

# 8

## EMERGING INFECTIOUS DISEASES: CONCEPTS IN PREPARING FOR AND RESPONDING TO THE NEXT MICROBIAL THREAT

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### OVERVIEW\*

Former U.S. Surgeon General William H. Stewart has been attributed with stating in the late 1960s that the time had come to “close the book” on infectious diseases as major threats to public health. Even though this statement’s authenticity has been questioned,<sup>1</sup> it is often used to convey the optimism expressed at the time by health experts and world leaders.<sup>2</sup> At the time, it did appear that the age of infectious diseases that had plagued humans for millennia was coming to an end. Vaccines and antibiotics had substantially reduced the incidence and mortality of many diseases. The smallpox eradication campaign was on its way and it was thought that eradication of other diseases (for example tuberculosis and polio) would not be too far behind. Improved food and water safety resulted in less exposure to disease-causing microbes, and the use of pesticides to control arthropod populations had reduced vector-borne diseases. It seemed the battle with the microbial world had been won, and it was time to focus efforts and funding on the looming threat of chronic diseases.

This confidence, however, largely ignored the burden of infectious diseases in the developing world. Five decades later, although great strides have been made to control infectious diseases, microbial pathogens are still major threats to public health throughout the world. The last few decades have unveiled new challenges: “old” pathogens once thought to be controlled by antibiotics have developed multidrug resistance, new pathogens have emerged, and traditional pathogens have appeared in new locations. Furthermore, factors such as increased global commerce and travel and the threat of the intentional release of pathogens have set the stage for infectious disease disasters with large numbers of casualties. In this chapter, “casualties” includes all persons with symptoms of the infectious disease, not just fatalities.

There is a wide body of knowledge on the emergence and reemergence of pathogens of public health importance. Humans are in a delicate balance with microbial cohabitants of the earth;

circumstances can tip that balance in favor of microbes with new or renewed pathogenic vigor. There will always be emerging pathogens, and consequently there is always the chance that a virulent microbe will cause extensive human disease and death. Exactly what the causative agent of the next big infectious disease disaster will be and when it will happen is not known. Using examples from past events, this chapter addresses the concepts and tools necessary to prepare better for and respond to infectious disease disasters in general.

### OVERVIEW

#### The Threat of Emerging Infectious Diseases

Infectious diseases are caused by microorganisms such as bacteria, viruses, fungi, and protozoa, and by proteinaceous particles called prions. The majority of microbes on earth are benign to humans; many are necessary for ecological stability, and even human and animal health. Microbes that do cause disease are collectively referred to as pathogens. There are more than 1,400 pathogens known to cause disease in humans.<sup>3</sup>

Some pathogens are prevalent at a constant and stable rate in a given population and are considered “endemic.” Other infectious diseases are not common to a given population but, at times, a number of cases occur that is higher than expected. This situation is considered an “outbreak” (for a more localized increase in disease incidence) or an “epidemic” (for a larger regional increase in disease incidence). The concept of the epidemiological triangle (Figure 8.1) is used to understand the factors involved in promoting such an outbreak or epidemic. This model highlights the interactions among an agent (e.g., *Salmonella*), a host (e.g., elderly patients at a nursing home), and an environment (e.g., undercooked chicken left at room temperature) that cause disease (e.g., acute gastroenteritis). Table 8.1 provides a comprehensive list of terms related to infectious disease biology.

Many pathogenic microbes have been associated with human disease for hundreds or thousands of years. Examples of infectious diseases with long human histories include smallpox, plague, cholera, malaria, tuberculosis, and syphilis. These diseases, and others, resulted in millions of deaths over the

\* The views expressed in this chapter are those of the authors and not necessarily those of the University of Cincinnati or U.S. Department of Veterans Affairs.

**Table 8.1. Infectious Diseases Biology Terminology**

	<i>Description</i>	<i>Example</i>
Airborne Transmission	The process whereby agents are spread by small-particle ( $\leq 5 \mu\text{m}$ ) droplet nuclei that can suspend in the air and travel by air currents or through ventilation systems; respiratory PPE (N95 respirator) is often required to prevent infection in responders.	<i>Mycobacterium tuberculosis</i>
Biological Incident	The presence of a pathogen in a population from a natural, accidental, or intentional exposure that has the potential to cause extensive public harm and/or fear.	2012 MERS emergence in the Middle East (natural); 2010 return of epidemic cholera to Haiti (accidental); 2001 dissemination of anthrax spores in U.S. mail (intentional)
Communicable	The ability of an infectious agent to be transmitted from one host to another; contagious.	Influenza, smallpox
Contact Transmission	The process whereby agents are spread by direct contact with a person or indirect contact with contaminated objects.	Direct contact: skin (MRSA); mucous membrane (HIV) Indirect contact: fecal-oral (norovirus)
Droplet Transmission	The process whereby agents are spread by large-particle ( $> 5 \mu\text{m}$ ) droplet nuclei produced by, for example, coughing and sneezing; agent does not remain suspended in the air for a long time and infection usually occurs when susceptible person is within 1 m of infected person. A surgical mask may offer protection.	Influenza Meningococcal disease
Endemic	A disease that is consistently present in a population at a certain level or rate without requiring introduction from another area.	Malaria in India and Africa
Epidemic	A level of disease that is higher than the expected level at a time or location. Similar to an “outbreak” but usually refers to disease incidence that spans a large region, country, or multiple countries for a prolonged period of time.	Cases of measles in Wales in 2012–2013 Chikungunya fever on La Réunion Island in 2005–2006
Host – Resistant	The state in which a person is immune to infection by a specific pathogen.	In general, a person who has had hepatitis A is resistant to subsequent infection with the hepatitis A virus.
Host – Susceptible	The state in which a person can be infected by a specific pathogen. May be due to lack of immunity and/or to host factors that promote infection (e.g., a specific receptor).	A person who has not had the Measles/Mumps/Rubella (MMR) vaccine is susceptible to the agents that cause these diseases.
Isolation	The separation of infectious disease cases from the general population to prevent transmission of the agent to susceptible people; instead of physical separation, may use barriers such as masks on cases to “isolate” the infection and prevent transmission (this may be necessary in disasters with many casualties).	In 2003, SARS cases were sequestered on specific hospital wards.
Mode of Transmission	The mechanism a pathogen uses to spread from one host to another.	Airborne transmission by small particles in the air
Outbreak	An increased incidence of a disease in a region. Usually on a smaller scale (regionally and temporally) than an epidemic.  A food-borne outbreak typically refers to disease caused by food(s) contaminated with a specific pathogenic microorganism.	<i>Neisseria meningitidis</i> outbreak on a college campus Norovirus outbreak on a cruise ship
Pandemic	The global spread of an epidemic.	1918 influenza pandemic 2009 H1N1 pandemic
Quarantine	A form of isolation that restricts the movements of <i>healthy people who were exposed</i> to a contagious agent to prevent contact with the general public. The duration of the quarantine period is usually the longest time for symptoms to appear after exposure (incubation time). Home quarantine refers to isolation of exposed persons in the home, provided that basic needs can be met and contact with other household members can be avoided. Work quarantine refers to permitting exposed healthcare workers and emergency responders to go to work using appropriate PPE so that disaster operations can remain intact; this modification does not apply to workers in the general public.	In Ontario, Canada in 2003, people who were exposed to SARS were quarantined for 10 days. At times during the epidemic, over half of the paramedics in the Toronto area were operating under work quarantine conditions.
Reproductive Rate ( $R_0$ )	For an infectious agent, the number of people to whom an infected person spreads the disease in the absence of control measures (such as vaccination, isolation of cases).	According to historical data, a person with pandemic influenza will transmit the disease to three other people

Table 8.1. (continued)

	Description	Example
Reservoir	The environmental niche of a pathogenic organism, usually another organism unaffected by the infectious agent.	Specific rodent species are the reservoirs for particular hantavirus strains. Human-made water sources for <i>Legionella</i> species infections
Vector	An organism (e.g., insects or other arthropods) that harbors and transfers agents that are pathogenic to another organism (e.g., humans).	<i>Ixodes</i> ticks transfer <i>Borrelia burgdorferi</i> , the causative agent of Lyme disease, to humans; <i>Anopheles</i> mosquitoes transfer <i>Plasmodium</i> sp, the causative agents of malaria, to humans
Zoonoses	Infectious diseases in which the pathogenic agent is transmitted to humans from animals.	West Nile virus encephalitis is transmitted to humans from birds (via the mosquito vector)

centuries and were the focus of targeted efforts of varying degrees around the world to reduce the burden of infectious diseases on human populations. Improvements to public health systems, such as sanitation, drinking water treatment, and education, reduced human contact with pathogens. Scientific advances, such as antibiotics and vaccines to treat and prevent infectious diseases, revolutionized the medical arsenal against microbes. As a result, by the middle of the twentieth century, the incidence of many infectious diseases plummeted, particularly in the developed world. It was widely thought that science had conquered the threat that infectious diseases posed to human health.

What is appreciated now is that microbes are constantly interacting with their environment and evolving. As they do, circumstances may allow for the emergence of new infectious agents/diseases, or the reemergence of previously controlled contagions. These emergences fall into many categories:<sup>4</sup>

- Microorganisms that have not been known previously and that cause new diseases (e.g., severe acute respiratory syn-

drome coronavirus [SARS-CoV] and Middle East respiratory syndrome coronavirus [MERS-CoV]; human immunodeficiency virus [HIV] that causes acquired immunodeficiency syndrome [AIDS]);

- Agents that have been known previously and that cause new diseases (hantavirus in the United States in 1993 that caused respiratory distress instead of kidney disease);
- Microbes that have been known previously to cause disease, but the incidence of disease is noticeably increasing in a region (e.g., whooping cough caused by *Bordetella pertussis* in the United States; diphtheria caused by *Corynebacterium diphtheriae* in Russia);
- New, and often more virulent, strains of a known pathogen that cause disease (e.g., *Vibrio cholerae* O139 and epidemic diarrheal disease; highly virulent *Clostridium difficile* NAP1/027 and increased incidence of *C. difficile*-associated disease in North America and Europe). Increased virulence often occurs when a pathogen acquires a genetic element that allows for the production of a new virulence factor such as a toxin (e.g., *Staphylococcus aureus* that produces TSST-1 and causes toxic shock syndrome);
- Microbial pathogens that cause disease in a new geographical location (e.g., West Nile virus encephalitis in North America; reintroduction of epidemic cholera in Haiti; Chikungunya virus in the Caribbean; Ebola virus in West Africa);
- Microbes of animal origin that infect humans (zoonoses). This includes animal-associated microorganisms to which humans are newly exposed (e.g., hantavirus pulmonary syndrome due to Sin Nombre virus from the rodent population in the United States), or animal-associated microbes that are newly able to infect humans (e.g., influenza virus from birds or swine);
- Microbial pathogens that have acquired the ability to resist the effects of antimicrobial agents (e.g., multidrug-resistant tuberculosis [MDR-TB]; methicillin-resistant and vancomycin-resistant *S. aureus*; amantadine-resistant influenza A virus; carbapenem-resistant Enterobacteriaceae [CREs]).

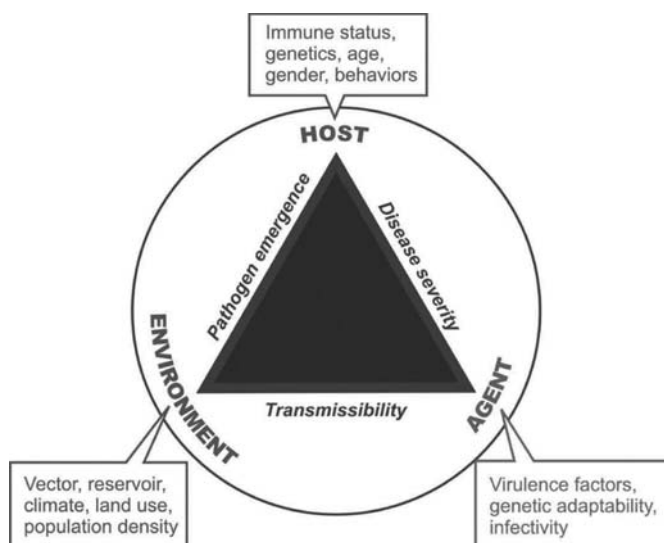


Figure 8.1. The epidemiological triangle. This type of diagram is widely used to represent the interconnectedness of the three major components involved in the emergence of infectious diseases. The “Host” is the organism that is affected by the pathogen or toxin and can develop disease. The “Agent” is the infectious microorganism (pathogen) or toxin. The “Environment” refers to the circumstances that influence the interaction between the Host and the Agent. Examples of influencing factors are given for each component.

The occurrence of emerging infectious diseases (EIDs) or reemerging infectious diseases in human history is not new. The great plague and influenza pandemics are well-known historical examples. The last few decades have witnessed a recrudescence of EIDs. Furthermore, as global surveillance of diseases has developed, the awareness that new EIDs are occurring has increased. Although exact numbers of EIDs are debatable due to differences

**Table 8.2. Factors that Drive the Emergence or Reemergence of Infectious Diseases**

<i>Factor in Emergence</i>	<i>Description</i>	<i>Example</i>
Microbial Adaptation	Microbes are under constant selective pressure from the environment to adapt genetically for survival. Evidence of adaptation includes: the evolution or acquisition of antibiotic resistance genes that allow bacteria to survive exposure to antibiotics, the mutation of genetic material, and the horizontal transfer of virulence genes from one microbe to another.	<p>The emergence of MDR-TB, which is resistant to at least two of the primary antibiotics used to treat the disease. Even more alarming is the appearance of extensively drug-resistant tuberculosis (XDR-TB), resistant to many first-line <i>and</i> second-line antibiotics.</p> <p>The emergence of CRE, for example by transfer of the New Delhi metallo-beta-lactamase-1 (NDM-1) gene, which confers resistance to a range of antibiotics to bacteria that carry it.</p> <p>The strain of Shiga-toxin-producing <i>E. coli</i> that caused an outbreak of food-related illness in 2011 in Germany and other countries was a rarely seen strain that had virulence factors from two different types of pathogenic <i>E. coli</i> and resulted in severe disease in a higher proportion of cases than usual.</p>
Human Susceptibility	The ability to stave off a pathogenic infection is predominantly due to host immunity, a multi-organ system involving physical barriers, complex cell–cell signaling, recognition, and memory to fight invading pathogens. A healthy immune system is a function of many factors. The extremes of age, poor nutrition, and presence of chronic and/or infectious diseases could result in an immunocompromised state.	The increased incidence of <i>Pneumocystis jiroveci</i> (formerly known as <i>Pneumocystis carinii</i> ) pneumonia in the United States as the HIV/AIDS population increased.
Climate and Weather	Changes in climate and weather affect every organism in a region. As plant and animal life is affected, so too is the interaction between humans and these organisms, and the microorganisms they may harbor. Climatic changes can also affect human activities. For example, a negative effect on crop production can increase malnutrition and render a population more susceptible to disease. Furthermore, agricultural practices may be altered, exposing populations to different vectors and microbial agents.	Certain species of zooplankton are associated with the presence of pathogenic <i>Vibrio cholerae</i> . In South America, the El Niño southern oscillation of 1991–1992 increased coastal water temperatures, zooplankton density, and, consequently, exposure of people to <i>V. cholerae</i> . The ensuing cholera epidemic was the first in the region in a century.
Changing Ecosystem	The environment can have a profound impact on the emergence of pathogens, predominantly through wildlife ecology and the interaction of humans with the vectors and animals that carry potential pathogens. Environmental changes in forestation, humidity, and predator density due to natural or anthropogenic causes can all affect vector and pathogen biology.	Dam building in Ethiopia to improve agricultural productivity had the undesired side effect of increasing mosquito breeding grounds, an outcome implicated in increases in malaria cases in children.
Human Demographics and Behavior	At over 7 billion people, the world population is four times as large as it was at the beginning of the twentieth century when advances in science, medicine, and public health first allowed for the widespread control of infectious diseases. The increasing population has resulted in crowded living conditions and habitation of previously undeveloped areas, exposing more individuals to new diseases. Human behaviors, often for economic gain, can also influence disease emergence.	<p>Live-animal markets that put humans and pathogens in close contact (e.g., SARS-CoV and influenza viruses).</p> <p>Commercial sex workers who engage in unprotected sexual intercourse (e.g., HIV emergence in Asia).</p>
Economic Development and Land Use	Globalization of national economies has resulted in an unprecedented interdependence in trade and commerce, and an increase in the volume of goods produced. Land use for industry and agriculture, and for population expansion, can influence emerging diseases.	Widespread deforestation in Malaysia for the expansion of plantations encroached on the natural habitat of fruit bats, the reservoir for the previously unknown Nipah virus. The fruit bats found food in the orchards that were adjacent to swine farms and infected the swine with Nipah virus. In 1988, human disease emerged.
Technology and Industry	<p>Medical technology has improved lives, but also has led to an increase in immunocompromised persons (e.g., transplant recipients).</p> <p>Technology has allowed for mass production in the food industry. Larger animal feedlots and processing plants facilitate the transmission of infectious agents from one animal to another. Refrigeration, packaging, and transportation networks allow foods from different regions and countries to be distributed throughout a nation.</p> <p>Advanced water distribution systems for consumption, hygiene, recreation, and indoor temperature regulation are comforts particularly associated with and expected in the developed world. With this technology comes the risk of mass distribution of pathogens.</p>	<p>Hemophiliacs who were infected with HIV from infected blood products</p> <p>Spinach contaminated with <i>E. coli</i> O157:H7 affected people in over twenty-five U.S. states in 2006.</p> <p>Viral gastroenteritis outbreaks associated with swimming pools</p> <p>Growth of <i>Legionella</i> bacteria in building water distribution systems and transmission to occupants resulting in Legionnaires' disease</p>

