health and the difficulty in implementing strategies, building effective coalitions, and mobilizing scientific communities that embrace One Health. Although there may be different definitions of One Health, there is broad consensus that a new framework for preventing infectious diseases is essential rather than the alternative of constantly responding reactively to these diseases.

The World Health Organization defines health as not merely the absence of disease but rather as a state of well-being and wellness that encompasses physical, mental, and spiritual health, resulting in healthier, safer, happier, and more productive lives. One Health is a concept that enables us to better understand this broad definition of health and that health is based on many factors and represents an ever-changing dynamic.

The factors determining health include genetics, social circumstances, environmental conditions, behavior, and medical care. The last, medical care, represents less than 25% of the total impact of determining our health status. In the United States, we spend approximately $2 trillion on health care per year, yet a very small and disproportionate amount of this total is spent on disease prevention and health promotion, where the greatest health impact can be achieved (16). One Health stresses prevention by incorporating other factors and shifting interventions upstream, closer to the source of the problem. Armed with this knowledge, scientists, researchers, and health care workers need to form One Health teams that cross disciplines and professions to better understand and improve health.

The concepts expressed as One Health are not new, but are predicated on the discoveries of others such as Louis Pasteur in the late 19th century, and were widely accepted before the advent of specialized medicine. These concepts have "reemerged" as One Health because they place the problem of infectious disease emergence within ecosystems, a relationship championed by the late Nobel laureate Joshua Lederberg. In his essay "Infectious History," Lederberg observed that "an axiomatic starting point for progress [against emerging infectious diseases] is the simple recognition that humans, animals, plants and microbes are cohabitants of this planet. That leads to refined questions that focus on the origin and dynamics of instabilities within this context of cohabitation. These instabilities arise from two main sources loosely definable as ecological and evolutionary" (17).

Adopting a One Health approach is an example of changing paradigms, as described by philosopher of science Thomas Kuhn in his seminal work, *The Structure of Scientific Revolutions* (18). With regard to medical science and addressing emerging diseases, we have reached an era when old models don't work as well but new models have yet to be created, a time when basic assumptions must be questioned and changed.

Such changes need not be led by the scientific community. The paradigm shift to One Health may be consumer driven. Indeed, One Health should be considered in terms of its economic benefits to stakeholders, and its value judged according to evidence of its superiority to current approaches. The evidence has to be based on metrics of reduced costs, reduction or elimination of cases and deaths, and greater effectiveness.

CONCLUDING REMARKS

There is nothing on the horizon to suggest that the factors and conditions driving the "perfect microbial storm" are lessening or abating. Our world continues to be more and more connected: trade, travel, and commerce are growing; populations of people, animals, and wildlife continue to grow and the interfaces between animals and people are both accelerating and intensifying; a global food system is expanding; pollution and contamination of our environment along with habitat destruction continue unchecked; climate change may alter our exposure to vector-borne and waterborne infections; our biodiversity of plants and animals is rapidly being lost; poor health continues to be both a cause and consequence of poverty; vulnerable populations are increasing in numbers; and microbes are gaining the upper hand through their ability to establish new niches and become resistant to antimicrobial agents. The result is a triple threat to the health of people, animals, and our environment. These factors also represent the principal evidence needed to mobilize health professionals toward adapting a new One Health approach to reduce these threats. Until we address the underlying factors that lead to disease emergence and reemergence, we will just continue to try to address these problems one at a time as we have done in the past. In today's world, we must commit and refocus our efforts holistically and collaboratively. We can no longer just focus on humans and microbes but rather must shift our attention to the interplay among people, animals, and the environment—One Health.

