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Emerging and Reemerging Infectious Diseases

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Glossary

Emerging infectious disease(s) Infections that are newly recognized in a population or have existed previously but are rapidly increasing in incidence or geographic range.
One health An interdisciplinary approach that brings together human, animal, and environmental health professionals to address complex global health problems.
Urban sprawl The uncontrolled movement of urban development away from a city central.
Vector Any organism, though usually an arthropod, that can transmit an infectious agent to a host.
Zoonoses Diseases that can be transmitted from an animal to human or a human to animal.

Introduction

Throughout history, infectious diseases have vastly impacted human civilization. This impact has been demonstrated by the relentless appearance of various infectious disease outbreaks, including plague that scourged Europe during the Middle Ages, yellow fever that decimated Napoleon's forces in Haiti during the early nineteenth century, and influenza that claimed the lives of as many as 50 million people in 1918 (Zietz and Dunkelberg, 2004; Patterson, 1992; Johnson and Mueller, 2002). In the twentieth century, public health knowledge and interventions increased, particularly in more developed countries, reducing the burden of infectious diseases (Armstrong et al., 1999). Industrialization and urbanization influenced improvements in sanitation, structural development (e.g., window screening), and vector control that collectively lowered transmission rates by reducing the population's contact with infectious agents (Armstrong et al., 1999). In addition, the discovery of penicillin in 1928 and the continual development of vaccines ushered in an age of treatment and prevention strategies that many believed could eradicate infectious diseases from the globe (Clardy et al., 2009; 1999).

This idea was personified by organizations that made pronouncements to 'take up arms' against the most burdensome diseases. A well-known example comes from the Rockefeller Foundation, an organization that allocated substantial resources in the early twentieth century to combat yellow fever in the United States and other highly impacted territories, efforts that established precedence for future work (Fosdick, 1989). After World War II, new health organizations were established, including the US Centers for Disease Control and the World Health Organization (WHO) that led multiple campaigns to completely eradicate specific infectious diseases. One of the most notable efforts was the vaccination campaign against smallpox, a highly infectious viral disease that was completely eradicated by 1980 (Henderson, 2009). These campaigns established a great confidence and optimism in the ability to combat and control infectious diseases worldwide.

Despite these achievements, infectious diseases still pose a considerable threat today (Jones et al., 2008). Currently, it is estimated that at least 25% of total global mortality is attributable to infectious diseases, translating into over 15 million deaths per year (Mathers et al., 2008). The majority of deaths occur among children less than 5 years of age, living in countries with low to middle incomes (Mathers et al., 2008). Certain diseases have greater mortality, such as acute respiratory infections, tuberculosis, diarrheal diseases, malaria, measles, and HIV/AIDS, which account for 9 out of every 10 infectious disease deaths (2001).

Data from the past 30 years reflect various degrees of resurgence or reemergence of different infectious diseases worldwide. Two important examples of this phenomenon include the increased incidence of wild-type poliomyelitis across geographic pockets of Northern Africa, as well as an increase in the number of individuals being infected by the mosquito-borne disease caused by dengue viruses. Additionally, novel infectious diseases continue to emerge in virtually every region of the world. Examples include Hendra virus, discovered in 1994 in Australia (Murray et al., 1995); Nipah virus, identified in 1999 as the causative agent of outbreaks among pig farmers in Malaysia (Chua et al., 2000); severe acute respiratory syndrome (SARS) responsible for an outbreak of respiratory disease in multiple countries in 2003 (Marra et al., 2003; Peiris et al., 2003); and the 2009 emergence of a new influenza strain, originating in North America, responsible for the first pandemic of the twenty-first century (2009b). In public health, these types of events are referred to as emerging or reemerging infectious diseases, or collectively known as emerging infectious diseases (EIDs). EIDs have been defined as infections that are newly recognized in a population or have existed previously but are rapidly increasing in incidence or geographic range (Morse, 2004; Morens et al., 2004; Fauci, 2005, 2001; Institute of Medicine (US). Committee on Emerging Microbial Threats to Health et al., 1992). EIDs can be considered emerging, recently reemerging/resurging, or deliberately emerging, depending upon the pathway of emergence (Morse, 2004; Fauci, 2005; Morens et al., 2008).

EIDs are influenced by a wide variety of often complex factors, including ecology, human behavior, globalization, microbial adaptation, and public health infrastructure (Morse, 1995, 2004; Lashley, 2003; Morens et al., 2004, 2008; Fauci, 2005; Jones et al.,

This article is a reprint of B.D. Anderson, G.C. Gray,Emerging and Reemerging Infectious Diseases, *Reference Module in Biomedical Sciences*, Elsevier, 2014.