Table 8.2. (continued)

Factor in Emergence	Description	Example
International Travel and Commerce	<p>The movement of people across regions means the movement of microbes and vectors as well. In addition to traveling for pleasure or for business, people move across borders for temporary employment, as military personnel, as immigrants, as refugees, as undocumented persons, or in situations of forced labor.</p> <p>Commerce is highly dependent on international production and trade of goods. For example, foods once considered exotic or seasonal are available in the United States year round due to importation from other countries.</p>	<p>One infected person spread the SARS-CoV from Guangdong Province, China to twelve guests at a Hong Kong hotel. The twelve people spread the virus to five other countries. In 6 months, the SARS-CoV spread from China to over thirty countries on six continents.</p>
Breakdown of Public Health Infrastructure	<p>Public health measures, such as sanitation, health education, vaccinations, and access to care, are critical for preventing infectious diseases. These measures must be consistently upheld, or microbial pathogens will return to the niche they once inhabited. Reasons for public health inadequacies or collapse include economic hardship, political instability, war, complacency, disasters, and lack of priority standing.</p>	<p>In the early 1990s, diphtheria reemerged in the former Soviet Union amidst a turbulent political, economic, and social environment.</p> <p>In 2000, approximately 2,300 people in Walkerton, Ontario, Canada became ill after consuming inadequately treated and monitored drinking water contaminated with <i>E. coli</i> O157:H7 and <i>Campylobacter jejuni</i>.</p>
Poverty and Social Inequality	<p>Increased populations, political unrest, and/or inadequate food production in some areas have resulted in increased numbers of persons who are malnourished and without access to medical care. Infectious disease outbreaks in these areas tax already overburdened healthcare systems. Inadequate resources spread disease by failing to reach the sick, transmitting the pathogen in the healthcare setting due to crowding and reusing supplies, and neglecting to educate the population on safe practices. In addition, the lack of adequate courses of medication leads to incomplete treatment of disease and the emergence of antibiotic-resistant pathogens.</p>	<p>The incidence of AIDS, malaria, and tuberculosis has reached alarming rates in developing countries where resources are scarce.</p>
War and Famine	<p>War often unsettles populations and increases the reliance on public health infrastructures to provide medicines, food, and emotional support to affected persons. These health systems are often inadequate during peacetime and cannot undertake additional responsibilities during unrest. Furthermore, poor health status in a population may result from: 1) substandard housing in refugee camps; 2) guerilla-controlled access to food and medicines; 3) elevated pollution; and 4) interrupted power and water distribution. Infectious diseases can spread from contaminated food or water, from persons with contagious respiratory diseases, or from sexual assaults. Famine, like poverty, deteriorates the health of populations and renders them more susceptible to old and new infectious diseases.</p>	<p>Cholera outbreaks in the 1990s among Rwandan refugees in the Democratic Republic of Congo resulted in thousands of deaths in weeks.</p>
Lack of Will	<p>Four segments of the global society that must commit to combating emerging infectious diseases are monetary donors, health professionals, governments, and patients and civil society. Donors, both private and public, are necessary to provide funding for research and for health programs. Health professionals must be available to design and implement intervention and prevention programs. Governments must prioritize infectious disease science, surveillance, and reporting; build public health infrastructures; and collaborate with other nations and global partners. And the community needs to motivate the other segments to act by voicing concerns and participating in intervention and prevention programs.</p>	<p>In the West, early efforts to understand HIV and determine intervention strategies were stalled by political and societal discomfort that the disease was spreading in the male homosexual population.</p> <p>Inadequate education on the myths and facts of sexually transmitted infection prevention led to widespread transmission of HIV throughout Africa and Asia.</p>
Intent to Harm	<p>There is heightened awareness of the threat of an intentional attack with a bioweapon. In addition to the unpredictability of when and where such an attack will occur, the type of microbe that will be used is largely unknown. There is concern that the agent used will be one not regularly encountered in the afflicted area. In effect, a bioterrorist attack could result in the emergence or reemergence of infectious diseases in an area, with the potential to cause many casualties. In addition, the social, political, and economic disruption could be far-reaching.</p>	<p>2001 release of anthrax spores via the U.S. postal system.</p>

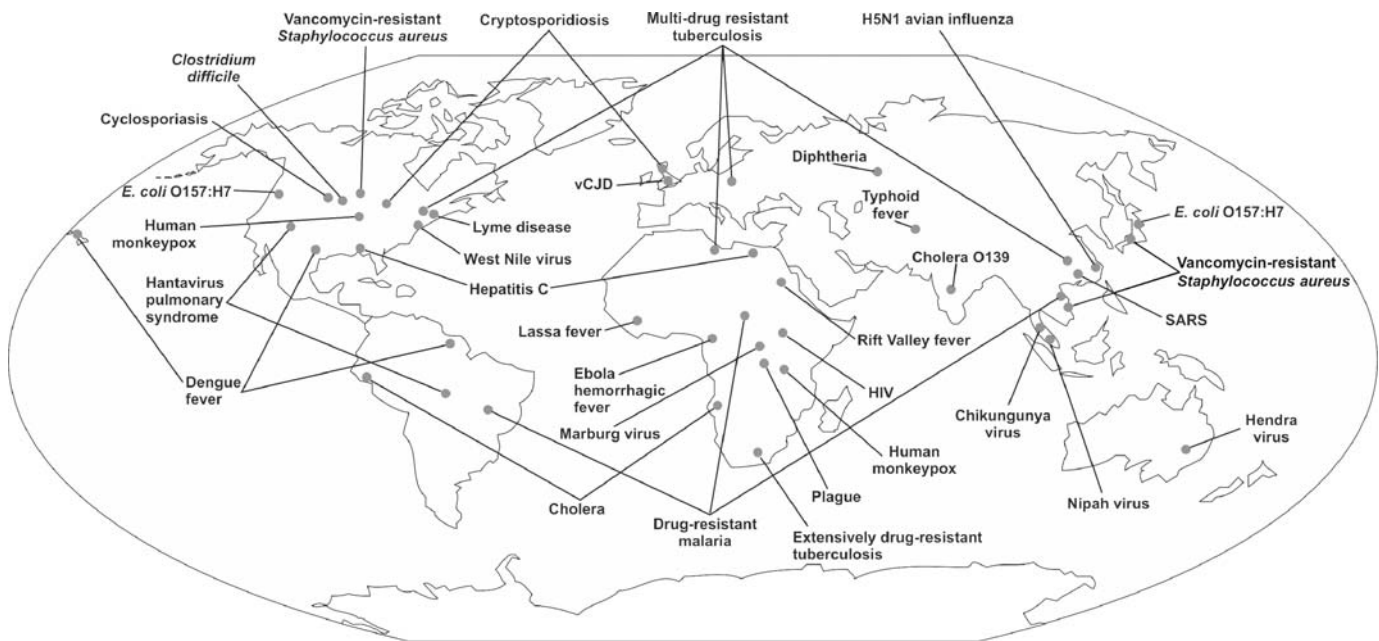


Figure 8.2. Emerging and reemerging infectious diseases/agents, 1990–2013. The diseases/agents in the black boxes with the white dots represent select emergences that have occurred since the first edition of this textbook was published in 2010. *E. coli*, *Escherichia coli*; vCJD, variant Creutzfeldt–Jakob disease; HIV, human immunodeficiency virus; SARS, severe acute respiratory syndrome; MERS, Middle East respiratory syndrome; NDM-1, New Delhi metallo-beta-lactamase-1. Adapted from the National Institutes of Health website ([www3.niaid.nih.gov/about/overview/planningpriorities/strategicplan/merge.htm](http://www3.niaid.nih.gov/about/overview/planningpriorities/strategicplan/merge.htm)).

in criteria used, Taylor and colleagues suggest that 175 of the 1,400-plus known human pathogens are EIDs (approximately 12%).<sup>3</sup>

Figure 8.2 shows recent EIDs and reemerging infectious diseases in both the developed and developing world.

The question then is: Why are EIDs occurring so frequently despite the optimism of past generations? In 2003, the Institute of Medicine (IOM) published *Microbial Threats to Health: Emergence, Detection and Response*,<sup>5</sup> which outlined thirteen factors that contribute to the emergence or reemergence of new pathogens.

Although now more than a decade old, the IOM report remains a seminal work in framing the understanding of why infectious diseases emerge. The factors reflect a very different world from previous decades. “Globalization,” often characterized by changes in global movement, economic development, and environmental and agricultural practices, has unwittingly exposed the world’s populations to microbial threats. Not all of the categories are necessary for every emerging pathogen; however, neither are they mutually exclusive. The emergence or reemergence of a pathogen is usually a function of many factors. An understanding of all the factors is necessary to prevent or quickly detect future EIDs and to determine how to effectively mitigate an EID disaster.

Table 8.3 uses pandemic influenza, dengue hemorrhagic fever, MDR-TB, HIV/AIDS, and cholera to demonstrate how these factors interplay in the emergence or reemergence of diseases.

Another example of the convergence of factors resulting in disease emergence and transmission is the Ebola virus disease (EVD) outbreak in West Africa,<sup>6</sup> the first such outbreak in that region and a situation still evolving at the time of this writing

in August 2014. With 3,069 cases and 1,552 deaths reported as of August 26, 2014 in Guinea, Liberia, Sierra Leone, and Nigeria, it is the largest EVD outbreak to date. The outbreak started in Guinea; phylogenetic analysis suggests evolution of the virus in the area as opposed to importation of the outbreak strain from other countries.<sup>7</sup> The initial EVD cases and transmission were unrecognized, likely a result of local clinicians’ unfamiliarity with the disease and its symptoms, and also due to inadequate healthcare availability and resources. Human behaviors in the area may have also played a role in the emergence and persistence of the disease, including: funeral practices that involve touching the deceased; food habits such as consumption of bats, a likely vector; mistrust of government officials, aid organizations, and healthcare workers resulting in delayed or avoided care; and fear, resulting in actions such as airplane flight limitations that affect resources and response capabilities. Indication that residents attacked and looted an EVD clinic in a poor neighborhood of Monrovia, Liberia suggests instability in the area is resulting in unconventional risks for further transmission of this disease. Likely the most critical factors related to the scope of this EVD outbreak compared to previous outbreaks are modernization and urbanization. Cases have occurred in larger cities with more mobile populations, and travel by land and air has transmitted disease between countries, hindering the comprehensive contact tracing necessary to prevent continued transmission.

Many of the thirteen factors outlined by IOM drive disease emergence by influencing the interaction of humans with animal reservoirs of potential pathogens. In fact, approximately 75% of recently emerged pathogens are zoonotic. The abundance, location, and behaviors of putative animal reservoirs, and human influences on them, are important factors in

**Table 8.3. Examples of How Multiple Factors Influence the Emergence or Reemergence of Infectious Diseases**

<i>Infectious Disease (Agent)</i>	<i>Pandemic Influenza* (highly pathogenic avian influenza [HPAI] virus)</i>	<i>Dengue Hemorrhagic Fever (dengue virus; transmitted to humans by mosquito vector)</i>	<i>Multidrug-resistant Tuberculosis (Mycobacterium tuberculosis)</i>	<i>AIDS (HIV)</i>	<i>Epidemic cholera in Haiti (Vibrio cholerae)</i>
<b>Emergence Factor</b>					
Microbial Adaptation	Reassortment of, or mutations in, influenza virus genes that allow for human–human transmission of HPAI virus	Adaptation of viral strains to urban mosquitoes facilitated emergence	Improper use of antibiotics allowed <i>M. tuberculosis</i> to develop resistances	Mutation of simian immunodeficiency virus to infect humans; emergence of drug-resistant HIV; high mutation rate complicates vaccine development	Mutations in toxin genes have resulted in an altered El Tor strain of <i>V. cholerae</i> with increased virulence
Human Susceptibility	Extensive viral adaptations means no inherent immunity in humans; no vaccine-enhanced immunity in the initial months of the pandemic	No cross-immunity to the four different viral strains; heterologous infection increases chance of severe disease	Increased tuberculosis in HIV-endemic areas	Lack of host immunity when virus emerged; no vaccine-enhanced immunity	Immunologically naive population on Hispaniola (Haiti and Dominican Republic) where cholera had not been seen for a century
Climate and Weather	Cold weather in some countries during flu season encourages social clustering and, consequently, viral transmission	Rainy seasons increase mosquito population			
Changing Ecosystems	Changing marshland habitats and waterfowl distribution	Repopulation of New World by mosquito species after mid-twentieth century mosquito eradication programs ended			
Human Demographics and Behavior	Increased worldwide poultry production to feed increased human population; cohabitation with potential zoonotic sources	Disease centers in overpopulated urban areas with poor housing and utility management that promote mosquito breeding grounds	Failure to adhere to medication regimens; people in remote areas hard to treat consistently; immigration of infected persons	Unprotected sexual activity; illicit intravenous drug use; prostitution	Disaster relief being provided in response to the 2010 earthquake
Economic Development and Land Use	Live markets put humans and infected birds in close contact	Dam building promotes mosquito breeding grounds			
Technology and Industry	Crowded poultry feedlots favor viral transmission between birds	Possible disease transmission through blood products		Disease transmission through blood products	
International Travel and Commerce	Global travel can rapidly spread disease; illegal exotic bird trade can transfer infectious birds	Travelers can spread strains between endemic areas; outbreaks in nonendemic areas with appropriate mosquito species (e.g., southern United States)	Dissemination of <i>M. tuberculosis</i> on airplanes via recirculation of air	Global travel spreads disease	Travel of international relief workers to Haiti to aid in the earthquake disaster response; relief workers from Asia, where cholera is endemic/epidemic, may have been incubating cholera at the time of deployment
Breakdown of Public Health Infrastructure	Prolonged nature of the pandemic strains resources	Lack of effective mosquito control; poor water and sewage systems in developing areas	Inability to monitor tuberculosis population; high treatment interruption rates in developing countries; HIV epidemic areas overwhelmed	Lack of education and intervention programs, overwhelmed workforce in developing countries	Disruption of already-poor sanitation, water treatment, and healthcare infrastructures by the earthquake disaster

(continued)

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<i>Infectious Disease (Agent)</i>	<i>Pandemic Influenza* (highly pathogenic avian influenza [HPAI] virus)</i>	<i>Dengue Hemorrhagic Fever (dengue virus; transmitted to humans by mosquito vector)</i>	<i>Multidrug-resistant Tuberculosis (Mycobacterium tuberculosis)</i>	<i>AIDS (HIV)</i>	<i>Epidemic cholera in Haiti (Vibrio cholerae)</i>
Poverty and Social Inequality	Rapid spread of the virus in the developing world	Developing countries that lack vector control programs risk high incidence	Expense of directly observed therapy inhibits consistent use in poorer nations	Expense of antiretroviral therapy; stigmatization of men who have sex with men, especially in early days of the emergence; marginalized women's rights in some societies	Occurrence in a developing nation with few resources for public health infrastructure and response; waning aid and funding
War and Famine	Increased global travel during World War I facilitated propagation of the 1918 influenza pandemic		Tuberculosis spreads quickly through refugee camps (e.g., in Somalia)	Treatment programs are difficult to administer in areas of conflict	Malnutrition in the population resulting in increased disease severity and poor outcomes
Lack of Will	Pharmaceutical industry and vaccine/therapeutic development	Poor surveillance in endemic countries	Inadequate infection control policies or practices	Initial low research and intervention priorities for an agent primarily spreading in men who have sex with men; refusal of officials in some developing countries to acknowledge HIV in the population	Low priority for vaccine development; initial reluctance of international relief force to acknowledge that response efforts may have contributed to the reemergence, leading to mistrust of the nation
Intent to Harm	Theoretical potential of genetically reconstructed 1918 pandemic influenza virus to be used in a terrorist attack				

\* At the time of this writing, pandemic HPAI has not reemerged. Based on knowledge from prior influenza pandemics and extensive studies on influenza virus epidemiology and genetics, experts have uncharacteristically broad insight into factors that affect how these zoonotic pathogens emerge.

disease emergence. Microbes often live in harmony with animal hosts and the pathogenic infection of humans is inadvertent.

### Infectious Diseases and Disaster Medicine

History has shown that infectious disease outbreaks, epidemics, and pandemics have the potential to afflict large numbers of people. Estimates for the next severe influenza pandemic suggest millions of cases in the United States alone with hundreds of thousands of flu-related fatalities. The 2001 deliberate release of anthrax spores in the United States through the postal system and the 2003 SARS pandemic are reminders that the scope of the disaster is not just a function of actual case numbers, but of the ability to manage the outbreak and to the public reaction during the event. Both situations taxed the available resources of some of the most sophisticated public health systems in the world despite relatively low numbers of cases.<sup>6,7</sup>

Disasters are commonly considered to be acute, often regional, events. Even in the realm of infectious diseases, the anthrax letters incident in the United States is often cited as an example of the type of response required for an infectious disease disaster. More likely, however, biological situations (of either intentional or unintentional origin) that strain response efforts will unfold in a more gradual manner. Furthermore, if disasters are defined as situations that require external resource

assistance, then the global AIDS pandemic (now decades long) can be considered a disaster. Disasters due to EIDs are of particular concern given the paucity of information on the biology of the agent, the course of disease, and mechanisms of treatment. Even a local outbreak of a known infectious agent can strain a response effort.

Management of infectious disease disasters shares many general aspects of the management of other disasters. The basic principles of leadership and collaboration, resource management, surge capacity, triage, and public relations are all important; however, the specifics of response activities can have special considerations when an infectious agent is the cause of the disaster.