Understanding the mechanisms that underlie newly emerging and reemerging infectious diseases is one of the most difficult scientific problems facing society today. Significant knowledge gaps exist for many studies of emerging infectious diseases. Coupled with failures in the response to the resurgence of infectious diseases, this lack of information is embedded in a simplistic view of pathogens and disconnected from a social and ecological context, and it assumes a linear response of pathogens to environmental change. In fact, the natural reservoirs and transmission rates of most emerging infectious diseases are affected primarily by environmental factors, such as seasonality or meteorological events, typically producing nonlinear results that are inherently unpredictable. A more realistic view of emerging infectious diseases requires a holistic perspective and incorporates social as well as physical, chemical, and biological dimensions of our global systems. The notion of One Health captures this depth and richness and, most importantly, the interactions of human and natural systems. Furthermore, there must be a synthesis of interdisciplinary approaches aligned with social-ecological approaches to garner an improved understanding of emerging infectious diseases, to better manage them, and to successfully address the wicked problems underlying the triple threat to health.

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Chapter 2

The Value of the One Health Approach: Shifting from Emergency Response to Prevention of Zoonotic Disease Threats at Their Source

David L. Heymann[1,2] and Matthew Dixon[1]

EMERGENCY RESPONSE TO NEWLY IDENTIFIED HUMAN INFECTIONS

When an infectious disease organism from an animal breaches the species barrier to infect a human, it enters an immunologically naïve population. Depending on incompletely understood risk factors, which depend on both the organism and the infected human, there are several possible transmission pathways: (i) no further transmission, with the human an endpoint as in rabies and variant Creutzfeldt-Jakob disease; (ii) nonsustained human-to-human transmission such as presently occurs in close human contact with persons with influenza A (H5N1) and human monkeypox (1–4); (iii) sustained human-to-human transmission following initial transmission from an animal source, as observed with influenza A (H1N1) that emerged as a pandemic in 2009; and (iv) sustained transmission that leads to endemicity (Fig. 1). HIV presents the most important recent example of the latter, but the pattern of animal infections becoming endemic in humans appears to have occurred throughout history, suggesting that most, if not all, endemic infections in humans have come from animals (5, 6).

The ecosystem in which microbes, humans, and animals exist is in delicate balance. Any changes to its equilibrium can afford increased opportunities for microbes to breach the species barrier. Opportunities occur through direct human contact with livestock and wild animals and/or their waste materials in shared ecosystems (7). They also occur through human-animal contact along the food production and marketing chain (8). These opportunities are increasing because of greater levels of infringement of human populations on animal habitats through urbanization, logging, mineral extraction, and recreation; and increasing demand for animal-based foods and other shifting dietary preferences that require more intensive animal husbandry and are based on international trade.

While human behavior plays a role in the type and extent of animal contact, and therefore the risk that an infectious organism will cross the species barrier, the inherent

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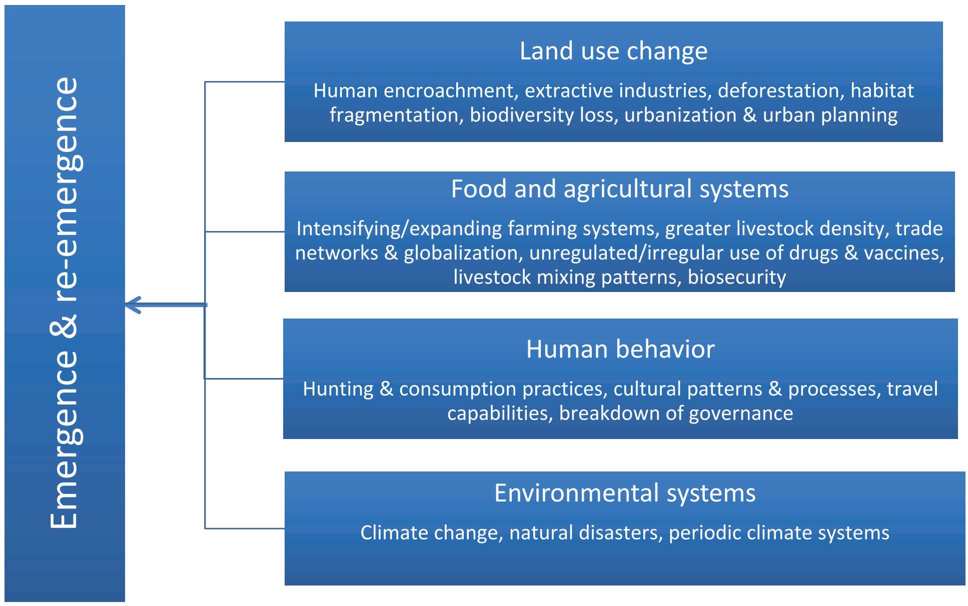