2008). More recently, the threat of bioterrorism, or the deliberate release of viruses, bacteria, or other agents used to cause illness or death in people, animals, or plants (Inglesby et al., 2002; Jernigan et al., 2002; Traeger et al., 2002), has added its own complexities to how EIDs affect global health. A number of recent bioterrorism events have had a dramatic impact on public health policies and resource allocations. New research and technology have provided better detection and response capabilities, as well as basic general knowledge of the various factors and determinants affecting the emergence and spread of EIDs; however, much is still unknown. This article offers a review of the most relevant literature associated with EIDs, as well as perspectives on how to address the most critical future public health questions.

Global Distribution

EIDs exist in most regions of the world, often with distinct and identifiable transmission patterns that are driven by various predictors or risk factors. These include the globalization of travel and trade, country and individual social–economic status, as well as population dynamics. Risk factors are used to identify trends in the movement of EIDs throughout various populations. When coupled with Geographic Information Systems mapping software, transmission patterns can be modeled, offering a pictorial view of EID distribution. These models are very useful, allowing for predictions to be made as to where future EID events are likely to occur and estimating the impact of public health interventions.

Globalization

Modern globalization has created ubiquity in world travel and trade. For example, a piece of fruit that is grown in Chile today can be purchased in a market on the other side of the world in 1–2 days. EIDs travel via these rapid global transport systems as made evident by the frequent international foodborne epidemics and zoonotic disease outbreaks that have occurred over the past few decades. SARS in 2003 demonstrated how quickly a highly transmissible respiratory pathogen can be spread, originating in China, and making its way to more than 15 countries in just a few months (Shen et al., 2004). Another example is the cholera outbreak that began in Haiti following a devastating earthquake in 2010, with genomic evidence suggesting that the epidemic *Vibrio* strain that ignited the outbreak was likely carried into the country by foreign security forces (Keim et al., 2011; Chin et al., 2011; Pun, 2011; Piarroux et al., 2011; Ali et al., 2011). These types of events make control extremely difficult, reflecting how quickly EIDs can be transmitted and established in new populations before public health officials can intervene.

EIDs and Economic Status

Geographically, EIDs are often more highly prevalent among underdeveloped and economically disadvantaged populations. Along with a high incidence of EIDs these populations also experience a greater severity from infections, often translated into higher rates of mortality (Farmer, 1996). This trend is attributed to various social determinants of health that elevate the susceptibility of an individual or population to infection (Marmot, 2005). Poverty both promotes and results from social determinants including access to health care, clean water, food, and other important environmental factors that influence disease transmission (Marmot, 2005). The cyclic nature of this relationship makes public health interventions complicated, since most, if not all, determinants must be addressed in order to have a lasting positive impact.

The socioeconomic status of a country can be an important determinant for the transmission of EIDs, influenced by both the availability of an appropriate public health infrastructure and the necessary resources to carry out prevention and control strategies. This could include instituting effective surveillance systems, as well as providing adequate health-care services to individuals affected by EIDs. Without this necessary capacity, a disease can quickly become well established or endemic in a population before a public health response can be initiated, if one is initiated at all.

Historically, tuberculosis, chiefly caused by *Mycobacterium tuberculosis*, is an EID associated with economics, often being coined a 'disease of poverty' due to the increased impact it has on economically poor individuals. Today, data indicate 95% of all tuberculosis cases and deaths occur in the developing world (2012b). In the past 30 years, tuberculosis has begun to reemerge across the globe, partly due to the emergence and spread of HIV, which is now a primary risk factor for tuberculosis transmission. Nearly half of all individuals in the developing world who have HIV also are coinfected with *M. tuberculosis* (2012b). This emphasizes the importance economics play as a driver for disease emergence and reemergence, as well as the treatment strategies available for those infected.

Despite a disproportional distribution of EIDs in low- and middle-income countries, high-income countries experience their own burden of EIDs. In the United States, West Nile virus continues to cause disease in man. Lyme disease is also well established with an annual incidence that has increased in over the past 10 years, reaching over 30 000 and 60 000 reported annual cases in the United States and Europe, respectively (Radolf et al., 2012). In 2003, the global pet trade contributed to an outbreak of monkeypox virus in the United States that originally infected individuals who had close contact with prairie dogs purchased as pets through a common supplier. Epidemiological studies traced the origin of this outbreak back to an exotic African rodent species that transmitted the virus to the prairie dogs during transport to the United States (Reed et al., 2004).