Table 8.4 provides a description of unique features of infectious disease disasters that are not usually encountered in many other disaster response efforts.

### The Infectious Agent

Infectious disease disasters, unlike physical and chemical incidents, are caused by biological entities that are diverse and under constant selective pressures to change. It may be clear that an outbreak has occurred due to the contagiousness and nature of the illness that characterize cases presenting to healthcare facilities; however, the identity of the agent that is sickening patients may be elusive, and any effort to mitigate the disease and spread



**Table 8.4. Challenges of Infectious Disease Disasters that May Differentiate Them from Other Types of Disasters**

Category*	Challenge
Infectious Agent	Novel agent or one not previously associated with disease
	No known treatment or cure
	Unknown reservoir
Disease	May not initially be recognized as the causative agent of the disaster
	Not characterized previously
	Medical community lacks experience identifying and treating
	Symptoms are similar to other infectious diseases
Transmission	People who are concerned about exposure but not truly exposed
	Contagious agent – large numbers infected over time
	Global response may be necessary to contain agent
	Multiple cities affected
Personnel	Disaster could last weeks, months, years or decades
	How to decide when the disaster is over
Resources	Exposure of response personnel to agent
	Healthcare workers' absenteeism due to concern of contracting agent
The Public	Isolation of cases in the healthcare facility
	Decontamination of hospital equipment
	Capacity of laboratory to process samples
	Distribution of limited supplies (drugs, equipment)
	May be other infectious disease outbreaks concurrently
Ethics and Law	Quarantine and Isolation
	Screening for symptoms (at hospitals, airports)
	Controlling movement (closed borders)
	Closing services (schools, churches, public transportation)
	Psychological fears
Terrorism	Media relations
	Mass vaccinations
	Quarantine/restriction of movement
	Allocation of resources
Terrorism	Demands on healthcare workers, first responders
	Balancing epidemiological and criminal investigations

\* The first three categories (agent, disease, transmission) are unique to infectious disease disasters. The remaining categories (personnel, resources, the public, ethics and law, and terrorism) may apply to other types of disasters, but the challenges listed are unique or particularly applicable to infectious disease disasters.

of the agent will be compromised. Cases of severe atypical pneumonia perplexed physicians in Guangdong province, China in 2002. Chinese officials maintained the causative agent to be a bacterium called *Chlamydia*.<sup>8</sup> It was not until months later, after global spread occurred requiring a then-unprecedented international response effort, that a new coronavirus was publicly identified as the cause of a heretofore-uncharacterized disease, SARS.

For a number of infectious agents, previously known or unknown, there is no specific treatment or cure. Medical management is limited to supportive care, which may require long hospital stays. Depending on the number of afflicted persons, this could affect resource availability (discussed later). The unknown nature of some pathogens also limits detection and diagnostic capabilities.

Infectious agents are often zoonoses. Human infection from the animal reservoir occurs when environmental and behavioral factors coincide to allow for transmission of the agent. In the case of EIDs, the identity of the animal reservoir may be unknown. Successful mitigation of disease spread is contingent on discovering the reservoir. The 1993 emergence of hantavirus pulmonary disease in different locations in the United States occurred due to increased contact between rodent and human populations; disease eradication followed reduction of human contact with rodent excreta.

### The Disease

In some situations, the medical literature may not have previously described the disease (e.g., the various viral hemorrhagic fevers that have emerged over the years), or a particular disease was not previously associated with a type of infectious agent (e.g., acute respiratory disease and hantaviruses). In either case, understanding the mechanism of disease is important to provide effective care and prevent future cases. Incomplete or incorrect disease classification hampers an effective response effort. Alternatively, a disease may be classically associated with an infectious agent; however, outbreaks are rare (e.g., SARS) or historical (e.g., smallpox) and the medical community lacks experience in identifying and treating the disease. This scenario can also affect the timeliness with which a disaster is controlled.

In many instances, an EID has similar symptoms to other diseases that are endemic to a region. SARS patients had general symptoms of fever, headache, and malaise that typically progressed to pneumonia. Healthcare workers had the daunting task of differentiating patients with respiratory ailments to properly isolate and treat the SARS cases.<sup>9</sup> Likewise, a 1995 *Neisseria meningitidis* outbreak in Minnesota occurred during flu season, overwhelming a hospital emergency department and complicating triage.<sup>10</sup> Additionally, some cases of EVD in West Africa in 2013 and 2014 may initially have been diagnosed as malaria<sup>6</sup> – a disease that requires different clinical and infection control practices to prevent illness and transmission.

Particularly during epidemics with common symptoms such as headache and fever, healthcare facilities may be inundated with the so-called worried well. Although psychology experts have advocated for abandoning this phrase and replacing it with more appropriate terminology such as “medically unexplained symptoms,” it is still often used to refer to persons who think they may have symptoms although they do not actually have the disease, or to well persons who present to healthcare facilities in the hopes of receiving prophylaxis “just in case.” These situations are understandable given the fear of contracting the

infectious disease and the desire to protect oneself and one's family. Communication with the public is an important component of the response. It provides information on the disease and actions to take if people think they have been exposed. Crowd control, screening, and triage may be necessary actions to separate infected and uninfected persons.

### **Transmission of the Infectious Agent**

An infectious disease may be contagious. This occurs when the reproductive rate ( $R_0$ ) – the average number of secondary cases to which an infected person spreads the disease when no control measures are used – is greater than 1. Some agents, such as *Bacillus anthracis* (the causative agent of anthrax) are not contagious ( $R_0 < 1$ ) and containment of the disaster is dependent on prevention of human contact with *B. anthracis* spores in the environment. Many other infectious agents are contagious ( $R_0 > 1$ ). Pandemic influenza  $R_0$  estimations vary, but most are approximately 2–3.<sup>11</sup> This means that one person with influenza will likely infect two other people. Interestingly, in the case of SARS-CoV, the  $R_0$  was usually approximately 2–4, yet some people appeared to be super spreaders, passing the virus to at least ten people.<sup>12</sup> This variance in  $R_0$  among different hosts complicates predictions of the magnitude of the epidemic.

There are many implications of a communicable disease agent for disaster relief. Large numbers of afflicted persons could result from a single “emergence” of an agent or from one bioterrorist attack because more and more people are exposed to the agent. Due to travel of infected persons (e.g., SARS in 2003, MERS in 2013), or environmental factors that influence animal ecology (e.g., hantavirus pulmonary syndrome in 1995), the infectious disease may affect many cities, straining the ability of national and regional agencies to assist in local response efforts. Furthermore, as multiple neighboring public health jurisdictions are affected, communication and collaboration becomes important. If the infectious agent crosses international borders, a global effort may be required to end the spread of disease. This could include travel restrictions, surveillance, and the sharing of resources (e.g., vaccines and antibiotics) and technology (e.g., diagnostics).

The communicability of an infectious agent can also affect the duration of the disaster. Rather than resulting in an acute incident, an infectious disease disaster could last weeks, months, or even years as waves of people are affected in a region or across the globe. Pandemic influenza is predicted to last 18–24 months. The AIDS disaster has lasted for decades. Sustaining disaster relief for years will be challenging – resource utilization, a fatigued healthcare workforce, even changing political administrations, can all affect response and recovery efforts. As mentioned previously, other infectious disease outbreaks will surely occur, requiring an even greater effort from an already overwhelmed system.

Transmissibility of infectious agents in the context of disaster medicine and infectious disease emergence is poignantly exemplified by the cholera epidemic in Haiti that followed the devastating January 2010 earthquake. The country, already burdened with suboptimal public health, medical, and sanitation infrastructures, was critically in need of assistance to respond to victims of the earthquake. The world reacted, and thousands of

aid workers descended on Haiti in the days, weeks, and months after. In October 2010, a new issue began to emerge – increasing cases of severe, acute gastrointestinal illness in areas along the Artibonite River that spread to all parts of the country. Surprisingly, the disease was cholera, which had not been seen in Haiti in over 100 years. It was possible that a local strain of the bacteria had reemerged after the earthquake. However, extensive analysis revealed an unexpected source – molecular characterization of the strain and epidemiological evidence strongly indicate that the epidemic strain of *Vibrio cholerae* was introduced to the region by a vessel of United Nations relief workers from Asia. It appears that sewage disposal practices on the ship introduced a particularly virulent South Asian strain of *V. cholerae* to the Artibonite River and eventually exposed millions of immunologically naive people to the agent, largely due to insufficient sanitation and healthcare systems. By the fall of 2013, hundreds of thousands of people had become ill and over 8,000 people had died in Haiti,<sup>13</sup> and the bacteria had spread to neighboring Dominican Republic and Cuba. This is the first widely documented case of the international disaster response resulting in a second large-scale disaster of an infectious nature. This occurrence has not only led to mass casualties, but also to the reemergence of an infectious disease in a region.<sup>14</sup>

Implementation of the incident command system for disaster relief of an acute event such as a fire is relatively straightforward, with a clear start and end point. The beginning and end of an infectious disease disaster can be much less clear. Often, a period of days occurs when no new cases are diagnosed, the outbreak is determined to be over, and public health response activities return to normal; then, the community experiences a second wave of cases and public health and healthcare entities must work quickly to reinstate outbreak procedures. This concept is illustrated by the 2003 SARS epidemics in Ontario, Canada and in Taiwan, with a focus on infectious disease transmission in the healthcare setting. The 2003 SARS epidemic curve for Ontario, Canada demonstrates two phases of increased disease incidence (Figure 8.3).

Provincial public health officials had assumed that the outbreak in Ontario was contained at the end of April 2003 because no new cases of SARS were diagnosed after April 20. World Health Organization (WHO) officials concurred; the travel advisory to Toronto was lifted on April 30 and Toronto was removed from the WHO list of locations with disseminated SARS on May 14, 2003. Ontario health officials relaxed the strict hospital infection control directives for SARS. Days later, the second phase of the epidemic in Ontario began. Apparently, patient-to-patient and patient-to-visitor spread of the virus was still occurring unnoticed at one hospital. When SARS control measures were lifted, viral exposure of hospital workers led to a resurgence of cases.

Once again, infection control directives were issued, the hospital ceased admitting new patients, and hospital workers faced restrictions and quarantine.<sup>15</sup> Taiwan also had transmission of SARS among healthcare workers.<sup>16</sup> In contrast to the Toronto experience, some patients and staff were quarantined in the affected healthcare facility, infection control practices were enhanced at all facilities, and extensive community

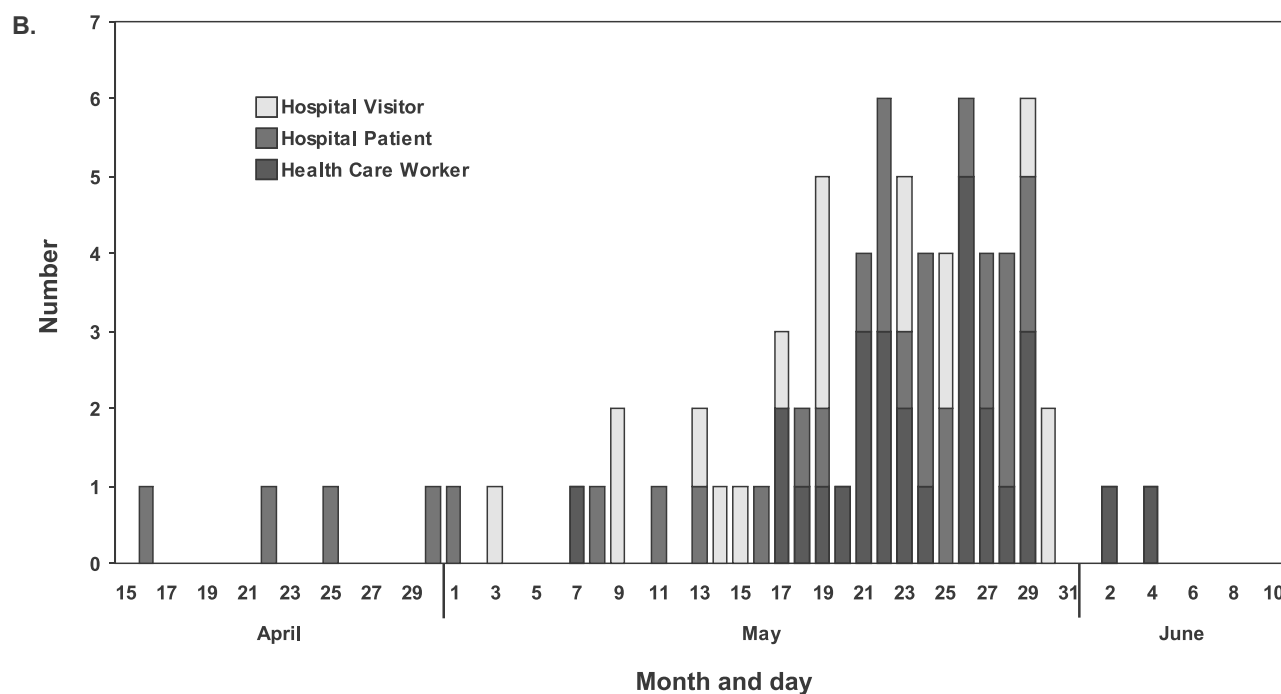
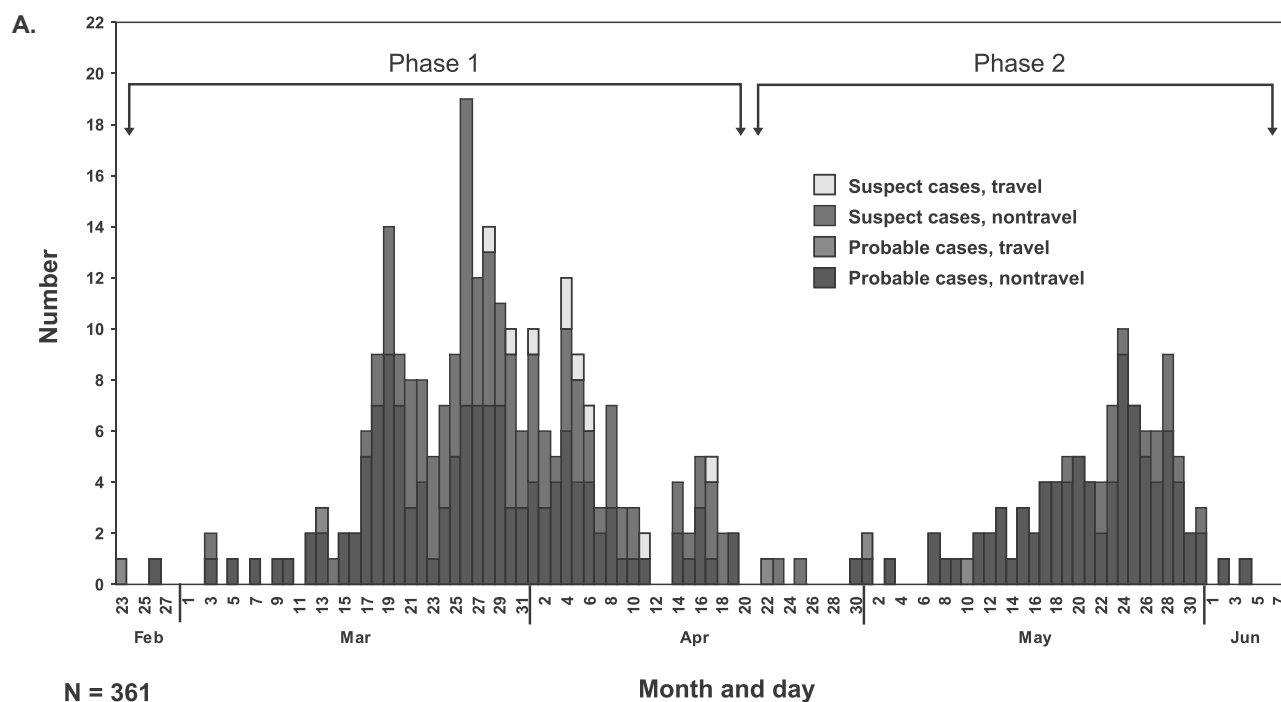


Figure 8.3. Reported SARS cases in Ontario, Canada in 2003 demonstrating the two phases of the epidemic. A) Number of reported cases of SARS by classification and date of illness onset – Ontario, Canada, February 23–June 7, 2003. B) Number of reported cases of SARS in the second phase of the epidemic by source of infection and date of illness onset – Toronto, Canada, April 15–June 9, 2003. Adapted from U.S. Centers for Disease Control and Prevention. 2003. Update: Severe acute respiratory syndrome – Toronto, Canada. *MMWR*; 52(23): 547–550.

screening, outreach, and infection control practices were instituted. Although the total case count was higher in Taiwan, the outbreak curve was not bimodal. The experiences of these two cities stress a number of points: 1) Surveillance is critical to limiting the spread of an infectious agent in the healthcare setting. All patients and healthcare workers should be monitored for development of symptoms. 2) Decision-makers must be wary of relaxing strict infection control measures too soon. Although officials in Ontario and at WHO waited at least 20 days (two incubation periods) before lifting the SARS directives, this action was complicated by the difficulty in differentiating SARS patients from patients with other respiratory ailments. 3) The psychological toll on affected citizens, and especially healthcare workers who may have witnessed their colleagues become sick and die, was immense in both cities and must be factored into the situational awareness for the event for determination of response actions. The very nature of infectious agents is often unpredictable, especially when the agent is newly emerging. This reality needs to be balanced with the desire to return an overwhelmed staff and system to normal operations.