Figure 1. Potential pathways after emergence. doi:10.1128/microbiolspec.OH-0011-2012.f1

biology and genetics of the infectious organism also play a fundamental role. Some microbes are genetically unstable—the genome may be prone to mutations, replication error, reassortment, or recombination during reproduction in the animal or human host. Such alterations in the genome can change the transmission properties and increase or decrease virulence. Modification of the microbial genome can thus equip a microbe with the ability to cause illness, to transmit, and/or to survive (9). RNA viruses in particular demonstrate a strong propensity to mutate and develop into human infections that emerge from animals and are transmissible from human to human (10).

The term "emerging infection" is often used to describe newly identified zoonotic infections at the animal-human interface. Often they are first identified many years after the breach in the species barrier has occurred (11). During the past 40 years newly identified zoonotic—or emerging—infections have been identified that range from Ebola and Marburg hemorrhagic fever viruses to HIV, the paramyxoviruses (Hendra and Nipah viruses), and certain food-borne bacterial infections (e.g., verocytotoxin-producing *Escherichia coli* O157) (12, 13). Most emerging infections have been first identified in humans, before the animal source was known, and many of them reemerge when the risk factors for cross-species transmission align.

In some situations, an infection with the putative zoonotic organism is asymptomatic or causes mild human illness. At other times it causes severe human illness and there is need for an immediate and potentially emergency response in the infected human population to save lives and contain the infection through treatment and/or disease management.

The clinical response to zoonotic infections is often costly, an economic burden that can be particularly difficult in low-income countries where health budgets are already heavily restricted. Postexposure prophylaxis for rabies, for example, has been estimated (conservatively) to cost $40 in sub-Saharan Africa and $49 in Asia, a cost that equals 5.8 and 3.9%, respectively, of the annual per capita gross national income (14). But zoonotic infections can also be costly in industrialized countries. Health services utilization, work absenteeism, and direct costs for hospitalization of persons with H1N1 in Spain have been estimated at €6,236 per inpatient (15).

Following an outbreak caused by an emerging infection, an epidemiological investigation helps to assess the risk to humans—and to determine the source, and if the source is an animal, to understand whether there is continued risk of transmission to humans. A range of emergency response measures must then be implemented, including surveillance, contact tracing, isolation, social distancing, vaccination or prophylaxis (if vaccines and/or medicines are available), and in some instances culling of the animal source. The revised International Health Regulations (IHR 2005) (16) require World Health Organization (WHO) member states to rapidly assess an emerging infectious disease outbreak and notify the WHO, and through WHO the global community, if the outbreak fits the criteria established for a public health emergency of international concern and causes a risk of international spread (17).

Intensive culling of cattle after research had identified causal links between bovine spongiform encephalopathy (BSE) in cattle and variant Creutzfeldt-Jakob disease in humans, for example, was estimated to have cost the United Kingdom government $5.75 billion, including $2 billion in lost exports (18); culling of flocks of H5N1-infected chickens, coupled with inadequate compensation in Asian countries, cost an average of $210 per farmer, a high cost in a population whose average monthly income is $120 (19) (Fig. 2). If an emerging infection becomes endemic in human populations, the disease burden and cost can have a major and prolonged economic impact. The impact of AIDS in terms of lost economic output is significant, particularly in the poorest countries;