Higher socioeconomic countries also experience a substantial burden of foodborne related EIDs, the more common pathogens being bacteria, including *Salmonella* spp., *L. monocytogenes*, *Brucella* spp., *Campylobacter* spp., and pathogenic strains of *E. coli* (Newell et al., 2010). Even with strict regulations on food production, outbreaks frequently occur due to the centralization and mass production by the food industry, which is capable of distributing large quantities of food over vast geographic areas. In this

type of system, if food becomes contaminated, then rapid dissemination of the pathogen before detection is much more likely. This is especially dangerous when the pathogen being disseminated is very pathogenic and the population is more susceptible. This was the case when a rare subtype of enterohemorrhagic *E. coli* (O104:H21) was responsible for a foodborne outbreak throughout Europe in 2011 that caused over 3800 cases and 54 deaths (Frank et al., 2011). Upon investigation, the source of the outbreak was found to be sprouts that were grown with contaminated seed attained from a supplier in another country (Buchholz et al., 2011).

Population Density and Expansion

Since 1960, the global population has more than doubled, from 3 billion to nearly 7 billion people (2012a). As the population has grown, population density has also increased, creating in some countries what are called megacities (e.g., Tokyo, Mexico City, New York City, etc.). These cities may have upward of 20 million people or more, sometimes residing in extremely confined geographic areas. These conditions promote the proliferation of new diseases, especially when the pathogen is highly transmissible, forming emerging disease 'hot spots' (Jones et al., 2008; Heymann and Rodier, 2001). In addition, some of these countries operate wet markets where livestock, including poultry and swine, are slaughtered in poor hygienic conditions and sold directly to the public (Webster, 2004). These practices further promote favorable environments for disease emergence, with SARS and highly pathogenic avian influenza (HPAI) virus being recent examples.

In response to rising population densities, many cities have seen an increase in urbanization, particularly away from a city central. This practice is often referred to developmentally as urban sprawl. While the practice has helped to reduce the rate of growing population density inside cities, it has concurrently moved more groups of people into previously undeveloped areas. This rapid expansion in land use and development has combined what was once fairly separated animal and human habitats, allowing for more frequent exposure of humans to potential disease reservoirs, increasing the risk of EID proliferation.

Pathways of Emergence

It has been proposed that EID events occur in two steps (Morse, 2004). A pathogen must first be introduced into a new population and then disseminated within that population. With this construct in mind, understanding the origin of novel microbes becomes critical. Microbes often exist in the environment in a nonpathogenic state, with limited contact with a viable host. However, when appropriate conditions are met, opportunistic microbes can exploit new niches, including human hosts, resulting in a successful introduction. Once successful, this type of event is sometimes referred to as a microbial 'jump' or 'crossover'. This crossing of the species barrier is often necessary before widespread dissemination can occur.

Dissemination is then dependent upon the transmissibility of the pathogen in the new population. Dissemination can occur directly from one host to another, or can establish an intermediate host in its transmission cycle, such as a vector. If a pathogen is unable to be transmitted beyond an immediate or intermediate host, then further dissemination is not possible. These interactions can often be complex, involving pathogen, environment, and host, making it challenging to understand and identify what contributes to the most optimal conditions promoting disease emergence.

Zoonoses

The transmission of a pathogen between animals and humans is known as zoonotic transmission or zoonosis. Zoonosis is perhaps one of the most important pathways of emergence, with an estimated 75% of all known EIDs originating from some type of animal reservoir (Taylor et al., 2001). Disease examples include HIV/AIDS, Lyme disease, plague, SARS, several hemorrhagic fevers, and zoonotic influenza. Each of these possesses a unique etiology, and though it is not an exhaustive list, it highlights the diversity of disease emergence related to zoonosis. Additionally, effectively controlling zoonotic diseases is particularly difficult, since recognizing an emerging zoonotic disease often does not occur until a major outbreak is already underway. If the responsible zoonotic pathogen is highly transmissible, then future epidemic spread occurs even after recognition.

As previously discussed, population growth has had a drastic impact on society. Greater zoonotic disease potential can result from this growth primarily due to an increased interaction between humans and animal habitats, Figure 1. Population growth has also resulted in a higher demand for food commodities. To meet this growing demand, industrialization of food production is increasing, especially in developing countries. This is true of all types of food, including meat production that has moved away from small farms toward large-scale cattle, poultry, and swine operations, Figure 2. These sites have been able to streamline meat production; however, it comes at the cost of creating favorable environmental conditions for the zoonotic transmission of opportunistic microbes (Drew, 2011).