Food-borne transmission of infectious agent adds other factors to the epidemiological investigation. Identification of the contaminated product(s) can involve: obtaining food histories from cases and controls, sometimes weeks after the initial cases surface; extensive laboratory analysis of food and environmental samples; consideration of food distribution networks and trace-backs to food sources; implications on the food industry and consumer perceptions; differences in local, regional, and national food outbreak surveillance protocols; and ramifications of/to the economy and international trade. The 2008 *Salmonella* serotype Saint Paul outbreak, associated with over 1,400 cases in the United States and Canada – initially attributed to tomatoes and then to Mexican hot peppers – has been the subject of numerous hearings and analyses to elucidate shortcomings in food safety and outbreak response in North America.<sup>17</sup> Likewise, the 2011 outbreak of *E. coli* O104:H4 in Germany and other parts of Europe, which resulted in about 4,000 illnesses and 53 deaths, was misattributed to Spanish cucumbers before Egyptian sprouts were identified as the likely transmission vehicle. International response included the banning of Spanish and/or European Union produce by some countries (e.g., Russia), a UN epidemiological investigation of Egyptian fenugreek seed suppliers, and the Egyptian government refuting claims that seeds from their growers were the source of the outbreak.<sup>18</sup>

### Response Personnel

The communicability of infectious diseases poses a unique threat to first responders, hospital emergency departments, and primary care providers. Although a radiological attack can result in exposure of healthcare workers, the mechanism and nature of the injuries is well-defined and the threat, once identified, can be relatively easily contained and avoided. In contrast, containing an infectious agent in the healthcare setting can be far more insidious – some people may be asymptomatic carriers of the agent, surfaces may be contaminated, and appropriate personal protective equipment (PPE) may not be in use. The infectious nature itself of a newly emerging pathogen, including whether it is contagious prior to symptom onset, may not even be recognized. All of these factors can result in exposure of healthcare workers to the agent. In the 1957 influenza pandemic, healthcare workers constituted a large proportion of the infected. The emergence of Ebola-Zaire virus in 1976 devastated the region, including the

clinic run by Belgian missionary Sisters. Almost 20 years later, 30% of physicians and 10% of nurses were infected with Ebola-Zaire during an outbreak in the Democratic Republic of the Congo (formerly known as Zaire).<sup>19</sup> SARS in Toronto primarily spread in the healthcare setting (72% of cases were healthcare related), and 44% of cases were healthcare workers.<sup>20</sup> MERS transmission in 2013 was also documented in the healthcare setting.<sup>21,22</sup>

It may be necessary to restrict the movement of individuals in a community to prevent spread of the infectious agent. This is particularly true in the healthcare setting where infectious people congregate and where immunocompromised patients can be exposed. During the SARS pandemic, many healthcare workers were directed to function under work quarantine. These workers were instructed to go to work or stay home, with minimal contact outside these areas. Many healthcare workers are stationed at different facilities or have more than one healthcare-related job. The movement of workers between facilities could expose many more patients to the infectious agent, yet prohibiting this movement would leave facilities understaffed.

Health professionals are a dedicated group of individuals who adhere to a code of ethics to provide care for the ill and injured (often referred to as “duty to care”); however, the management of infectious disease outbreaks is stressful. The long hours often due to understaffing, high volume of patients, duration of the outbreak, and publicity can have adverse psychological impacts on responders and primary care providers. If the infectious agent is emerging and unknown, highly communicable and/or highly lethal, it is possible that healthcare workers will be unwilling or unable to perform their duties. Various studies have been conducted to assess healthcare worker willingness to provide care during infectious disease disasters (notably SARS<sup>23</sup> and influenza pandemics<sup>24</sup>) and the contributing factors for refusing the duty to care. An analysis of published, peer-reviewed articles found that personal obligations and protection of self and loved ones from disease via availability of antiviral medication and/or vaccine were important determinants in willingness to report to work.<sup>25</sup>

The personnel “on call” during an infectious disease disaster are not just the direct patient care staff. Public health staff (nurses, epidemiologists, sanitarians, and laboratory technologists) will be involved from the beginning to determine the extent of the disaster and how to stop the spread of the infectious agent, and to identify the infectious agent source. These efforts necessitate long work hours for days and often weeks. A second unrelated infectious disease outbreak or disaster could occur during or shortly after the first disaster, requiring the same personnel to act without respite. This protracted demand on the workforce may require recruitment of additional personnel not specifically trained for a particular task to maintain the increased level of service (surge capacity). For example, in the 1995 *N. meningitidis* outbreak in Minnesota, extra people were needed to dispense antibiotics, a job that legally could only be performed by a registered pharmacist until the licensing board provided emergency authorization for others to do so. Understanding surge capacity needs is critical to timely, consistent, and effective remediation of the event.

### Resources

The availability of resources in public health is a concern even in the absence of a disaster situation. The 2004 shortage of seasonal influenza vaccine in the United States resulted in long lines, distribution issues, and public attention – the shortage itself

became a disaster of sorts. This scenario of limited vaccine availability was heightened in the 2009 H1N1 influenza pandemic,<sup>26</sup> even though disease severity was not high. During an outbreak or epidemic, mobilization of potentially large volumes of preventive and/or prophylactic medicines to the affected area(s) is necessary in a short period of time. Approximately 10,000 courses of ciprofloxacin were required to treat the people *possibly exposed* to anthrax spores in the United States in October 2001.<sup>27</sup> The 1995 *N. meningitidis* outbreak in Minnesota resulted in the vaccination of 30,000 people, more than half the population of the town. The vaccine stock was not available locally and it took 2 days to deliver the medication to the impacted area. In the 2010 emergence of cholera in Haiti, oral cholera vaccine was not used based on a number of factors including unavailability of enough doses for the population and logistical issues with implementing a vaccination campaign in the aftermath of the earthquake.<sup>28</sup>

Healthcare workers and other response personnel at risk of exposure must use appropriate PPE to prevent exposure to the infectious agent. U.S. hospitals use national guidelines for the types of PPE required based on the mode of pathogen transmission (e.g., contact, droplet, or airborne). Details on the types of PPE required for the different modes of transmission are available at the U.S. Centers for Disease Control and Prevention (CDC) website.<sup>29</sup> The World Health Organization also espouses use of PPE for response to infectious conditions.<sup>30</sup> Public health experts may recommend extra precautions when the agent initially emerges and there is incomplete information on the mode(s) of transmission. For example, evidence suggested that SARS-CoV was not spread by airborne transmission (characterized by dissemination through the air on small particles); however, healthcare workers were often directed to wear airborne PPE (N95 respirators). Consideration should be given to ensuring that PPE can be used properly in an emergency situation (e.g., some respirators need to be fit-tested for optimal functioning) and to contingency plans if PPE availability is insufficient.

The healthcare workforce is a resource itself. As workers become ill, stressed, or quarantined, fewer people will be available to care for patients (in fact, the number of patients may increase as workers become patients). Some of the most qualified people to treat disease will be on the front lines at the beginning of the disaster and at increased risk of contracting disease. This may require less experienced individuals from other departments to fill the void. Many healthcare workers died from SARS in 2002 and 2003, including Dr. Carlo Urbani, the WHO infectious diseases specialist in Vietnam who is credited with discovering the outbreak and taking steps to prevent its spread.

Even with the proper use of PPE, a contagious microbe can spread in the healthcare setting. Examples include patient-to-patient or patient-to-visitor transmission. Therefore, the isolation of infectious patients to one area of the facility is recommended. This may necessitate extra equipment and supplies dedicated for use in the isolation area. Patients infectious with pathogens spread by airborne transmission (or with emerging pathogens for which airborne transmission is suspected) should be sequestered in negative pressure rooms from which air is released directly outside or filtered before recirculation throughout the facility. There are, however, limited numbers of these units and a large infectious disease disaster may require cohorting multiple patients in the same room or even the establishment of facilities committed to treating only infectious patients. During other types of large disasters, patients are often transferred to various hospitals in the region. Although this has been suc-

cessfully accomplished in some infectious disease disasters (e.g., in Singapore during the SARS epidemic), any patient transfer risks further spreading of the disease and should be undertaken within the context of overall containment strategies. Furthermore, in systems that allow it, neighboring hospitals may be unwilling to accept patients from hospitals with confirmed cases due to concern of the disease spreading to their own patients and staff. If the original hospital is designated as an infectious disease facility, these other hospitals may be willing to accept nonexposed patients in transfer, thereby increasing capacity for contagious patients within the original facility.

Equipment that is used to treat multiple patients, ranging from stethoscopes to ventilators, must be properly managed between patients using disposal or decontamination processes as appropriate. This may be particularly difficult for new infectious agents for which effective decontamination protocols are not known. Furthermore, taking equipment out of circulation, even temporarily, may delay treatment of patients.

There are usually two general aspects to mitigating an infectious disease outbreak: the care of individual patients (to alleviate disease and suffering) and the population epidemiological investigation and response (to prevent further transmission). In both cases, laboratory testing of human and/or environmental samples for evidence of the pathogen is important to ensure the correct intervention strategies are directed to the right people and areas. Although an increase in the number of patient samples during an outbreak is often expected, the number of environmental samples can be quite large. At times, the magnitude of testing required is overwhelming to even the larger regional, national, and international laboratories, whose services are required for sizeable incidents and/or for the testing of certain pathogens. For example, thousands of analytical assays were performed on environmental samples in the 1993 U.S. hantavirus pulmonary disease epidemic, in the 1999 West Nile virus emergence in the United States, in the 2001 U.S. anthrax attacks, and in the 2012 *E. coli* O104:H4 outbreak in Germany. The response to an EID outbreak may be largely dependent on the local public health workforce, but this response may be directly reliant on the capacity of other health departments and agencies.

### The Public

The 2003 SARS epidemic in Toronto provides numerous examples of unique considerations for interacting with the public during an infectious disease disaster. The etiology of SARS was initially unknown, but it was apparent that person-to-person transmission was occurring. Therefore, voluntary quarantine measures were implemented, representing the first time in 50 years that such measures were used in North America to control disease transmission in a community. Approximately 23,000 people were asked to adhere to home quarantine (remain at home, wear a mask, have limited contact with family members, and measure their temperatures twice a day) and/or work quarantine. Studies after the epidemic ended suggest that complete compliance to home quarantine requirements was low.<sup>31</sup> Respondents to a web-based survey indicated confusion over the quarantine instructions and inability to contact public health officials for clarification. Furthermore, the quarantine period was necessarily 10 days, a relatively long time for most people to be away from work and community activities.

For this pandemic, it was not necessary to close borders (within and/or between nations) to general travel. Diseases with higher transmission rates, such as smallpox from a bioterrorist

attack (estimated  $R_0 = 10$ ),<sup>32</sup> may require such stringent measures. Issues to consider are enforcement, the effect on businesses, and the effect on the supply chain for disaster management. Institutions within a community where people congregate may require closure, including schools and places of worship.

Whether or not movement or quarantine measures are implemented, public concern and psychological trauma will likely be high for both contagious and noncontagious diseases. This concern will be a function of exposure risk to the agent and subsequent infection, the severity of illness, and the availability of treatment for oneself and one’s dependents. Media coverage during the disaster influences community resilience and either exacerbates or alleviates fears, depending on perceptions of the mitigation effort and truthfulness and accuracy of the messages.

**Ethics and Law**

There are many ethical and legal considerations in the management of an infectious disease disaster. The following issues are illustrative:<sup>33</sup>

- The process of making population-based decisions for infection control during a disaster (e.g., mass vaccinations, quarantine, and movement restrictions) will raise concerns about the legality and necessity of infringements of individuals’ rights.
- A scarcity of resources such as vaccines, therapeutics, or hospital equipment will require difficult decisions about who receives the resources and who does not.
- In the event of a disaster caused by a highly contagious, highly virulent, uncharacterized, and/or genetically engineered agent, to what extent should first responders and other healthcare workers be expected to comply with “duty to care” orders for the public good?

**Terrorism**

This chapter will not elaborate on preparedness and response for infectious disease events caused by bioterrorism because their presentation and management is similar to that for other microbial threats. Criteria include most of those already described, albeit some may be particularly relevant (e.g., public fear, the number of areas affected, and laboratory capacity). The U.S. Department of Health and Human Services (HHS), specifically CDC, and the U.S. Department of Agriculture, Animal and Plant Health Inspection Service jointly administer the Federal Select Agent Program, which maintains and oversees use of a list of select agents and toxins that “have the potential to pose a severe threat to public, animal or plant health or to animal or plant products.”<sup>34</sup> Diseases caused by many of the agents on this list, including anthrax, smallpox, and the viral hemorrhagic fevers, are not commonly encountered by the medical community in the Western hemisphere. A bioterrorist may use an agent that has been genetically engineered to be highly virulent, resistant to therapeutics, and/or to cause a novel disease. In these cases, health professionals will be at a further disadvantage to prevent disease and death.

As with every terrorist attack, a criminal investigation should ensue after a bioweapon is used. In other types of attacks, this investigation begins immediately after the actual incident has occurred (e.g., an explosion), during the aftermath and rescue efforts. When a bioweapon is used, it may be days or longer before exposed people develop symptoms. Depending on the agent used, it may be an even longer time before a crime is

**Table 8.5. Indications that an Infectious Disease Outbreak May Be Due to a Bioterrorist Attack**

Category	Indication of Bioterror Attack*
Agent	The disease or agent is not usually seen in the region (e.g., smallpox anywhere in the world; plague caused by <i>Yersinia pestis</i> on the East Coast of the United States).
	Multiple geographically distant areas have disease outbreaks occurring at the same time due to a genetically identical strain of an agent. (e.g., identical <i>Francisella tularensis</i> strain causes outbreaks in Washington, DC, St. Louis, MO, and Las Vegas, NV). Note: unintentional food-borne outbreaks may display this incidence pattern if the contaminated product is widely distributed.
	Genetically engineered to be resistant to multiple antibiotics, particularly those commonly used to treat disease (e.g., ciprofloxacin-resistant <i>B. anthracis</i> ).
Host/ Environment	Genetically engineered to cause a novel disease for that agent (e.g., incorporation of genes that cause symptoms of a chronic disease).
	Genetically engineered to be more virulent than usual (e.g., incorporation of genes for toxin production; reconstructed 1918 influenza virus).
	Larger number of casualties in a region in a short period of time compared to expected incidence.
Environment	Cases do not have risk factors for exposure (e.g., brucellosis cases without known exposure to contaminated foods or infected animals). This may indicate an unconventional infection route, such as aerosolization of the <i>Brucella</i> pathogen.
	Cases may have risk factors for exposure, but no common exposures (e.g., all salmonellosis cases ate from restaurant salad bars, but they ate different foods at different restaurants).
	Case distribution and/or environmental distribution of the agent follow wind trajectories (e.g., accidental release of anthrax spores in Sverdlovsk, USSR in 1979).
	Other types of attacks (e.g., chemical, radiological) occur at the same time.
	More than one outbreak (with potentially larger numbers than usual) in a region caused by different agents, especially if one or more agents is uncommon.
	An outbreak of disease in an unexpected season, or that does not follow usual global incidence trends.
	Unnatural distribution mechanism of the agent (e.g., anthrax spores in letters).

\* More than one indication may be present after an attack. Indications listed do not necessarily mean a bioterror attack has occurred, and should be substantiated with epidemiological and/or criminal investigations.

suspected. The site or mechanism of the actual agent release may never be known. If the agent used in the attack occurs naturally in the region, foul play may not even be suspected.

Table 8.5 lists some clues that suggest an outbreak could be due to criminal activity. Although the criminal investigation

will focus on finding the perpetrators of the attack, a second investigation – an epidemiological investigation – will be progressing as well to determine the cause and spread of disease. Both public health and law enforcement investigations will require sample analysis and interviews with the public and must progress in a collaborative manner despite each entity having different goals.

The amount of microbiological sampling after an act of bioterrorism will likely be extensive. Contaminated areas could have very high concentrations of the bioweapon, risking cross-contamination of PPE and transfer of the agent to other surfaces in the area, or other regions. The criminal investigators must take precautions to avoid contracting disease. In the 2001 U.S. anthrax attacks, investigators had to develop microbiological methods specifically for dried spores. Despite these precautions, handling the most contaminated samples, including both the attack letters and cross-contaminated letters, created aerosolized spores and a very hazardous situation.<sup>35</sup>

## STATE OF THE ART

As with other types of events, the response to an infectious disease incident of any origin is only as effective as the monitoring and relief infrastructure in place. In the United States, heightened awareness of infectious disease threats followed the 2001 anthrax attacks. An era of preparedness ensued, with the U.S. Congress allocating unprecedented sums of money to enhance the public health response to bioterrorism. Internationally, a significant driver for public health preparedness has been the International Health Regulations (2005) which entered into force in 2007. The immediacy for response action plans was amplified by the 2003 emergence of SARS,<sup>36</sup> and has been reinforced by other international biological incidents such as the 2009 H1N1 influenza pandemic, the 2012 emergence of MERS-CoV, human cases of H7N9 avian influenza in China in 2013, and Ebola virus disease in 2014.

Preparedness is the state of being ready to act. In the infectious disease disaster context, it broadly refers to the ability to detect a pathogen, act to prevent its spread, and mitigate disease in humans (or animals or plants). Related components include an ability to forecast emerging incidents and to provide reliable situational awareness as a biological incident progresses. Accomplishing this is challenging, given the large number and variability of pathogenic microbes, the potentially rapid global spread of disease, and the extent of communication required between individuals, agencies, governments, and nations. Furthermore, the working definition of “infectious diseases disaster preparedness” and the mechanisms and priorities to achieve it can vary widely between jurisdictions and nations. Because the exact nature of the infectious disease in a disaster situation cannot be known in advance, planning procedures are largely dependent on assessment and subsequent remediation of response vulnerabilities (often identified from previous events and training exercises).