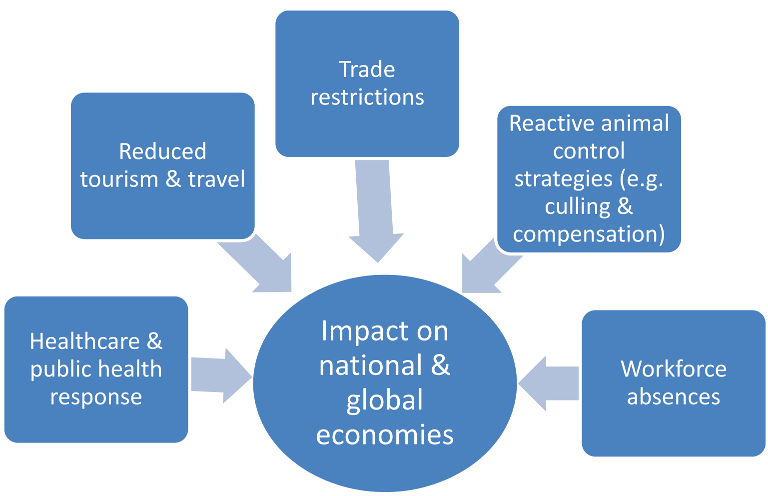

Figure 2. Economic impact of recent emerging infection events.
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reductions of 2 to 4% in the national gross domestic product have been calculated, for example, across a range of African countries (20).

Severe acute respiratory syndrome (SARS) was the first major emerging infection identified in the 21st century. A close examination of its origins, the outbreak and human sickness and death that it caused, the international response, and the effect it had on Asian economies provides a clear lesson of the impact of emerging infections and the reasons they must be assessed and managed with urgency to ensure a rapid and effective response.

First detected because it caused a severe atypical pneumonia, SARS soon became a burden in hospitals in the Guangdong Province of China, where many patients required respiratory support and broad-spectrum antibiotics had no effect. Hospital workers caring for these patients became infected as well, and one of them—a medical doctor who had treated patients in the Guangdong Province—traveled to Hong Kong, where he stayed in a hotel on the same floor as both Chinese and international guests. Some of these other hotel guests became infected, but it is not clearly understood how—hypotheses ranged from transmission through the hotel ventilation system to transmission in a shared closed environment such as occurs when people use the same elevator (21).

Those who became infected at the hotel were admitted to Hong Kong hospitals when they became ill or traveled to other countries, many times while still in the incubation period, to become seriously ill at their next destination. Hospitalized, they too became sources of infection of hospital workers, who in turn unintentionally infected other patients and family members.

Molecular and epidemiological investigation suggested that the infection of the index case (never identified) was a onetime event. As more information became available, it was further hypothesized that this initial infection was due to close contact with an infected animal, probably a civet cat, thought to have been a carrier of a coronavirus that mutated, either in the animal or an infected human, in such a way as to cause severe human illness (22).

The world's interconnectivity through air transport facilitated the international spread of SARS. Its electronic connections also permitted a virtual collaborative effort for surveillance, and for an emergency outbreak investigation, management, and containment: the most favorable patient management regimens and modes of transmission were rapidly identified; the causative organism was identified and characterized; international travel advisories were recommended to stop international spread; and after human-to-human transmission had been interrupted, the scientific evidence that was collected during the outbreak was used for guidelines in preparation for another outbreak should it occur (23).

SARS resulted in 8,422 probable infections and 916 (11%) deaths; in addition, the economic impact of the outbreak on gross domestic product was estimated at $30 billion to $100 billion from decreased commerce, travel, and tourism (24). Unlike HIV, the SARS coronavirus did not become endemic, and economic recovery was rapid.

Research to examine various hypotheses of transmission and to develop medicines and vaccines was active during the outbreak, but it came to a standstill during the following year when there was no recurrence of human infection and resources were then shifted to other research priorities.

SARS and other emerging infections share a common theme: infection is often first detected in human populations, in which an emergency clinical response and hypothesis-generating outbreak investigation begin before the source of infection is understood.