Other food acquisition practices pose a greater risk of acquiring an EID. This includes the long-standing practice in Africa, Asia, and the Americas of hunting and consuming wild animals, also called bushmeat. Eating bushmeat has been associated with a number of new diseases, including two highly fatal hemorrhagic diseases caused by Ebola and Marburg viruses (Peters, 2005; Wolfe et al., 2005). Additionally, the practice of consuming raw or unpasteurized milk products (e.g., milk, cheese) can increase the transmission risk of certain zoonotic bacteria, such as *L. monocytogenes*, *Brucella* spp., and *Camylobacter* spp. This is particularly common in areas where pasteurization is not an accepted practice.

Figure 1 The risk of zoonotic transmission of a pathogen is increased with man's close and frequent contact with other species.

Figure 2 Large dense populations of animals, particularly in herds, can promote zoonotic pathogen transmission to man.

Vectors

Some EIDs are vector-borne, caused by the transmission of a pathogen through the feeding activity of a vector, usually an arthropod. Some of the most common and effective vectors are insects including flies and flees, as well as arachnids such as ticks and mites. These vectors are often attracted to humans and animals because they are obligate blood feeders, using biting or piercing mouthparts to obtain a blood meal from their host. Pathogens have coevolved with vectors to exploit this behavior, often relying on transmission to allow for the propagation of new progeny. An example of a model vector that does this is the mosquito, which is the most widely distributed and abundant vector in the world. Mosquitoes are of particular concern due to their sometimes aggressive feeding behavior and ability to effectively transmit a broad range of pathogens, causing diseases such as malaria, dengue fever, and many others.

In terms of importance to emergence, it has been suggested that vector-borne EIDs constitute nearly a quarter of all EID events occurring in the last decade (Jones et al., 2008). Also, there has been an increase in the total number of vector-borne EIDs during this same time period, while other types of EIDs have slightly decreased (Jones et al., 2008). Increased human population density and changing demographics seem to be associated with this rising trend of vector-borne EIDs, as well as climate change that some have suggested is promoting an expansion in vector distribution and range (Jones et al., 2008; Epstein, 2001).

Animals are also important in the life cycles of vector-borne diseases, since many can be competent hosts and serve as reservoirs for different pathogens. In fact, some EIDs only occur when humans become an incidental or dead-end host in an already established transmission cycle between an animal and vector. This is true for Japanese Encephalitis (JE), a flavivirus transmitted by certain mosquitoes, causing viral encephalitis cases primarily in Asia. For JE, humans are dead-end hosts, capable of infection if bitten by an infected mosquito, but unable to amplify and transmit the virus further, whereas, swine and other wild birds are able to propagate the virus and maintain a complete transmission cycle. Hence, if humans are removed from the environment, the virus would still be sustained as long as the vector, pathogen, and reservoir were to remain.

Factors Associated with EIDs

Since the early 1990s, discussion has been centered on the factors that are most associated or attributable to EIDs. A report published by the Institute of Medicine in 1992 originally identified six contributing factors (Institute of Medicine (U.S.). Committee on Emerging Microbial Threats to Health et al., 1992). Since the list was published, new emerging threats have resulted in additional factors being added, all thought to be important contributors by the global health community, Table 1.

This list provides guidance as to where research efforts and interventions should be targeted. It is important to note that many of these factors are often interrelated with each other. For instance, a lack of political measures will often result in the breakdown of public health measures. Economic development and land use can be associated with technology and industry, as well as changing ecosystems, and shaping conditions of poverty. Hence, effective interventions must be multidimensional for sustained change.

Ecological Changes

Perhaps one of the most apparent and pervasive factors affecting the incidence of EIDs is environmental alterations that result in a drastic change in ecology. One common ecological model works from a premise that disease occurs at the intersection of environment, pathogen, and host, Figure 3. A change to any one of these entities could impact the disease outcome. It has been suggested that classical ecological tools are limited in their ability to effectively assess the multifaceted complexities of EIDs. This is clearly indicated by the limited number of published studies that have effectively evaluated EIDs from an ecological perspective (Meentemeyer et al., 2012). An ecological relationship could be as simple as the symbiosis of certain types of fungus and plants where no other factors play a role in the survival of everyone. Others can be much more complicated, such as the multistage life cycle of the guinea worm (cause of the disease dracunculiasis), a parasitic nematode that uses two different species, a copepod and humans, to complete its life cycle. These parasites are impacted by human movement, water availability, copepod abundance, as well as climate, all of which can impact the nematode life cycle.