Figure 8.4 shows a general schematic of selected response stakeholders and the activities that occur before, during, and after a biological incident. While not all-inclusive, the diagram serves to illustrate: 1) the ongoing nature of EID preparedness, surveillance, and response; 2) the complexity of the response; 3) the overlapping responsibilities of stakeholders; and 4) the current “feedback” approach to EID preparedness. The light grey

circle just outside the heavy black line (designated “Biological Incident Occurs”) is the “incident threshold.” This circle represents the time it takes for detection of the biological incident (during which time agent transmission progresses essentially unchecked), and can determine the extent of response measures necessary. This section of the chapter discusses the components of infectious disease preparedness that aim to facilitate response activities and minimize the duration, disruptiveness, and impact of the incident. The discussion uses the U.S. perspective to illustrate one approach to EID preparedness. Other countries may address these issues differently. Nonetheless, the section highlights conceptual considerations for infectious disease disaster preparedness.

## Disaster Response Plans

As illustrated by Hurricane Katrina in 2005 and Super Storm Sandy in 2012 in the United States, the earthquake in Haiti in 2010, and the Tōhoku Earthquake and Tsunami in 2011, a large-scale event can overwhelm a response system in both developed and developing nations. The predicted characteristics of infectious disease disasters outlined in the previous section, coupled with evidence from past incidents, serve as tools for understanding the challenges of the next EID disaster. Questions such as “Who is in charge?” and “How well do different jurisdictions or nations interact?” have been the subject of many workshops, symposia, and planning meetings that have occurred at local, regional, national, and international levels.

An important distinction between typical infectious disease disasters and many other disasters is the lack of a specific and immediately recognized incident initiation point (rather, there is an “incident threshold” period). By the time a biological incident is detected and response plans are initiated, many people in diverse areas may already be affected. Biological incidents also have the potential to spread internationally, meaning that response capabilities, plans, and actions in one country can potentially affect many others.

### *International Plans – the International Health Regulations (2005)*

WHO has had international regulations for preventing the spread of disease since 1951, although narrow in scope to select infectious diseases. In May 2005, the World Health Assembly adopted the International Health Regulations (IHR)<sup>37</sup> – this edition is extensively revised and expands the scope beyond a few diseases to any potential “public health emergency of international concern.” In this way, the IHR will remain relevant as infectious diseases emerge or reemerge. The overarching purpose of the IHR is “to prevent, protect against, control and provide a public health response to the international spread of disease in ways that are commensurate with and restricted to public health risks” while limiting unnecessary interruption of global traffic and trade. In general, State Parties to the IHR became bound by the agreement on June 15, 2007. State Party obligations for compliance with the IHR include, among others, reporting of biologic events that are potential public health emergencies of international concern to WHO, and developing minimum core public health capabilities (e.g., surveillance, laboratory capabilities, reporting, implementation of control measures, workforce training) for effective and prompt response to biologic events. The core capabilities were to be achieved within 5 years of the IHR entering into force; evidence suggests, however, that less

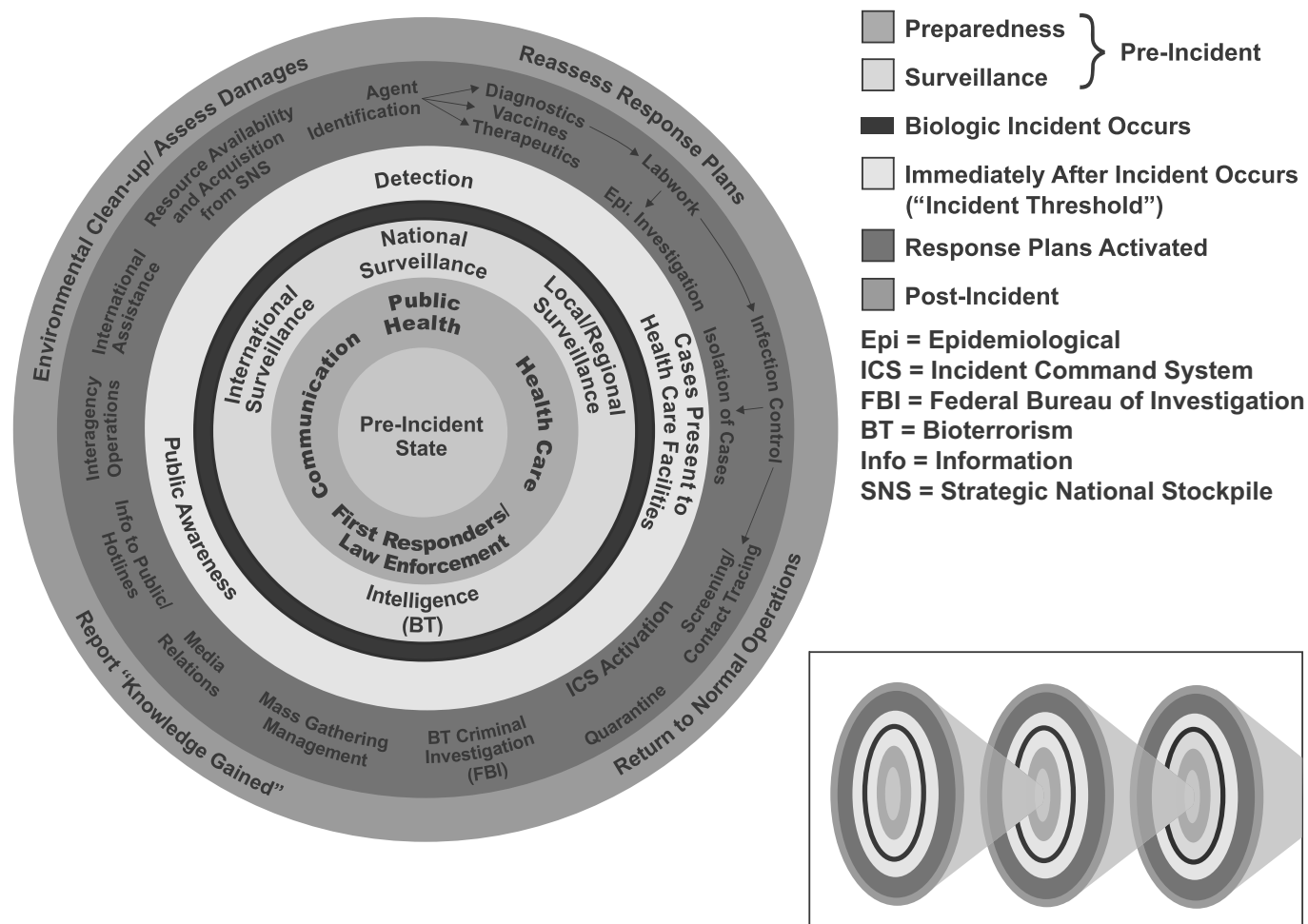


Figure 8.4. Schematic of events before and after a biological incident. “Incident” refers to the exposure of a population to a newly emerging disease (e.g., SARS), to an infectious disease with the potential for extensive casualties and/or public concern (e.g., *Neisseria meningitidis*), or to an act of bioterrorism. Represented are examples of the factors that need to be considered before, during, and after an incident. Increased size of the concentric circles generally corresponds with the progression of time; however, events in larger circles may “feed back” on smaller circles. The use of circles symbolizes the interconnectedness of entities and events within each ring.

The center of the diagram (“Pre-Incident State”) represents the situation prior to a biological incident; during this phase, the various response stakeholders (e.g., Public Health, Healthcare, First Responders/Law Enforcement and Communications) enhance preparedness by, for example, improving response plans and participating in practice exercises. This aims to fortify comprehensive preparedness plans (second ring labeled “Preparedness”) and surveillance activities (third ring labeled “Surveillance”). The heavy black line represents the occurrence of an actual biological incident. After this happens, a period of time ensues when response stakeholders should become aware of the incident (fourth ring labeled “Incident Threshold”), either by active detection through surveillance efforts or passively by presentation of cases to healthcare personnel. Depending on the agent, the incident may not be initially apparent. The border between the occurrence of the incident and the incident threshold is blurred, representing the often unknown occurrence and/or nature of the emergence when it happens. Response plans are activated (fifth ring labeled “Response Plans Activated”) when the incident is recognized. Some elements of the response are shown to illustrate the types of actions the preparedness stakeholders may need to take. This includes agent identification and development of diagnostics/vaccines/therapeutics, activities that will not be timely for an EID unless solid scientific programs are in place in the Pre-Incident State. The events in the final circle (sixth ring labeled “Post-Incident”) largely occur in the post-incident phase when disease transmission has been controlled and no new cases are detected. Some actions such as the clean-up of environmental contamination may initiate sooner to prevent disease transmission. Disaster mitigation efforts are analyzed in the post-incident phase. “Knowledge Gained” is used to optimize preparedness plans for the next potential biological incident (this flow of information is symbolized in the inset). Effective planning and surveillance in the circles before an incident occurs can reduce the incident threshold time and make the events of the subsequent circles easier to manage.

than 20% of the 194 parties to the IHR had met this obligation by the June 2012 deadline.<sup>15</sup> A number of challenges have been described, for example, gaps in resources, insufficient laboratory infrastructure, difficulty in capacity building at the local level, and lack of priority due to the need to address other endemic health and healthcare issues.<sup>38</sup> These challenges highlight that compliance capabilities are not globally uniform but a reflec-

tion, at least in part, of disparities between the developed and developing world.

#### U.S. Local, State, and National Systems

Management of an infectious disease outbreak usually begins with local authorities as the first cases of disease are reported. Therefore, local preparedness plans can be essential for



preventing dissemination of the infectious agents to other regions. This is particularly important when more than one locality is affected concurrently, straining national and international assistance mechanisms. In the years after the terrorist events of 2001, the U.S. government appropriated over a billion dollars to states to augment disaster preparedness. The CDC Public Health Emergency Response Guide, version 2.0 (April 2011) provides guidance and information to U.S. local, state, and tribal health departments for initiating public health response activities in the first 24 hours of an emergency or disaster. The guide includes the following preparedness assumptions that health departments must develop prior to an incident in order to effectively respond to an emergency or disaster:

- establishment of working relationships between local public health partners (e.g., neighboring health jurisdictions, emergency management agencies and services, fire and law enforcement, volunteer/aid organizations, emergency planning committees and response coordinators, academic institutions, and private businesses)
- risk and hazard assessments for the area
- a risk communication plan
- resource capacity assessment and surge capacity plan
- operational plans consistent with those used by other response agencies in the community
- procedures that are consistent with the U.S. Department of Homeland Security (DHS), National Response Framework (NRF), and the National Incident Management System (NIMS)
- surveillance systems to monitor public health
- a trained public health workforce (e.g., on proper use of PPE, emergency operations procedures, incident command system)
- exercises to evaluate and review response plans<sup>39</sup>

Specific plans for biological incidents should address operations in the event that the agent spreads to or from neighboring jurisdictions.

Within the U.S. system, the NRF (second edition, published in 2013) emphasizes involvement of the whole community for “implementing nationwide response policy and operational coordination for all types of domestic incidents.” The NRF is structured in alignment with the NIMS framework, a unified command approach to disaster response that directs different organizational branches as required and is scalable, flexible, and adaptable as incidents change in size, scope, and complexity. When the scope of an incident is expected to surpass the response capabilities of the local and state governments, federal assistance can be requested by the state under the Stafford Act. The all-hazard approach of the NRF necessarily gives broad guidelines for the organization of the response so that procedures apply to many situations. The NRF also outlines more specific considerations for certain types of incidents; for example, depending on the nature of the incident, certain Emergency Support Functions (ESFs) can be implemented. The Biologic Incident Annex outlines “the actions, roles, and responsibilities associated with response to a human disease outbreak of known or unknown origin requiring Federal assistance.”<sup>40</sup> This annex, coordinated by HHS, evokes primarily ESF 8 – Public Health and Medical Services. This ESF defines the core functions for supplemental federal aid to be the assessment of public health and medical needs, public health surveillance, medical care personnel, and

medical equipment and supplies. The Biologic Incident Annex also delineates special considerations (e.g., surreptitious nature of a bioterrorist attack, the importance of surveillance systems), policies (e.g., collaboration with the Environmental Protection Agency in the case of environmental contamination, involvement of the Federal Bureau of Investigation during a bioterrorist attack), concepts of operations (e.g., effective response elements such as detection and containment), and planning assumptions (e.g., multiple jurisdictions may be affected, disease transmission mode is important) that are unique and/or fundamental to a biological incident response.

### *Hospital Emergency Management Systems*

Hospitals should be aware of the unique aspects of large infectious disease outbreaks that could compromise the usual functioning of a disaster management system. These include the transmissibility of the infectious agent to persons not involved in the initial outbreak, the protracted nature of the incident as the agent spreads through the community, and the possibility of infection and absenteeism in hospital staff. Contagious agents necessarily confer an environment of population-based decisions to prevent widespread transmission to the community, which differs from the individual-based care customary of critical care and emergency medicine.

Hospitals should be prepared to operate using an Incident Command System (ICS) during an infectious disease disaster situation. Functioning within an ICS has the advantages of pre-empt assignment of roles, ease of coordination of multiple facility responses, and scalability of the response as the disaster progresses or is resolved. Within the United States, hospitals and healthcare facilities (i.e., those that receive medical and trauma patients on a daily basis) that receive federal preparedness funding are required to be NIMS compliant, which allows for the coordination of response efforts on a national level. Compliance includes the implementation of a number of elements in the areas of command and management systems, preparedness planning, workforce training, preparedness exercises, resource management, and communication and information management.<sup>41</sup> Within these areas, hospitals and healthcare facilities must plan for possible bioterrorism or large-scale infectious disease events. For these types of disasters, infectious disease specialists and infection control experts should be included in the incident command organizational chart to provide guidance on the management of potentially infectious patients with respect to triage, medical care, further assessment, and the handling of infectious decedents.<sup>42</sup>

An important component of the hospital response to a communicable disease is infection control policy to prevent the spread of the agent within healthcare settings. This concept was exemplified by the transmission of MERS-CoV in hospitals in Saudi Arabia, where a WHO mission to the country in May 2014 cited lapses in implementation of WHO-recommended hospital infection prevention and control measures as contributing to a surge in cases.<sup>43</sup> Hospital ICS plans for communicable disease disasters must account for prevention of transmission within the facility, and must also assume that a proportion of the people in the command structure will be unavailable for duty due to illness or personal obligations such as the need to care for ill family members. Preparedness includes a mechanism for real-time alternate assignments for each role in the command structure. Hospital infection control may also result in the temporary discontinuation of elective procedures. With adequate prior

training, personnel from these areas can be diverted to critical response areas that are overwhelmed.

In an infectious disease disaster, potentially exposed persons present to many hospitals in a region. A coordinated incident command Emergency Operations Center for all hospitals in a region is a particularly relevant system given the issue of resource limitations; however, cooperation between facilities may be challenging. Hospitals not yet affected by the disaster must balance the responsibility to assist in the emergency and accept patients with the need to prevent spread of a contagious agent. Transfer of resources such as ventilators and prophylactic medications to overwhelmed facilities may also be hindered because hospitals not yet involved anticipate future casualties. Therefore, hospital preparedness plans for mass casualty bioevents should also include response actions in the situation of limited outside assistance. Additional recommendations have been published on infection control, the types of interventions to use, deciding who should be treated, and who should administer care.<sup>44</sup> These recommendations, although developed for an intentional attack, can guide planning for all types of infectious disease disasters.

The need for extensive infectious disease disaster management plans is controversial. Some experts argue that the threat of an infectious disease disaster with a high human toll, such as pandemic influenza, is greatly exaggerated. Supporting this viewpoint, the 2009 H1N1 influenza pandemic – the first global influenza emergence since the focus on preparedness plans in the new millennium – did not result in the disease incidence or severity expected. Furthermore, modern day medicines and technologies have provided an arsenal against microbes not available during historical epidemics. Yet preparedness needs are difficult to gauge for novel pathogens, including new pandemic influenza strains. Nonetheless, some assert that the constant barrage of reports on the lack of preparedness only serves to either reduce public confidence or foster an atmosphere of complacency.<sup>45</sup> SARS is often used as an example: public concern and economic losses were extensive, but there were only approximately 8,000 cases and 750 deaths worldwide. It would seem that the world overreacted. Recall, however, that the causative agent, reproductive rate, transmission mode(s), treatment, and mortality of this new respiratory infection were not known at the beginning of the pandemic. During this time of uncertainty, global spread occurred only weeks after international awareness of a new disease. Fortunately, the SARS-CoV was not as infectious as initially thought. This pandemic serves as a warning that preparedness plans are necessary, especially in the event of an EID with high transmissibility.

### ***Mechanisms to Prevent Disease Transmission in the Community***

Specific actions taken by responders during an infectious disease disaster will depend on the nature of the agent. In general, the reproductive rate will determine the extent of the measures necessary for containment. There may be uncertainties at the beginning of an EID outbreak. Epidemiological data on the initial cases will guide predictions. In the event that the agent is transmissible from person to person, mechanisms of varying degrees of restriction can be implemented. The concepts of isolation, quarantine, evacuation, shelter-in-place, and social distancing are important containment strategies. Whether these measures are implemented on a voluntary or mandatory basis will depend on characteristics of the agent, and on legal and

ethical considerations. Control of a contagious disease may also require contact tracing, which involves identifying and locating the people with whom an infectious person has come in contact, and the mass distribution of prophylactic medication or vaccination, if available. Implementing controls at national borders to prevent inbound travelers from importing the infectious agent are an option but may be very difficult in some countries and may not be highly effective. Models of pandemic influenza in the United States, for example, suggest that even if incoming infections were reduced by as much as 99%, this would only delay peak disease incidence by approximately 3 weeks.

