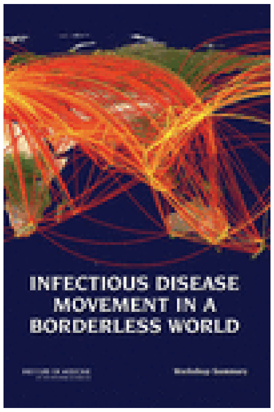


**Infectious Disease Movement in a Borderless World: Workshop Summary**

David A. Relman, Eileen R. Choffnes, and Alison Mack, Rapporteurs; Forum on Microbial Threats; Institute of Medicine

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# INFECTIOUS DISEASE MOVEMENT IN A BORDERLESS WORLD

## Workshop Summary

*Rapporteurs:* David A. Relman, Eileen R. Choffnes, and Alison Mack

Forum on Microbial Threats

Board on Global Health

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The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

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Willing is not enough; we must do."*
—Goethe

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# Reviewers

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

**Peter Daszak,** Wildlife Trust
**Lawrence O. Gostin,** Georgetown University Law Center
**William B. Karesh,** Wildlife Conservation Society
**Howard Markel,** University of Michigan Medical School
**Kevin Russell,** Department of Defense, Global Emerging Infections System

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the final draft of the report before its release. The review of this report was overseen by **Dr. Melvin Worth**. Appointed by the Institute of Medicine, he was responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.



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# Acknowledgments

The Forum on Emerging Infections was created by the Institute of Medicine (IOM) in 1996 in response to a request from the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH). The purpose of the Forum is to provide structured opportunities for leaders from government, academia, and industry to meet and examine issues of shared concern regarding research, prevention, detection, and management of emerging or reemerging infectious diseases. In pursuing this task, the Forum provides a venue to foster the exchange of information and ideas, identify areas in need of greater attention, clarify policy issues by enhancing knowledge and identifying points of agreement, and inform decision makers about science and policy issues. The Forum seeks to illuminate issues rather than resolve them; for this reason, it does not provide advice or recommendations on any specific policy initiative pending before any agency or organization. Its value derives instead from the diversity of its membership and from the contributions that individual members make throughout the activities of the Forum. In September 2003, the Forum changed its name to the Forum on Microbial Threats.

The Forum on Microbial Threats, and the IOM, wishes to express their warmest appreciation to the individuals and organizations who gave their valuable time to provide information and advice to the Forum through their participation in this workshop. A full list of presenters may be found in Appendix A.

The Forum is indebted to the IOM staff who contributed during the course of the workshop and the production of this workshop summary. On behalf of the Forum, we gratefully acknowledge the efforts led by Dr. Eileen Choffnes, director of the Forum; Kate Skoczdopole, senior program associate; Sarah Bronko, research associate; K. C. Ostapkovich, research associate; Kenisha Peters, senior



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## BOXES



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# Workshop Overview[1]

## INFECTIOUS DISEASE MOVEMENT IN A BORDERLESS WORLD

> *Infectious disease is a kind of natural mortar binding one creature to another, one species to another, within the elaborate edifices we call ecosystems.*
>
> David Quammen (2007)

The advance of human civilization has brought people, plants, animals, and microbes together in otherwise improbable combinations and locations. While such biological introductions were once rare occurrences, human actions have all but eliminated the spatial and temporal barriers between species and ecosystems (Carlton, 2004). The profound consequences of human-mediated biological introductions include emerging infectious diseases: those caused by pathogens that have increased in incidence, geographic or host range; or that have altered capabilities for pathogenesis; or that have newly evolved; or that have been discovered or newly recognized (Anderson et al., 2004; Daszak et al., 2000; IOM, 1992).

Today, international travel and commerce (most notably the explosive growth of commercial air transportation over the past 50 years) drives the rapid, global distribution of microbial pathogens and the organisms that harbor them (IOM, 2003). These include humans, whose movements have been implicated in the

[1]The Forum's role was limited to planning the workshop, and this workshop summary has been prepared by the workshop rapporteurs as a factual summary of what occurred at the workshop.



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spread of diseases, including influenza (IOM, 2005); severe acute respiratory syndrome (SARS; IOM, 2004); drug-resistant malaria (IOM, 2003; Martens and Hall, 2000); and chikungunya[2] in Europe (Angelini et al., 2007). Indeed, it is possible to travel between most places in the world in less time than the incubation period for many infectious diseases (Wilson, 2003), as was illustrated in spring 2009 by the rapid, global spread of the new, swine origin, influenza A (H1N1) virus (Dawood et al., 2009; Khan et al., 2009).

Travel is not only becoming increasingly rapid and more socially widespread, but is also more ubiquitous. Travelers and tourists connect once-remote areas, which serve as both "sources" and "sinks" for emerging infectious diseases, to more developed regions. International trade in food and other agricultural commodities, as well as in wildlife, has also increased markedly among an ever-widening network of producers and markets. Pathogens accompany live animals, plants, and their byproducts across continents and oceans; microbes and vectors also hitch rides in ballast water[3] and in shipping crates and containers. Upon arrival in industrialized countries, such as the United States, potentially disease-containing goods can be redistributed nationwide within hours.