However, the research that does exists suggests that the most important ecological changes encouraging EIDs are those that put humans in closer or more frequent contact with current or potential pathogen reservoirs. For instance, the incidence of Lyme disease in the United States and Europe seems to be associated with the number of available hosts in a given area. Deer and small mammals play an important role in the life cycle of ticks that vector the spirochete causing Lyme disease. Studies have shown that host populations directly correspond to tick abundance, often influenced by ecological factors that promote population growth (Levi et al., 2012). When this is coupled with urbanization and reforestation, transmission can drastically increase, since both the host and environment serve as the drivers for disease emergence.

Climate Change

Evidence shows that the earth's average surface temperatures have increased at least 0.6°C over the past century (Houghton and Intergovernmental Panel on Climate Change. Working Group I., 2001). While many agree with the empirical evidence of rising temperatures, there is still controversy as to why the earth is warming. Some argue that the earth is experiencing a natural temperature fluctuation similar to what has occurred throughout history, citing previous ice ages and warming periods. Others have suggested that the rising temperatures are attributed to increased atmospheric concentrations of carbon dioxide related to the

Table 1 Factors of emerging and reemerging infectious diseases

- Microbial adaptation and change
- Human susceptibility to infection
- Climate and weather
- Changing ecosystems
- Human demographics and behavior
- Economic development and land use
- International travel and commerce
- Technology and industry
- Breakdown of public health measures
- Poverty and social inequality
- War and famine
- Lack of political will
- Intent to harm

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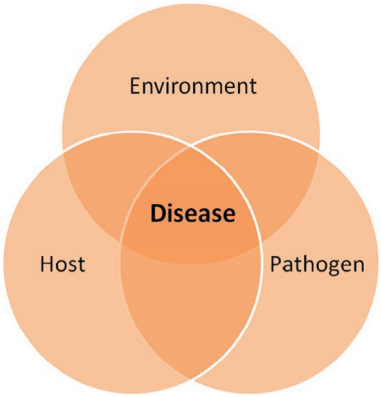

Figure 3 A basic ecological model illustrating the interaction of host, pathogen, and environment in disease.

burning of fossil fuels and deforestation. Despite the discourse, the reality of climate change in the context of EIDs remains an important topic, with research showing associations between disease indicators and climate factors (Patz et al., 1996; Epstein, 2001).

Climate change primarily impacts the range of infectious diseases, particularly those that are transmitted by vectors. Warmer temperatures allow vectors to more readily survive conditions at higher altitudes and latitudes, as well as having shorter periods of overwintering. Weather patterns are also influenced, as the hydrolytic cycle can be disrupted by warmer ocean temperatures, causing severe weather at greater frequency. Particularly concerning are weather events that release high volumes of rain, as they may result in temporary explosions in vector populations, especially mosquitoes.

Microbial Adaptation and Change

From a pathogen perspective, microbial adaptation and change significantly contribute to the likelihood that a microbe will become pathogenic in a population. As mentioned, when certain environmental conditions are met, a microbe can experience alterations in genetic makeup that can affect its pathogenicity or virulence. This type of adaptation can either occur gradually or rapidly by means of random mutations, reassortments, or adaptive pressures brought on by stressors such as antimicrobial agents.

A good example of microbial adaptation is demonstrated by the influenza A virus, an RNA virus that has been shown to undergo both gradual and rapid genetic changes. Just in the last 20 years, new variants of influenza have caused major human outbreaks, including HPAI subtype H5N1, first detected in 1997 (1997) and the pandemic influenza subtype H1N1, first detected in 2009 (2009a). Influenza A contains two surface proteins (glycoproteins), called hemaglutinin (HA) and neuraminidase (NA): HA proteins are associated with viral attachment and cell entry using a fusion pathway, while NA proteins regulate the release of progeny virus from an infected cell. Antigenic drift and shift are two mechanisms that create variations in the antigenic properties of these two proteins that allow influenza A to bypass the acquired immunity of a population, Figure 4. Antigenic drift occurs when small point mutations accumulate gradually, altering the antigenic properties of the two surface proteins. This can cause population immunity to partially decrease, resulting in seasonal epidemics. Antigenic shift involves major changes in proteins, sometimes through the swapping of entire gene segments. The genetic reassortment occurs when two or more unique viruses infect the same cell and generate mixed progeny viruses (Chen and Deng, 2009; Kaye and Pringle, 2005). In particular, genetic reassortments of the HA antigens may result in large worldwide epidemics or pandemics. Waterfowl are thought to be the largest source of diverse viruses from which gene reassortment may occur, as they are known to carry viruses with 16 different HA proteins. When a population has no or little immunity to a new subtype and the new subtype is highly transmissible, pandemics may result.