Some infectious disease outbreaks may require rodent or arthropod control programs to eliminate reservoirs or vectors that carry the agent. This can be challenging for EIDs of unknown (or mistaken) etiology. An outbreak of suspected St. Louis virus encephalitis in New York in 1999 prompted mosquito control and public education activities. Experts soon realized that the encephalitis cases were actually caused by West Nile virus, a closely related virus not previously associated with disease in North America that is transmitted by a broader range of mosquitoes. Initial intervention strategies were sufficiently expansive to be constructive but were optimized with the new diagnosis to the different habitat and activity patterns of West Nile virus-carrying mosquitoes.<sup>46</sup>

Control of zoonotic diseases may require extensive elimination of animals of agricultural importance. The emergence of Nipah virus in Malaysia and avian influenza in Asia in the early 2000s resulted in the slaughter of millions of pigs and fowl, respectively.<sup>47,48</sup> Although arguably necessary to prevent disease transmission to humans, this type of activity can have negative consequences. Economically, segments of the agricultural industry may be devastated due to decreased production, costs of disease containment and clean-up, trade embargoes, and reduced consumer confidence. Associated industries such as transportation, suppliers, and food service would also be negatively affected.

### **Science and Technology**

Scientific advances in molecular biology over the last half century, and particularly in the last 25 years, have greatly benefited infectious disease public health. The successes of the core goals of public health in any infectious disease disaster, namely detection of an outbreak, prevention of its transmission, and mitigation of disease, are all functions of the body of scientific knowledge on the pathogen and the technological capabilities to translate that knowledge into action. In the case of an EID, this specific kind of knowledge may initially be sparse. This highlights the need for solid work in basic infectious disease biology, because EIDs will often (but not always) be novel strains/species of known infectious agents.

Basic scientific research on the bioterrorism potential of select agents has increased dramatically in the last decade, providing insight into their pathogenic mechanisms. These advances can lead to the discovery of targets for novel countermeasures and/or to new diagnostic tools. Some critics have suggested that extensive funding for specific select agents is detrimental to preparedness goals. Biodefense research needs to be translatable to infectious diseases in general, and to public health policy.

### ***Identification and Characterization of the Agent***

Standardized techniques, such as microscopy and culture, are useful in determining the nature of the agent (e.g., the type of

bacteria) and whether any known therapeutics are active against it. Further genetic and molecular analyses, including polymerase chain reaction and immunofluorescence techniques, can differentiate the agent from other similar microorganisms. Along with these types of assays, genome sequencing (the identification of the nucleic acid composition of the organism's entire DNA) can determine whether the etiological agent is a known or a novel pathogen. For example, the SARS coronavirus is only distantly related to other known human coronaviruses (an etiological agent of the common cold) and produces a very different disease, so it is considered to be a newly emerged variety of this type of virus.<sup>49</sup> Similarly, the epidemic of respiratory illness in 2012 and 2013, primarily in the Middle East, is caused by a coronavirus genetically distinct from SARS and therefore represents a new viral emergence – the MERS coronavirus.<sup>22</sup>

There are many obstacles to rapid and definitive identification and characterization of a novel agent. Known animal models may not exist, precluding the ability to link the isolated agent with disease or establish transmission modes. Culturing techniques to grow microbes in the laboratory are very specific for different types of agents, even within the same genus. Due to the unknown nature of transmission and disease severity, specialized containment labs with specifically trained staff may be required. Many regional testing laboratories do not have the equipment or experience to conduct molecular testing.

### **Diagnostic Assays**

Diagnostic assays are important to quickly identify new cases of disease, to differentiate between cases and noncases with similar symptoms, and to determine environmental sources of the pathogen. Genetic tests are often developed due to the rapidity and relatively high analytic sensitivity (ability to detect small amounts of the agent) and analytic specificity (ability to differentiate the agent from other organisms) of the results compared with conventional laboratory techniques. Time is often required to create these assays. During an EID situation, significant pressure exists for rapid development of diagnostics so that clinicians and epidemiologists have tools to identify new cases. These first-line diagnostics are useful, but an understanding of the sensitivity (i.e., true positive rate), specificity (i.e., true negative rate) and accuracy of the diagnostics is important for assessing the interpretation and limitations of any results.

### **Therapeutics**

Antimicrobial drug discovery waned in the 1960s when pharmaceutical companies turned their attention from the supposedly declining threat of infectious diseases to the more pressing and lucrative concerns of chronic illnesses. In modern times, in the face of increasing antimicrobial resistance and emerging agents, new therapies are needed. Scientists are using molecular and structural biology techniques to understand microbial pathogenesis. This information can enhance approaches to discovering novel classes of drugs that block pathogenic processes. Despite an increasingly alarming understanding of the emergence and burden of antimicrobial-resistant pathogens, the drive for the discovery of new drugs effective against bacteria and viruses has not been an industry priority. From 1998 to 2003, only nine new antibacterial drugs were approved, the same number as those approved for just one virus alone, HIV, in the same period. Importantly, only two of the nine antibacterial drugs had novel mechanisms of action.<sup>50</sup> A review published in 2013 indicates that the “innovation gap” of novel antimicrobial agents

continues, with only three new classes of antibiotics approved for use since 2000.<sup>51</sup>

Emerging agents provide a unique challenge for therapeutic design. As noted previously, treatment options for EIDs may be limited, with even broad-spectrum antimicrobial drugs having little or no effect. Information is learned about the causative agent and the disease as the outbreak or epidemic progresses; however, using conventional therapies that work for similar diseases, or emergency use of pre-event approved therapeutics, is risky without efficacy and/or safety studies. In a systematic review of more than fifty published studies that assessed treatment efficacy during the 2003 SARS pandemic, no therapy (including antivirals, corticosteroids, intravenous immunoglobulin, convalescent sera, and type I interferon) conclusively improved patient outcomes. In fact, some studies reported possible harmful effects of treatment with ribavirin or corticosteroids.<sup>52</sup> The development of novel drugs for an EID is challenging. Even if a molecular target is discovered, the design, development, and approval of a therapeutic agent would not be rapid. For example, in the United States it takes approximately 8 years for a new drug to complete clinical trial phases, gain approval, and be marketed. Furthermore, factoring in 1) the high cost of drug development, 2) the relatively low numbers of cases of an EID initially, and 3) the chance that the epidemic will end with no further cases, pharmaceutical companies would be unlikely to even initiate the discovery process without government intervention and/or incentives.

### **Vaccines**

Vaccines are one of the most successful public health tools to improve the health of populations. By preventing infectious diseases, vaccines limit human suffering and the spread of contagious agents. There are many infectious diseases that are endemic in parts of the world for which no vaccines are available. Finding mechanisms to produce effective vaccines is the subject of extensive basic research. Molecular and genetic advances have vastly improved the understanding of immune system regulation and of vaccine delivery methods. Translating this knowledge into approved vaccine products has been slow for numerous reasons. In some cases, the knowledge base on the infectious agent is simply not advanced enough to make a vaccine. For example, some viruses have high mutation rates; consistent vaccine efficacy is difficult because mutated forms of the viruses arise that are not affected by vaccine-enhanced immune functions. As with therapeutic development, pharmaceutical companies are hesitant to engage in vaccine design. The return on investment is relatively low, demand for vaccines that target sporadically occurring agents is unpredictable, some vaccines for endemic diseases are not extensively used (e.g., yellow fever in Africa and South America), and safety and liability issues abound.

### **Government Incentives**

After the terrorist attacks of 2001, the U.S. federal government passed the Project BioShield Act in 2004 (and reauthorized portions in 2013) to “accelerate the research, development, purchase, and availability of effective medical countermeasures against biological, chemical, radiological, and nuclear (CBRN) agents.”<sup>53</sup> The three main goals of Project BioShield are to 1) provide funding for the procurement of critical medical countermeasures (MCMs); 2) give authority to the National Institutes of Health of HHS to prioritize the granting procedure for research and development of critical MCMs; and 3) assist in the

use of MCMs during an emergency. BioShield lays the groundwork for increased vaccine and drug development for bioterrorist agents. Major pharmaceutical companies have not widely used this funding system primarily due to concerns about liability protection for expedited MCMs. Funding smaller biotechnology companies can help fuel an industry, but there are risks for both parties involved. Some companies may be unable to produce the contracted pharmaceutical after receiving federal funding, or the government may opt to purchase less of the product than projected.

The U.S. pharmaceutical industry needs motivation beyond Project BioShield to expand antimicrobial therapeutic and vaccine development. In this regard, the Pandemic and All-Hazards Preparedness Act was approved in December 2006. This act directed the formulation of the Biomedical Advanced Research and Development Authority (BARDA) within HHS. BARDA is charged with promoting the translation of scientific research into antimicrobial products, including provisions to induce participation by the pharmaceutical industry. The creation of BARDA was criticized. Consumer advocacy groups questioned the safety of using expedited drugs, even in emergency situations. Scientific associations were concerned about the lack of transparency of BARDA activities and decisions, the potential for gaps in or duplication of research efforts, and funding sources and amounts.<sup>54</sup> In 2013, the U.S. government passed the Pandemic and All-hazards Preparedness Reauthorization Act. This legislation clarifies and expands on U.S. Food and Drug Administration authority for supporting preparedness and rapid response capabilities, including components that address refinement of, or additional authorities for, emergency use of MCMs, pre-event positioning of MCMs, shelf-life extension of MCMs, and regulatory/review processes for MCM development.

### Dual-Use Risk

The 2001 U.S. anthrax attacks heightened public awareness about bioterrorism. To increase preparedness against future strikes, the American government allocated billions of dollars for biodefense research on certain pathogens and toxins, termed “select agents.” The select agents are categorized as those that affect humans, those that affect agriculture (animals and plants), and those that can affect both humans and agriculture. Policymakers realized that increased research on select agents could increase the risk that the agents, or scientific information learned about them, would fall into the hands of terrorists. As a result, measures have been taken through the Biopreparedness Act to limit access to the select agents, regulate genetic manipulations of these agents, and restrict publication of information that could lead to enhanced virulence of the select agents. The Biopreparedness Act also mandates FBI clearance rules for scientists working with select agents. The National Science Advisory Board for Biosecurity (NSABB) was formed to oversee the balance between increasing scientific research to prepare better for a bioterrorist attack and preventing potential adversaries from accessing scientific reagents and information.

Since the first adoption of the act, changes to “dual use” legislation and implementation have occurred. Revisions in 2012 to the select agents list removed a number of them to focus regulatory efforts on the agents of most concern to public or agricultural health. In addition, some agents, such as Ebola virus, botulinum neurotoxin and *Bacillus anthracis*, were designated as “Tier 1” to indicate the subset most at risk for deliberate misuse and with greatest potential for mass casualties, economic

or infrastructure devastation, or erosion of public confidence. Additionally, rules for publication of research on pathogens with pandemic/bioterrorism potential that are engineered to increase pathogenicity or transmissibility came into question in 2011 after two research groups, one in the United States and one in the Netherlands, independently submitted manuscripts to scientific journals describing such work. NSABB initially recommended that the work not be published in full; the journals delayed publication, the research community halted work on related research until the issue could be resolved, and eventually NSABB reversed its recommendation to withhold publication of each paper after the manuscripts were revised to remove methodological details.<sup>55</sup>

### Surveillance

Broadly speaking, public health surveillance refers to “the collection, analysis, and use of data to target public health prevention.”<sup>56</sup> There are four basic components to surveillance: monitoring for disease, detection of disease, analysis of data, and dissemination of findings. A relatively newer term is “bio-surveillance,” which is often used to denote the assessment of health-related and other data for rapid recognition (i.e., “early warning”) of a biologic incident or “real-time” situational awareness as an incident progresses. The sooner the detection of an infectious disease outbreak or emergence occurs, the faster the response can be to prevent spread of the agent and human disease. In addition, early detection can prevent the dissemination of the pathogen to other regions or countries and potentially prevent an epidemic or pandemic. The Surveillance Resource Center on the CDC website is an online clearinghouse of guidance and practice tools for surveillance capabilities.

Surveillance is also an assessment tool for the general functioning of a public health system. Monitoring disease incidence, morbidity, and mortality can indicate regions that must boost existing public health infrastructure. These regions are at increased risk for large numbers of casualties during an infectious disease disaster compared to regions with more robust infrastructures.

### International Surveillance Efforts

Globalization has conversely made international infectious disease surveillance both increasingly necessary and possible. Emerging infectious agents can arise in any country and potentially spread globally due to travel and commerce. Quick determination of the emergence of an outbreak will give public health officials, clinicians, and researchers throughout the world an opportunity to prevent dissemination and to develop diagnostics and therapeutics. Increased global interactions, which can promote spread of a disease agent, can also encourage cooperation in surveillance efforts. The IHR obligates Member Parties to develop a minimum core surveillance capability for the detection of biologic events that may constitute a public health emergency of international concern.

Disparities exist in the capabilities of different countries with respect to workforce, tools, and effort. In Europe, where resources for surveillance were prioritized as in North America, sophisticated systems have been developed to collect, analyze, and disseminate information for public health action (e.g., the European Surveillance System). Many developing countries have a strained public health infrastructure that cannot expand to support intensive surveillance efforts. Therefore, global partnerships that link networks from many regions and countries, such as those

supported by WHO Member States, serve to share expertise and information. For example, the WHO Integrated Disease Surveillance Programme is a strategy adopted by most countries in the WHO African Region for strengthening core surveillance capabilities at the district level.

Reporting is a critical component of effective global surveillance. The IHR includes reporting of potential public health emergencies of international concern to WHO as a core capability so that global response activities can be initiated if necessary. The obligation to report such events is intended to prevent countries from delaying reporting to avoid stigmatization and negative impacts on travel and trade, or assumptions that an outbreak is under control and of little threat for further spread. The situation of the emergence of SARS reinforced the need to include reporting in the IHR: although cases of SARS first appeared in Guangdong Province in November 2002, Chinese officials only confirmed the outbreak to WHO in February 2003 after international surveillance networks were alerted through media and Internet reports.<sup>57</sup> Chinese public health officials worked with WHO to control the outbreak, but international dissemination had already occurred. In response to the SARS pandemic, the Chinese government has overhauled its infectious disease surveillance and reporting systems.

The public health infrastructure problems that delayed the Chinese response are not unique to that country. This substantiates the need for international collaborations to detect EIDs and support mitigation efforts. Implementation of the IHR for reporting has not been uniform across nations, but the regulations provide a framework of expectations. In China, transparency in reporting cases of H7N9 influenza in 2012 and 2013 has been lauded by WHO as exemplary adherence to the IHR,<sup>58</sup> and is distinct from the experience with the lack of early reporting of cases of SARS a decade earlier. In contrast, Saudi Arabia has been accused of being less than forthcoming with information on the emergence of MERS, even in light of the IHR.<sup>59</sup>

### **National Surveillance Efforts – U.S. Model**

Healthcare practitioners play a central role in the surveillance process by notifying public health authorities regarding patients with reportable diseases or atypical symptomatology. For example, U.S. physicians in the early 1980s noticed that young men were contracting *Pneumocystis carinii* pneumonia (now known as *Pneumocystis jirovecii* pneumonia) and/or certain malignancies not normally associated with that demographic group. This was one of the first indications that a new immunocompromising infectious disease (now known as AIDS) was circulating in the population.

This classic method of outbreak identification is a key component of disease control in a population, but relying on it solely is problematic. Recognition of cases that should be reported and subsequent data submission are not always timely. There is heavy reliance on subjective determination of what should be communicated to public health and not all infectious diseases are reportable. Furthermore, early surveillance opportunities that could potentially prevent human disease and death may be missed. In the first North American outbreak of West Nile virus in 1999, unexplained bird deaths had been noticed 2 months prior to the human outbreak investigation, but no extrapolation was made to possible human consequences.

Recognizing the value of time, many health departments, health agencies, academic institutions, and governments have developed a number of surveillance systems and networks to

more rapidly and consistently detect disease events. Examples of the types of systems include those that 1) monitor the environment for the presence of bioterrorism agents (e.g., BioWatch in the United States); 2) use health and other data for early detection of outbreaks (i.e., syndromic surveillance; Chapter 13); and 3) aim to foster collaboration and information sharing among biosurveillance stakeholders (e.g., the U.S. National Biosurveillance Integration System).

The U.S. government executive leadership published a National Strategy for Biosurveillance in 2012 to emphasize that early detection of biological threats, and accurate and timely information for situational awareness, is important for decision making at all levels to save lives and protect national security.<sup>60</sup> This strategy aims to strengthen U.S. government national biosurveillance by leveraging and integrating existing national capabilities, building capacity, fostering innovation, and strengthening partnerships. These activities are in the context of maintaining a global health perspective by promoting reinforcement of international partnerships and encouraging surveillance development and integration across countries.

### **Workforce Preparedness**

Workforce preparedness is the state of readiness of public health, public safety, and healthcare employees to act in an infectious disease emergency. Workforce readiness is primarily related to workforce capacity and education/training. The concept is often used to describe readiness at the community and state level, but EID or large biological incidents will likely require participation on a national level as well. The jobs performed by these employees are critical to the proper and sustainable functioning of the other preparedness requirements such as surveillance and resource management. Furthermore, training exercises and past disasters have demonstrated that mitigation and response are improved by good working relationships between public health, public safety, and healthcare workers.