Like influenza A virus, other pathogens undergo similar mechanistic adaptive changes and sometimes variation results from external pressures that promote microbial evolution. Antibiotic resistance is an example of this kind of adaptation. Since their discovery, the use and variety of antibiotics have greatly increased over time and many pathogens have adapted to their presence. These antimicrobial resistant pathogens are having an increased impact upon clinical care and medical costs.

Bacteria, such as methicillin-resistant *Staphylococcus aureus* and multidrug resistant *M. tuberculosis*, are good examples of the severe impact that this type of microbial adaptation can have on individual health outcomes. Individuals infected with these bacteria are often prescribed newer and more expensive, 'last defense' antibiotics. These diseases may be life-threatening and require specialized care. Hospitalized patients with these resistant pathogens may seed the hospital staff and environment and cause nosocomial transmission among immunocompromised patients.

Important EID Examples

EIDs result from a large variety of causative agents, each one possessing a unique etiology and ecology. Agents may be organized according to transmission pathways, genetic markers, or the pathology a pathogen might exhibit in a population. Most often,

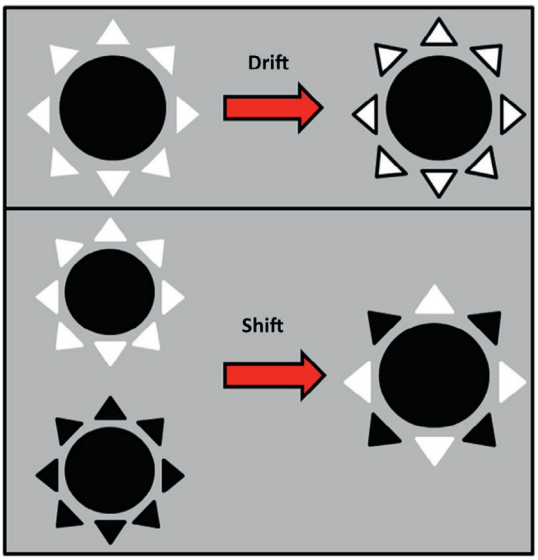

Figure 4 Graphical representation of antigenic drift and shift among influenza A viruses. Top panel: Antigenic drift – minor genetic changes (e.g., through mutation) lead to slight changes in surface glycoproteins or season variation in strains. Bottom panel: Antigenic shift – exchanges of entire segments of genome lead to major changes in the surface glycoproteins, which may lead to pandemics.

however, EIDs are categorized into bacteria, virus, fungus, parasites, and more recently prions. Table 2 presents key examples of each of these disease categories.

Conclusions

As the world's population rises and public health problems increase in complexity, it will be critical to establish innovative and dynamic strategies to counter EID threats. These strategies should include the reinforcement of public health systems, better diagnostics for EIDs, stronger surveillance systems, and better interdisciplinary and international collaborations. A novel interdisciplinary strategy, called One Health, is gaining popularity as an approach that attempts to focus efforts on complex public health issues such as EIDs.

Public Health Infrastructure

Public health infrastructure is critical to the current mitigation and future prevention of EID events. An effective infrastructure should include the following: a legal framework that allows for enforcement of public health measures and a system to monitor outcomes; dissemination and utilization of health knowledge, including the training of health workers; and physical environments or services conducive to targeting important health threats, like sanitation infrastructure (e.g., sewers). Infrastructure can subsist on a local level, but most often relies upon the coordination and leadership of nationallevel governments, providing guidance for task prioritization and implementation. However, national and international organizations can also provide assistance by supporting government-led efforts with technical and financial resources, or filling in the necessary gaps of a fragmented infrastructure.

EID Diagnostics

Diagnostics are an important tool for identifying and characterizing infectious disease agents from both clinical and environmental samples. Common techniques include molecular assays, such as multiplexing, microarrays, deep sequencing, and traditional and real-time polymerase chain reaction, as well as immunoassays, including variations of the enzymelinked immunosorbent assay and other techniques exploiting antigen and antibody binding activity. The variety and availability of these techniques have greatly improved over the last two decades, with significant increases in sensitivity and specificity, as well as marked decreases in costs. For instance, the cost of full genome sequencing of a moderately large virus has seen substantial reductions in the past decade, dropping from tens of thousands of dollars per run to a couple thousand dollars, with much more accurate analysis. Much of this improvement can be attributed to new technological developments, such as third and fourth generation sequencing that is greatly improving novel pathogen detection capabilities.

Table 2 Examples of recent human emerging infectious disease threats

Emerging infectious disease threat	*Pathogen*	*Emerging/reemerging*	*Primary transmission*	*Key geographic area(s)*
Bacteria				
Bartonella infections	*Bartonella spp.*	Emerging	Zoonotic	Australia, Europe, United States
Vancomycin-resistant *Staphylococcus aureus* infections	*Staphylococcus aureus*	Reemerging	Person-to-person	Worldwide
Pathogenic *Escherichia coli* infections	*Escherichia coli*	Emerging	Foodborne	Europe, United States
Cholera	*Vibrio cholerae*	Reemerging	Waterborne	Africa, Asia, South America, Haiti
Plague	*Yersinia pestis*	Reemerging	Vector-borne	Africa, Asia, South America, United States
Typhoid fever	*Salmonella typhi*	Reemerging	Foodborne, waterborne	Africa, Asia, Latin America, Carribean
Diphtheria	*Corynebacterium diphtheriae*	Reemerging	Respiratory (person-to-person)	Eastern Europe, India
Multidrug-resistant tuberculosis infections	*Mycobacterium tuberculosis*	Reemerging	Respiratory (person-to-person)	Worldwide
Lyme disease	*Borrelia spp.*	Emerging	Vector-borne	Eastern Asia, Europe, United States
Fungal				
Cryptococcus gattii infections	*Cryptococcus gattii*	Emerging	Environmental exposure	Australia, Canada
Parasite				
Cyclosporiasis infections	*Cyclospora cayetanensis*	Emerging	Foodborne, waterborne	Worldwide
Drug-resistant malaria	*Plasmodium spp.*	Reemerging	Vector-borne	Africa, Asia, South America
Protein				
Variant Creutzfeldt–Jakob disease	Prion	Emerging	Zoonotic, foodborne	Europe
Virus				
West Nile fever	West Nile virus	Reemerging	Vector-borne	Africa, Asia, Europe, North America
Hantavirus pulmonary syndrome	Hantavirus	Emerging	Zoonotic	Canada, East Asia, Europe, South America, United States
Dengue fever	Dengue virus	Reemerging	Vector-borne	Central Africa, Central America, Latin America, Southern Asia
Yellow fever	Yellow fever virus	Reemerging	Vector-borne	Central Africa, South America
Lassa fever	Lassa fever virus	Emerging	Zoonotic	Central and Western Africa
Marburg hemorrhagic fever	Marburg virus	Reemerging	Zoonotic	Central Africa
Ebola hemorrhagic fever	Ebola virus	Reemerging	Zoonotic	Central Africa
Rift Valley fever	Rift Valley fever virus	Reemerging	Vector-borne	Africa
Hendra virus infection	Hendra virus	Emerging	Zoonotic	North-eastern Australia
Nipah virus infection	Nipah virus	Emerging	Zoonotic	Asia
Highly pathogenic avian influenza	H5N1 influenza virus	Emerging	Zoonotic	Asia
Severe acute respiratory syndrome	SARS coronavirus	Emerging	Respiratory (person-to-person)	Asia[a]
2009 pandemic influenza	2009 H1N1 influenza virus	Emerging	Respiratory (person-to-person)	Worldwide
Japanese encephalitis	Japanese encephalitis virus	Reemerging	Vector-borne	Asia

[a]Originated in Asia, but had rapid global transmission.

Reproduced from Armstrong, G.L., Hollingsworth, J., Morris, J.G., Jr., 1996. Emerging foodborne pathogens: Escherichia coli O157:H7 as a model of entry of a new pathogen into the food supply of the developed world. Epidemiol. Rev. 18, 29–51; Rey, M., 1996. Resurgence of diphtheria in Europe. Clin. Microbiol. Infect. 2, 71–72; Collinge, J., 1999. Variant Creutzfeldt-Jakob disease. Lancet 354, 317–323; Wongsrichanalai, C., Pickard, A.L., Wernsdorfer, W.H., Meshnick, S.R., 2002. Epidemiology of drug-resistant malaria. Lancet Infect. Dis. 2, 209–218; Crump, J.A., Luby, S.P., Mintz, E.D., 2004. The global burden of typhoid fever. Bull. World Health Organ. 82, 346–353; Mackenzie, J.S., Gubler, D.J., Petersen, L.R., 2004. Emerging flavi viruses: the spread and resurgence of Japanese encephalitis, West Nile and dengue viruses. Nat. Med. 10, S98–S109; Shen, Z., Ning, F., Zhou, W., He, X., Lin, C., Chin, D.P., Zhu, Z., Schuchat, A., 2004. Superspreading SARS events, Beijing, 2003. Emerg. 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A major need is the better recognition of EIDs, especially in low-resource areas where EIDs are common. This can be accomplished by prioritizing laboratory infrastructure development, continuing to direct efforts in targeting disease 'hot spots' where EID outbreaks are most likely to occur. Emphasis should be placed on making new diagnostic assays timely, affordable, and feasible for laboratories with limited resources. In addition, employing assays that are able to detect multiple agents in a single specimen is important in EID management. This kind of technique allows for more rapid identification of causative agents, an important component in how public health responses are planned and delivered.