### **Public Health Workforce**

Inadequate public health workforce numbers and expertise are not limited to developing nations. For example, it is well established that decades of budget cuts and neglect have resulted in an understaffed public health infrastructure in the United States. This has compromised the ability to respond effectively during an infectious disease disaster. In some jurisdictions and facilities, especially smaller ones, the roles of public health nurses, laboratory technologists, epidemiologists, and infection control practitioners are accomplished by staff with multiple duties. Furthermore, these positions are often characterized by staff who are reassigned when needed, by employees working overtime, and/or by the use of temporary workers. These options will be limited during an infectious disease disaster as demand for these employees will increase and movement between facilities will be restricted.

Formal education of public health workers in the United States for epidemic situations is accomplished mainly by the CDC. The Epidemic Intelligence Service (EIS) is a well-known program. For more than 60 years, the EIS has trained public health professionals with hands-on field experiences in epidemiology. CDC Environmental Public Health Leadership Institutes prepare environmental public health workers for leadership positions at the state and local levels and promote networking between jurisdictions. CDC also funds Preparedness

and Emergency Response Learning Centers at university schools of public health across the United States to train the public health workforce on core public health competencies.

Laboratory technologists are a fundamental part of infectious disease disaster management teams. Timely surveillance, detection, and diagnosis are all dependent on laboratory services and can reduce transmission and disease severity during an infectious disease disaster. Chronic underfunding has left many public health laboratories understaffed. As demonstrated by the 1999 West Nile virus emergence, 2001 anthrax attacks, and 2003 SARS pandemic, the laboratory workforce can quickly become overwhelmed with samples. The U.S. CDC implemented the Laboratory Response Network in 1999 to act as a networking platform for laboratories (local, state, federal, international, military, veterinary, and agricultural) in response to terrorism. This role has since been expanded to include EIDs and other public health emergencies.

The general public expects the public health workforce to provide accurate information. Such timely and reliable data are a vital resource for control of an epidemic. However, knowledge of the characteristics of an emerging biologic incident may change frequently as the incident unfolds, and messaging and resource planning may need continual assessment and updating. Public health telephone hotlines are a common mechanism to disseminate information and to answer specific questions. Disaster plans do not, however, always consider the volume of calls that an information hotline receives. Over 316,000 calls were placed to the Toronto SARS hotline, which was established the day after the first Toronto SARS case was announced at a press conference. Almost 60% of the callers selected the “listen to recorded information” option. Of the calls in which the “speak to a staff person” option was selected, almost 80% (104,852 calls) were *not* answered by a staff member.<sup>61</sup> This number illustrates the overwhelming service requirements that can be associated with infectious disease disasters. Case numbers alone do not always correlate with workload. The prevalence of use of social media will likely reduce the importance of telephone hotlines.

### **Public Safety Workforce**

First responders such as law enforcement, firefighters, and emergency medical services personnel are important segments of the public workforce for management of an infectious disease disaster. These workers will be involved in the distribution of resources, crowd control at mass gatherings, the transfer of patients, and any criminal investigations resulting from a bioterrorist attack. In some countries, first responders have the advantage of extensive ICS training and experience; however, as outlined previously, biological incidents are unique in many facets. As one of the primary interfaces with the general public, first responders are at risk for exposure to infectious agents. Jurisdictions must determine in advance how best to protect first responders in the event of a contagious infectious disease disaster. The U.S. CDC website provides information for state, local, and tribal public health directors, and for first responders with respect to emergency response after a biological incident. These recommendations include use of PPE by first responders and suggestions for the handling of contaminated mail or containers. Preparedness also includes an understanding of public health law with respect to quarantine orders and other public movement restrictions, and plans for enforcing these orders.

### **Healthcare Facility Workforce**

A component of NIMS hospital compliance in the United States is workforce training in core competencies so that hospital personnel will be able to function in a coordinated fashion during a disaster. The U.S. CDC found that the ICS format for disaster response was critical for providing stability and continuity to response efforts after Hurricane Katrina. As a result, the CDC pandemic preparedness plan uses the ICS to structure response efforts during a prolonged disaster with high staff turnover. Hospital ICS plans for an infectious disease disaster should account for reduced workforce capacity as the disaster progresses due to illness, absence to care for ill family members, refusal to work, and psychological stress. In that regard, healthcare workers should be trained in advance to understand possible implications of a contagious infectious disease disaster and methods to contain the disease. This training should include proper use of PPE, duty-to-care expectations, and infection control practices. Workforce preparedness must also address psychological consequences of a prolonged disaster. The toll on those expected to respond to disasters is significant and this stress has usually received inadequate attention. This is especially important when the workforce is already understaffed.

### **International Workforce**

Infectious diseases affect more people in developing nations than in other areas of the world. An underdeveloped and understaffed public health workforce contributes to this poor outcome. For example, early management of the 2014 EVD outbreak in West Africa was hindered by insufficient numbers and training of local healthcare and public health staff. Response to the outbreak was largely reliant on clinical volunteers from international aid organizations, with little assistance from local or international governments until the threat of international dissemination of the virus increased.

Augmenting fields such as epidemiology and infection control in developing nations can reduce human suffering and increase detection of emerging pathogens and impending pandemics. International partnerships among aid organizations, government agencies, and industries have resulted in programs to develop global information networks and workforce alliances that train public health workers in developing countries. WHO's Global Health Workforce Alliance and Integrated Disease Surveillance programs are examples of international efforts to improve workforce capacity and training in developing nations.

### **Response Communications**

Many aspects of successful management of an infectious disease disaster are dependent on timely and accurate communications between different stakeholders. Examples of such aspects include surveillance, implementation of scientific advances, resource allocation, and delivery of assistance.

### **International Communication**

As previously outlined, infectious disease disasters and emerging new pathogens can rapidly become global in nature. Communication among governments and agencies is fundamental to limiting the extent of an infectious disease disaster. The initial delay in disclosure of a new severe respiratory disease to the world was a likely factor in the global spread of SARS. Once it was clear a new disease had emerged, the international response

demonstrated unprecedented cooperation and communication. WHO, facilitated by the Global Outbreak Alert and Response Network, established secure communication networks and websites for the daily exchanges of information on surveillance, epidemiology, and disease characteristics. The utility of this networking system was nowhere more evident than in the discovery of the etiological agent. The Laboratory Network, which consisted of eleven laboratories in nine countries, shared data and information. Together, they identified the causative agent of SARS, sequenced its genome, and developed diagnostic tests, all in a matter of weeks. These laboratories were already in communication prior to the SARS pandemic via the well-established WHO Influenza Surveillance Network, substantiating the value of ongoing partnerships.

### **National Response Communication**

One of the primary ways that new, cleared information is shared in the United States regarding urgent public health incidents is the CDC's Health Alert Network (HAN), which publishes CDC advisories and updates on clinical and epidemiological information, often as an incident is unfolding. For example, numerous HAN communications were published in 2012 regarding the multi-state outbreak of fungal meningitis resulting from injection of people with fungus-contaminated medications.<sup>62</sup> Communication between jurisdictions and between levels of government is vital during an infectious disease disaster due to the transmissibility of the agent. It can be the difference between a contained localized outbreak and a national epidemic. Unlike many other disasters, communications interoperability will likely remain intact during an infectious disease disaster. This is in contrast to the situation during Hurricane Katrina, where widespread physical disruption of communication systems made information exchange between response teams difficult. Without a distinct starting point for the biological incident, however, extensive and formal interagency and intergovernmental communication through the NRF may be delayed. This could undermine unified command and result in multiple and disparate efforts toward similar goals. Even in non-disaster situations, past experiences suggest that poor communication results in conflicting actions. For example, during the 2004 U.S. influenza vaccine shortage, agencies at different governmental levels gave inconsistent messages, recommending vaccination of different age groups.<sup>63</sup>

### **Communication with the Public**

Communication of disease and containment information to the community by the public health system can determine, to a large degree, the extent of an epidemic. WHO held the first Expert Consultation on Outbreak Communication symposium in Singapore in 2004 to discuss risk communication to the public. It is widely agreed that providing the public with accurate and timely information is necessary to prevent spread of the infectious agent. Yet, these tasks are usually very difficult because the information may change as the epidemic unfolds. Inconsistent messages may be viewed as untrustworthy. Furthermore, while response plans should include general requirements for crisis and emergency risk communication to the public, the messages need to be tailored for each biological incident or circumstance. For example, although the Ministry of Health in Saudi Arabia recommended that people at high risk for contracting MERS cancel their participation in the 2013 Hajj pilgrimage, a French study found that all 179 survey-takers with conditions that put

them at high risk for contracting MERS still planned to participate even after pre-travel educational consultations.<sup>64</sup> Most, however, were receptive to prevention practices such as wearing masks. The authors suggest that risk perception may be influenced by cultural and religious beliefs, and risk messaging should account for that context.

The media is a powerful tool for disseminating information. In a survey of people quarantined in Toronto during the SARS epidemic, more people claimed that they got helpful information on the quarantine orders from the media than from public health officials or from their healthcare providers. Good working relationships between health department public relations liaisons and local news stations before an incident occurs can encourage cooperation during an outbreak. In a large disaster, it may be necessary to establish an information center to coordinate messages for the public. In addition to the disaster itself, the media also report on the management of the emergency.<sup>65</sup> Some decisions will need to be explained or justified. As defined by the ICS structure, a credible spokesperson should be selected as the point of contact with the media to ensure delivery of consistent and accurate messages to the public.

### **Resource Management**

In a biological incident, critical resources are needed for detection of the pathogen in the community and for appropriate patient care. Yet, real outbreaks from the past and tabletop preparedness exercises have ascertained that resources will be limited.

### **National Resources**

Within the United States, HHS and CDC maintain the Strategic National Stockpile (SNS).<sup>66</sup> The SNS is a supply of critical resources that includes antibiotics, antitoxins, ventilators, N95 respirators, and medical equipment for use in the event of a public health emergency. CDC distributes SNS resources to supplement local capabilities on request from the governors of affected states and on assessment of need. Aid is in the form of 12-hour Push Packages and Vendor Managed Inventory. The 12-hour Push Packages are designed for distribution of nonspecific critical resources from regional warehouses within 12 hours of federal approval of allocation. The Vendor Managed Inventory supplies additional and more specific resources within 24–36 hours directly from pharmaceutical companies; CDC may choose to supply Vendor Managed Inventory instead of a Push Package. CDC deploys Stockpile Service Advance Group staff to assist in receiving, organizing, and distributing the supplies.

The SNS is an extensive cache, but insufficient for a catastrophic disaster effecting multiple jurisdictions. A large infectious disease disaster, such as a bioterrorist attack, is an example of an event that will affect many areas at one time. CDC may have to prioritize which states receive aid from the SNS based on severity of the outbreak. Some SNS resources may even be reserved in the event of a second attack. Furthermore, the 12-hour response time refers to distribution from federal stocks to state authorities; it is up to the states to then determine which localities will receive the supplemental aid. Given all of these circumstances, hospitals should stockpile *at least* a 48-hour supply of PPE and drugs likely to be used during a mass casualty infectious disease event. A 3–7-day supply may be necessary in the event of a large or widespread disaster.

### *Hospital Resources*

A large biological attack or epidemic could result in hundreds of people a day presenting to hospital emergency departments during peak disease incidence. As the number of ill patients increases, hospital critical care providers will have to assess resource capacity and may need to determine allocation procedures to save the most lives instead of focusing the majority of resources on a few critically ill patients. This is a difficult task because intensive critical care for the very ill in non-disaster situations may result in improved outcomes.

As discussed previously, hospital plans must include provisions for isolating infectious patients. These should include requirements for beds, equipment, and staff dedicated for that purpose. The availability of mechanical ventilators is a particular concern during an infectious disease emergency. Many microbial pathogens cause respiratory complications that require mechanical ventilation. Yet preparedness assessments have demonstrated that hospitals cannot accommodate ventilation for all patients, even operating under surge capacity guidelines. For example, during a Minnesota drill, regional vendors could only provide sixteen extra ventilators.<sup>67</sup> Proper allocation of resources is also a function of knowing what resources are available. An up-to-date list of available staffed beds, ventilators, and other limited resources can help with the triage process.

The hospital infectious disease triage system is an important process to quickly determine patient health and susceptibility status. People efficiently and accurately categorized as “susceptible,” “exposed and/or infectious,” or “immune” (due to vaccination or prior recovery from the disease) can receive the appropriate management with minimal suboptimal use of resources.<sup>68</sup> In the midst of a disaster, the tendency is to either over-classify people as “exposed” or to protect individuals who are at minimal risk. Both of these situations can result in increased numbers of people unnecessarily using limited hospital resources.

### *Allocation of Resources*

Preparedness plans need to include guidelines for resource allocation in the event that supplies are limited. In other words, algorithms are needed to help identify which patients may not qualify for treatment. Making these decisions at the time of an infectious disease disaster without prior consideration can lead to heightened confusion among providers, contention among policymakers, and anger among the public. Legal, social, and political factors will be as much a part of the decision-making process as patient care.

Most agree that to save the most lives, the patients most likely to survive (that is, the least critically ill) should be treated with limited resources first. Whatever system is adopted, administration must be equitable and transparent to all patients and to the public. One mechanism to promote the just allocation of limited resources is to numerically code the survivability of patients based on clinical assessment. Resource distribution is then based on patient scores.

### *A Specific Case: 2009 H1N1 Pandemic Influenza and Resource Availability*

For many years prior to the emergence of the novel H1N1 influenza A virus in April 2009, the threat of pandemic influenza was often used to examine resource availability in public health. The 2009 novel H1N1 event (declared a pandemic by WHO on June 11) highlighted that disease emergence characteristics can be unpredictable despite well-informed “best guesses.” Viral

emergence and disease were first detected in North America, not Asia; the pandemic virus was a novel H1N1 quadruple reassortant of swine, human, and avian genes, not (yet) a highly pathogenic H5N1 avian virus with increased transmissibility in humans; transmission and disease continued during the summer months in the United States; and worldwide disease severity was mild or moderate with low mortality rates. Unlike disease transmission and global spread, disease severity was not officially factored into the WHO decision to elevate the pandemic alert phase, but this pandemic demonstrated that concern for public overreaction and for response activities tied to elevation of alerts necessitated a carefully worded declaration statement addressing that disease was moderate. In 2013, based on knowledge gained from this pandemic, WHO issued interim guidance that proposed a revised influenza pandemic alert system. This system has four phases instead of six, with the pandemic phase accounting for “a period of global spread of human influenza caused by a new subtype. Movement between . . . phases may occur quickly or gradually as indicated by the global risk assessment, principally based on virological, epidemiological and clinical data.”<sup>69</sup>

In the United States, the initial wave of the 2009 H1N1 influenza pandemic illustrated some of the suspected resource challenges of a novel disease outbreak, including increased volumes of patients in emergency departments, management of changing recommendations and information overload, scarcity of PPE (e.g., requirements for and availability of surgical masks and N95 respirators), viral resistance to existing therapeutics, hospital employee issues (e.g., absence due to influenza-like illness, wage compensation for absence after exposure, fatigue), availability of diagnostics, and lack of a vaccine at the onset. The anticipation of a second wave of H1N1 disease in the fall of 2009 coupled with the arrival of seasonal influenza led response stakeholders, such as the American College of Emergency Physicians, to issue guidance on the necessary resource and surge capabilities for management of novel H1N1 outbreaks.<sup>70</sup>

The 2009 H1N1 influenza pandemic marked the highly unusual situation where two viruses coexisted in elevated phases in the WHO pandemic alert system (novel H1N1 at pandemic level and avian H5N1 at phase 3). Viral unpredictability precludes definitive expectations of a “double influenza pandemic.” Nonetheless, such a situation has serious consequences for response capabilities; robust pandemic preparedness is especially important for resource management, continuity of operations, and patient care.

### **Preparedness Training Exercises**

Infectious disease disasters are rare events, yet a state of complacency or underpreparedness by response stakeholders can result in increased casualties when one does occur. Preparedness is more than just having meetings and written plans. Exercises are the current state of the art in testing the readiness of response systems and in identifying areas that need improvement. The time and resource commitments for this practical training must be balanced with those for normal operations, and an avoidance of “preparedness fatigue.”

Some exercises are supplements to didactic lessons at institutions of higher learning, such as nursing and medical schools. Nurses and physicians may be the first to recognize that an infectious disease disaster is looming and/or they will be on the front-line of the response. It follows then that nursing and medical students should receive dedicated education and training in the



mechanics of the response. The exercises are usually in the form of case scenario discussions that address the clinical, operational, and ethical issues of infectious disease disaster management.

Policymakers, resource managers, public health departments, first responders, and healthcare facilities often use tabletop exercises and drills to assess preparedness. These types of activities are useful for practicing coordination of efforts within and between different parties. The exercises usually involve the mock release of a biological agent such as the smallpox virus, with informational updates given by the exercise administrators to participants as the disaster unfolds. Factors such as resource availability and allocation, protection of healthcare workers, and public unrest are usually components of the exercise. Table 8.6 lists criteria typically considered for the development of a training exercise.

Since the anthrax attacks of 2001 and the 2003 SARS outbreak, regional preparedness drills are now commonplace throughout the world. In the United States, there have been large-scale national disaster exercises such as Dark Winter and TOPOFF (for “top officials”) exercises starting even prior to 2001. These congressionally mandated exercises were designed to examine national preparedness. They involved officials and responders from all levels of government. All of these exercises substantiated the validity and importance of the preparedness factors that are outlined in this section. For example, TOPOFF 4, which occurred in October 2007, had over 15,000 participants and included the U.S. territory of Guam. It was designed to assess the response to multiple coordinated attacks with a Radiological Dispersal Device. TOPOFF 3, which took place in April 2005, included a bioterrorism component and participation from Canada and the United Kingdom. It was the first national practice of a response based on implementation of the NRF (then known as the National Response Plan) and NIMS in the capacity of the Homeland Security Operations Center. Concerns raised by the DHS Office of Inspector General<sup>71</sup> after completion of the exercise included: 1) insufficient understanding and training of participants on NRF and NIMS procedures, which resulted in “bureaucrat confusion” and operations under multiple different protocols; 2) confusion over the declaration of an Incident of National Significance and the consequences of such an action; 3) challenges with information collection and reporting; 4) inadequate collaborations between government and the private sector; 5) the high cost of TOPOFF 3 to participating states; and, importantly, 6) repeated weaknesses from TOPOFF 2.

Although not really “drills,” recent outbreaks, epidemics, and events are arguably the most appropriate tools for assessing disaster responses. Public reaction, media relations, and interagency communication in a high-pressure situation are components not easily reproduced in an exercise. Response limitations in recent events such as the 2001 anthrax attacks (e.g., laboratory capacity), the 2003 SARS pandemic (e.g., contact tracing, implementation of quarantine, and healthcare worker safety), Hurricane Katrina in 2005 (e.g., interagency communication), and the 2009 H1N1 influenza pandemic (e.g., vaccine production and allocation) serve as reminders that certain aspects of preparedness plans are consistently deficient. Even local outbreaks of foodborne illnesses can inform health departments on areas in need of improvement. For exercises to be useful to a jurisdiction, government, or institution, they need to occur at regular intervals. Policies will change over time due to data from previous exercises, new legislation, and funding constraints. In addition, personnel

**Table 8.6. Considerations for Exercise Development**

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<b>Participants</b>	
■	Health departments/Public health
■	Government officials (local, state, federal)
■	Hospital workers
	Management
	Patient care providers
	Laboratory technologists
	Epidemiologists/Infection control
	Pharmacists
	Health information management
	Support personnel (e.g., housekeeping, security)
■	Law enforcement
■	First responders
	Emergency medical services
	Fire
■	Media representatives
■	U.S. Federal Bureau of Investigation and equivalent in other countries (bioterrorism exercises)
<b>Areas for response assessment</b>	
■	Resource availability
	Hospital patient care areas and supplies
	Therapeutics and vaccines
	Personal protective equipment
	Personnel
■	Resource allocation
■	Response coordination/Incident Command
■	Infection Control
	Spread of the agent through the community
	Protection of healthcare workers and responders
■	Communication
	Interagency
	Among jurisdictions or regions
	Among levels of government
	Media relations/Information to public
■	Triage
■	Information management
■	Personnel management
	Within facilities and agencies
	Mobilized for large-scale action (vaccine distribution, epidemiology)
■	Management of public reaction
	Public fear
	Civil unrest
	Mass gatherings for resources
■	Psychological ramifications
	Response personnel
	Public
■	Understanding of legal implications of decisions
■	Cost of implementing decisions
<b>Exercise Evaluation</b>	
■	Assessment of whether processes and outcomes of the response met goals
■	Comparison of evaluation to previous exercises
■	Cost of the exercise

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Adapted from Bardi J. Aftermath of a hypothetical smallpox disaster. *Emerg Infect Dis* 1999; 5(4): 547–551.

turnover necessitates repeated training so that new employees can function within the system. The utility of the exercises is also contingent on proper evaluation after they are completed. An exercise with flawed design and/or execution can lead to a false sense of preparedness. For example, participants in the TOPOFF 3 exercise noted that federal assistance was provided in an

unrealistically fast manner and may not correspond to the timing in an actual disaster.

### Modeling

Given the rarity of infectious disease disasters, mathematical models are used as prediction and forecasting tools. These models use existing data from previous outbreaks, epidemics, or pandemics to provide insight into putative future transmissions of infectious diseases and/or ramifications of preparedness decisions. This is important because the process of designing and interpreting models can serve as a guide for discussions on the variables and assumptions involved in controlling disease. The uncertainty regarding use of various inclusion and exclusion parameters and the potential errors in selection of data values brings into question the significance of the models.

Epidemic emergence models using climatic data have been developed with success for *V. cholerae* O139, a pathogen endemic to certain regions of the world.<sup>72</sup> Modeling of novel or rare pathogens, such as pandemic influenza or intentionally released smallpox, is more problematic. Here, specific characteristics of the agent (transmissibility or drug resistance) and the host (susceptibility, super spreaders, public reaction and compliance) are unknown and must be assumed.

Modeling is also used for preparedness plans to determine how decisions will affect the progression of the epidemic. Models related to resource allocation, antimicrobial use, vaccination strategies, health economic implications, and public control (quarantine, isolation, social distancing) have all been published.<sup>73–77</sup> How to best validate these models (and the decisions they support) and incorporate their recommendations into the formulation or optimization of preparedness plans remains a challenge.

### Evaluation

Since 2001, many countries have spent large amounts of money on public health preparedness for a biological event. For example, the United States has spent billions of dollars on surveillance, workforce preparedness, response strategies, and exercises and drills to prepare for an attack using biological weapons. Formal evaluation of these activities is crucial to ensuring that outcomes are properly reviewed and that funding is being used effectively. This mandates more than the simple creation and publication of after-action reports. Preparedness programs should be designed with the inclusion of specific evaluation components to empirically determine whether goals are being met and provide data for improvements. This type of evaluation is critical because some assessment questions may give a skewed sense of readiness. For example, in assessing a workforce readiness training program, asking whether or not people are trained (a structural measure) is different from asking how well employees perform their duties after training (a process measure) or even whether the training was successful in reducing the morbidity and mortality of an infectious disease disaster (an outcome measure). This last type of assessment is challenging given the rarity of infectious disease disasters and the difficulty of defining “success.”<sup>78</sup>

The complexity of preparing for infectious disease disasters lies in the unknown nature of future threats. Because of this, individuals involved in their management may disagree on the necessity and requirements for effective preparedness plans. This is particularly true for bioterrorism preparedness, because the per-

ceptions of the necessity for such specific plans vary widely.<sup>79,80</sup> For example, the campaign in the United States in 2003 to vaccinate 500,000 healthcare workers against smallpox had very low compliance. This was due, at least in part, to perceptions that the threat of a smallpox bioterrorist attack was low and concerns over the unknown safety of the vaccine.<sup>81</sup> Evidence-based assessments of the needs and priorities of response preparedness efforts and the probability of success (from sociological and scientific perspectives) are critical to preventing this type of program collapse. This is particularly important because the failure of these large programs causes the public to question the utility and funding of any EID preparedness initiative.

### RECOMMENDATIONS FOR FURTHER RESEARCH

The traditional paradigm regarded pathogens as enemies to be battled as they emerged. As a better understanding of the relationship between humans and the microbial world is gained, the war analogy in approaching EID management has become insufficient.<sup>82</sup> It has become clear that relying on the current antimicrobial arsenal to react to EIDs is inadequate. With the exception of post-exposure prophylaxis, this is predominantly a treatment strategy for those who have already developed disease. Preventing acquisition of infection or disease is preferable to treatment to avert potential disaster situations. There have been successes with preventive mechanisms, such as vaccines to specific infectious disease agents; however, the diversity of EIDs and the potential for microbial adaptation and change precludes using current strategies against all known pathogens, and especially for still undiscovered or yet-to-emerge agents.

The emergence of infectious diseases, largely fueled by human practices, poses worldwide disaster threats. Immediate needs to expand the local and global public health infrastructure and workforce are obvious. The ultimate future of infectious disease disaster management rests on improving two broad but interrelated areas:

1. Preparedness strategies that surpass the usual unresolved obstacles by promoting multidisciplinary program design, and by substantiating early surveillance/detection and prevention of disease;
2. Research into novel countermeasure development, host-microbe relationships, host-immune responses, surveillance tools, and analysis of how behaviors of the human host and perturbations of the environment (whether at the macro- or micro-molecular level) affect infectious disease emergence. These essentially encompass a fresh perspective reevaluation of the approach regarding the understanding of the epidemiology of infectious diseases.

### Preparedness

#### *Preparedness Strategies*

Repeated drills are used to determine areas for preparedness plan improvements; however, the usefulness of drills diminishes when identified obstacles are not addressed. Areas consistently identified for further improvement include resource allocation, communication between response stakeholders, and understanding of governmental roles. Current templates for planning need modification to first address why these “lessons learned” are not, or cannot be, actually implemented. This necessitates

the study of the barriers to implementation of findings from previous drills and disasters by multidisciplinary teams that include social scientists, communications experts, and human factors specialists. Ultimately, drills should be used as a rehearsal tool for workforce training (i.e., to identify improvement goals on an individual basis), not as a mechanism for developing preparedness plans.

### ***EID Surveillance***

Although improved response preparedness is reassuring, preventing disease transmission will do much to reduce the dependence on limited resources and other preparedness obstacles. EID management needs to be changed beyond the state of relying on disease treatment when cases appear at the hospital doors. In essence, it must move from the conventional reactionary EID response to a more proactive approach.<sup>83</sup> Improving early EID detection can reduce the “incident threshold” and expedite agent characterization, assessment of response needs, and education of the public. This must be a global effort. Although new agents can emerge from any area, developing countries bear the burden of global infectious disease incidence and the likelihood of witnessing the development of new pathogens. The developed world has a responsibility to provide assistance in surveillance for both humanitarian reasons and the need for self-protection. Great strides have been made in global surveillance of human infectious diseases, especially after the infectious disease events of the new millennium and efforts to comply with IHR, but there are still political, social, and economic obstacles to further advancement.

As discussed, non-human sources of microbes can lead to emergence of human infectious diseases. A research need exists to broaden and strengthen surveillance beyond human symptom and disease reports. Past evidence shows that understanding animal infectious disease trends can benefit human health. Linking animal disease surveillance (including zoological, agricultural, and wild and companion animals) with human disease surveillance clearinghouses can potentially alert public health officials sooner to possible human infectious disease disasters, whether global in nature or constrained to a small location. The specificities of such tactics are complicated, given the current inconsistencies in animal disease surveillance and reporting and the unproven value of many human disease surveillance systems.

## **Research**

### ***Basic Research***

The understanding of pathogens has been transformed by genomics and proteomics, fields of molecular biology that study the overall functions and regulation of the genes and proteins of an organism in an environment. These technologies allow scientists to identify disease-causing agents and comprehensively characterize microbial pathogenic mechanisms in a fraction of the time needed in previous decades. Future efforts must include the development of technologies to translate this knowledge into functional applications such as rapid screening of people and/or animals during an EID disaster, the development of sensitive handheld devices for remote screening applications, and more rapid determination of antimicrobial resistances and application of therapies.

For effective EID management, other areas of basic research must be enhanced to complement the more common agent-specific programs. Namely, there is a need to expand research

on diverse biological disciplines associated with zoonotic and vector-borne diseases, such as reservoir ecology and entomology. Ideally, these specialties would be housed in interdisciplinary academic EID departments that include infectious diseases, molecular biology, and veterinary and conservation medicine experts to foster a collaborative atmosphere that has been increasingly referred to as a “One Health” approach to understanding disease emergence.

### ***Drug and Vaccine Development***

Improved pharmaceuticals alone will not be adequate to change the burden of EIDs on society, but they have an important role in mitigating disease severity, human suffering, and infectious agent transmission. The need and incentives for antimicrobial drug development has already been outlined. The future lies in the discovery of novel targets and mechanisms active against a broad spectrum of agents. This requires a more comprehensive understanding of host–pathogen relationships: how the host recognizes an invading pathogen, how pathogens evade host defenses, how hosts and microbes interact in nonpathogenic relationships (symbiosis), and how host–immune responses to pathogens can be modulated by drugs or by beneficial bacteria.

Revolutionary advances in understanding cellular immunology, structural biology, nanotechnology, diagnostics and monitoring, and bioinformatics have all contributed to the field of vaccine development. Scientists are on the brink of unlocking the secrets of improving vaccine efficacy by targeting both the innate and adaptive immune response.<sup>84</sup> DNA vaccines hold promise as future EID countermeasures because they can be designed and manufactured relatively rapidly, they can induce cross-strain immunity, and they can be administered by different routes.<sup>85</sup> As the basic sciences continue to inform the understanding of human and microbial biological processes, progress must be made in moving these advances to novel vaccine design and product development that result in effective vaccines. Thus far, such progress has been slow and effective vaccines against some long-studied, and globally-relevant, pathogens (e.g., HIV, *Plasmodium falciparum*) remain elusive. Further understanding of vaccine-induced protective immune responses in humans and immune evasion mechanisms in microbes is needed to accelerate next-generation vaccine development.<sup>86</sup>

The international community must take a more collaborative approach to drug and vaccine design for EIDs. Nowhere is this more evident than in the case of pandemic influenza vaccine. Current production capabilities may limit the number of courses available during an infectious disease disaster. Scientific research is necessary to: 1) develop rapid in vitro methods for vaccine component production; 2) increase vaccine efficacy at lower doses; 3) investigate less-specific vaccines that can be made and stockpiled prior to a pandemic; and 4) increase the shelf-life of vaccines. Advances in all four of these areas can benefit both influenza pandemic preparedness and vaccinology in general. WHO has convened meetings with international stakeholders to formulate plans for increasing the international production capacity of influenza vaccine. Such plans will need to address international differences in complicated issues such as production regulations, acceptable clinical safety data, and intellectual property.

In 2010, the Infectious Diseases Society of America (IDSA) called for a global commitment to antibiotic development; the “10 x 20 Initiative” challenges the development of ten new antibiotics by 2020.<sup>87</sup> Essential to the success of the initiative is a global

approach that builds on international capabilities to foster an ongoing research and development infrastructure. In the European Union, the Innovative Medicine Initiative launched its New Drugs for Bad Bugs (ND4BB) core element in the sixth call for proposals in May 2012, and subsequent calls for proposals have also included topics that address antimicrobial development.<sup>88</sup> Despite the heightened attention given to antimicrobial research and development by key groups, it is not yet clear whether this high-level attention has yielded results. An update report from IDSA in 2013<sup>89</sup> deemed progress to be “alarmingly elusive,” suggesting that efforts thus far to spur global innovation, funding, and regulatory progress have been largely unsuccessful. What more, then, is necessary? So and colleagues<sup>90</sup> suggest that the public-private dynamic important for fostering innovative antimicrobial development would be advanced by mechanisms and priorities that promote the sharing of the “3Rs”: Resources (e.g., sharing of data from pharmaceutical companies that would not provide a competitive advantage), Risks (e.g., public funding for research that would share the risks with private companies), and Rewards (e.g., product development partnerships).

### **EID Surveillance Research**

A more expansive approach to surveillance that encompasses monitoring beyond human and animal health is under investigation. Sometimes termed “conservation medicine,” it utilizes interdisciplinary networks that examine the ecology of microbial interactions with animals, plants, and humans in the context of the drivers of disease emergence.<sup>91</sup> These networks should include the expertise of health workers, veterinarians, plant biologists, epidemiologists, ecologists, climatologists, and conservation biologists. Environmental specialists and global geologists must be involved in such endeavors to ensure inclusion of environmental aspects that may affect EIDs. Computational and theoretical biologists, and epidemiologists with expertise in transmission, host–agent interaction, host–environment interaction, and agent–environment interaction, need to develop cooperative research programs among themselves and with other specialists. The goal of such collaboration is to produce, and more importantly, validate, predictive models of disease occurrence. This holistic approach to surveillance is exemplified by geographical information systems that integrate infectious disease incidence, prevalence, and distribution data with satellite environmental data to predict disease emergence in other locations with similar conditions.<sup>92</sup>

The ultimate goal is the capability to predict human EIDs before they occur, or at least to detect an emergence earlier. These types of broad surveillance tools that include environmental components have been used for years by plant biologists to predict disease emergence in agricultural crops. The basic epidemiological triangle of host, agent, and environmental interactions described earlier in this chapter was officially conceptualized decades ago by plant biologists.<sup>93</sup> The link between environmental factors and plant diseases may be obvious, but the time is overdue to integrate this same approach into understanding human infectious diseases.

That said, in addition to improving methods for achieving better surveillance, *what* is monitored needs further assessment. The perceived pressing need for surveillance systems, especially in the United States after the 2001 terrorist attacks, has resulted in much research, development, and implementation of such systems using a variety of data and information, often incorporated due to availability. The general, albeit likely unintentional,

assumption has been that such systematic analysis of “any” data and information will be useful and an improvement over a surveillance system vacuum. Now, over a decade later, it becomes clear that the field would benefit from the comprehensive study and development of mechanisms to assess whether or not data sources are relevant for the purposes of biosurveillance systems (early detection and situational awareness of outbreaks). Research is also needed to assess and advance the often-cited but heretofore largely unrealized capability to integrate information from different surveillance systems and efforts to provide a more comprehensive picture. Significant obstacles include lack of common architecture among systems, inability or unwillingness for entities to share systems or data, sustainment of efforts and collaborations, and lack of priority.

Finally, the EID surveillance field needs further research on analysis and interpretation of results. Ultimately, the goal of using surveillance tools is to provide information in “near real-time” to decision-makers regarding a disease emergence or progression of an outbreak. However, the expectation of timely information may not allow for the rigorous assessment that information providers would like to conduct before conveying results that may be used for actions. The ability to quantify, with some reliability, the confidence in the information will provide decision-makers valuable data when determining response activities.

Infectious disease disaster medicine is itself a growing field and has been the focus of extensive preparedness efforts. Further research on the impact of politics, international relations, social behavior, and public health policies on EID disaster management is warranted to develop sound and realistic action plans. As noted throughout the chapter, this multidisciplinary focus of effort toward the fields of infectious disease biology and epidemiology is a nascent application that holds promise for the future of both infectious diseases and disaster medicine.

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