Global Surveillance and Communication

Disease surveillance is defined as the ongoing systematic collection, consolidation, and analysis of outcome specific data for the purpose of planning, implementation, and evaluation of various health-related events (Thacker, 1988). Many information and surveillance networks that are currently in place can be characterized as fragmented or unrepresentative of actual disease circulation in a population, making it difficult to estimate actual incidences. There have been some successes in improving surveillance capabilities, particularly passive surveillance that uses techniques such as monitoring healthcare clinics and emergency rooms for various health outcomes indicative of an EID.

For instance, global influenza surveillance, following the 2009 H1N1 pandemic, received substantially more prioritization and resource allocations from countries that were lacking such capabilities beforehand. This has resulted in a rather comprehensive collection and dissemination of data to stakeholders worldwide, through a network called FluNet. This network is overseen and coordinated by WHO, and helps provide a more comprehensive resource regarding the incidence and circulation of different strains of influenza. Information is used not only to enhance outbreak response, but is also the source of prototype strains that are used in annual seasonal vaccination manufacturing. This is an example of how successful surveillance can greatly improve the public health response capabilities.

For EIDs this may be more difficult, only since it takes a large amount of coordination and resources to create global surveillance for any specific pathogen. Furthermore, loweconomic countries often do not have the necessary resources to carry out such endeavors. The Internet may be useful in supporting countries that lack traditional surveillance capabilities, as has been demonstrated by the international e-service called ProMED-mail. This service is a consortium of public health professionals that disseminate disease outbreak updates, often in real time, through a global e-mail distribution list. Since telecommunications are becoming well established, even in low-economic countries, this has proven to be a very practical approach, providing the international community with reliable information and even sometimes serving as a first report of an index case. Further developing these types of approaches will be useful in communicating EIDs, pre- and postevent.

International Collaboration

Today, EIDs impact our entire world. It will be important that governments and agencies concur with the need for strong international communication and collaboration regarding EID events. This will include the sharing of resources and knowledge, particularly regarding EIDs that are considered a global threat. It is also ideal that low-economic countries receive priority in the enhancement of their public health systems, since a large proportion of EID risk exists in these areas. Collaborations offer unique diversity in expertise, improve cultural competencies, and enhance response efforts in the event of an EID outbreak.

'One Health'

It is clear that EID ecology is often complex, requiring a sophisticated, interdisciplinary response to mitigate disease impact. One attempt to address these complexities has been coined 'One Health'. One Health is a moniker for the interdisciplinary approach, bringing together human, animal, and environmental health professionals, to address complex global health problems. While the terminology may be relatively new, the foundations of the approach are not. Throughout history, individuals from different disciplines have often worked together to create solutions for some of the most important health threats. One Health attempts to convert those cooperative successes into a practical methodology to be used in future public health problems.

One of the strongest arguments for One Health is the role zoonoses play in the emergence of new infectious diseases, and the recognized long-standing gap of cooperation that has existed between the fields of animal and human health. As previously described, the global impact of HIV, H5N1 avian influenza, SARS, and 2009 H1N1 pandemic influenza, all diseases with origins from animal reservoirs, have led to a consortium of doctors, veterinarians, and public health officials beginning to work together to identify effective solutions that bridge the gap between each discipline. In addition, experts from fields of geography have begun to pursue new models to help predict the movement of different EIDs. Engineers are developing new technologies, based upon the recommendations of field workers that may mitigate contamination of food and water supplies. Economists are calculating the cost effectiveness of vaccination campaigns to help guide policy makers in better using resources.

Overall, One Health is an approach that can improve effectiveness of public health response and interventions, as it allows for a more targeted application of multiple areas of expertise, not relying on a single discipline approach that may not address all of the minute facets that accompany most public health problems of today. To be successful, it will require an intentional effort of current public health professionals reaching out to one another, to strengthen collaborations, communication, and the ability to be open to novel ideas. Since this approach promotes flexibility, it should be able to adapt to the rapid changes demonstrated by emerging

diseases in the last two decades. It is this characteristic that makes One Health not just a temporary solution, but a philosophy that can have serious long-term impact on EID morbidity and mortality.

Acknowledgments

We thank Whitney S. Krueger, PhD, for her much appreciated editorial review of this work.

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