Travel and trade have been linked with disease since antiquity. People instinctively feared and isolated ill travelers long before the causative agents of infectious diseases were known or described (Gushulak and MacPherson, 2000). Quarantine laws, established to prevent the importation of plague—without success—in fourteenth-century Venice, were eventually adopted throughout Europe and Asia (Fidler et al., 2007; Markel et al., 2007).

International endeavors to contain infectious diseases commenced more than 150 years ago and are today embodied in the International Health Regulations (IHR), which provide the legal framework for global cooperation on infectious disease surveillance (IOM, 2007; Stern and Markel, 2004). While ideally there are strong incentives for nations to support global efforts to address infectious disease threats, such efforts have from their outset been characterized by a lack of authority for enforcement and weak inducements for participation (Stern and Markel, 2004).

More subtly, but no less importantly, introduced animals, plants, and microbes can disrupt ecosystems in ways that increase the potential for infectious disease outbreaks. Such changes can be more difficult to predict than the movements of pathogens, and more daunting to prevent. The term "invasive species" is widely used to describe plants and animals that spread aggressively when introduced to and established in new environments freed from the constraints found in their native environments (Dybas, 2004). Given both the similarities and characteristics of such invasions with those of pathogenic microbes, it may prove fruitful to view the origins of disease emergence, establishment, and spread through the

[2] A mosquito-borne viral disease.
[3] Water that is loaded and unloaded to balance cargo weight in ships.

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larger ecological lens of invasive species, and consider intervention strategies and approaches aimed at preventing and mitigating the far-reaching consequences of biological invasions.

On December 16 and 17, 2008, the Institute of Medicine's (IOM's) Forum on Microbial Threats hosted a two-day public workshop in Washington, DC, on Globalization, Movement of Pathogens (and their hosts), and the revised IHRs. Through invited presentations and discussions, participants explored a variety of interrelated topics associated with global infectious disease emergence, detection, and surveillance including the historical role of human migration and mobility in pathogen and vector movements; the complex interrelationship of travel, trade, tourism, and infectious disease emergence; national and international biosecurity policies; and obstacles and opportunities for detecting and containing globalized pathogens, thereby reducing the potential burden of emerging infectious diseases.

## Organization of the Workshop Summary

This workshop summary was prepared for the Forum membership in the name of the rapporteurs and includes a collection of individually authored papers and commentary. Sections of the workshop summary not specifically attributed to an individual reflect the views of the rapporteurs and not those of the Forum on Microbial Threats, its sponsors, or the Institute of Medicine. The contents of the unattributed sections are based on the presentations and discussions at the workshop.

The workshop summary is organized into chapters as a topic-by-topic description of the presentations and discussions that took place at the workshop. Its purpose is to present lessons from relevant experience, to delineate a range of pivotal issues and their respective problems, and to offer potential responses as discussed and described by the workshop participants.

Although this workshop summary provides an account of the individual presentations, it also reflects an important aspect of the Forum philosophy. The workshop functions as a dialogue among representatives from different sectors and allows them to present their beliefs about which areas may merit further attention. The reader should be aware, however, that the material presented herein expresses the views and opinions of the individuals participating in the workshop and not the deliberations and conclusions of a formally constituted IOM consensus study committee. These proceedings summarize only the statements of participants in the workshop and are not intended to be an exhaustive exploration of the subject matter or a representation of consensus evaluation.

## Globalization: Processes, Patterns, and Impacts

The inexorable migration of the human species has profoundly influenced Earth's ecology. As our ancestors wandered across the African continent, onward

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**BOX WO-1**
**Factors Involved in Infectious Disease Emergence**

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

SOURCE: Reprinted from *Lancet Infectious Diseases*, Morens et al. (2008), with permission from Elsevier.

to Asia, Australia, Europe, and eventually to the Americas, as we explored the ends of the Earth and beyond the confines of this planet, the vast entourage of animals, plants, and microbes that have accompanied us on our journeys has only amplified the impact of our species on every ecosystem that we have encountered.

Among these "fellow travelers," pathogens have flourished in new surroundings, while other microbes have colonized incoming migrant host species. Such introductions, abetted by additional genetic, biological, social, and political factors associated with infectious disease emergence (see Box WO-1), have given rise to epidemics throughout recorded history (IOM, 2003; Morens et al., 2008). The current era of "globalization" affords frequent and widespread opportunities for disease emergence, several of which are described in detail in later sections of this overview. This section summarizes two presentations that opened the workshop by exploring the history and ongoing political and public health significance of human migration and mobility.

*Human Migration: Past, Present, and Future*

In his overview of the history of human migrations, speaker Mark Miller, a professor of comparative politics at the University of Delaware, emphasized migration's growing political importance (see Miller in Chapter 1). Considering

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the present status of global migration as an indicator of future trends, he observed that, "increasingly, the questions of peace and war revolve around migration."

Highlights of Miller's whirlwind tour of historic migrations included the fourth-century convergence of a "crazy quilt" of ethic groups to establish the country we now call France; the movement of Celts and Jews into Europe; the travels of Vikings throughout the North Atlantic; and the eastward migration of Germans, counter to other population flows across Europe. He noted that between 8000 B.C.E. and the seventeenth century, four civilizations achieved "a rough kind of equilibrium" on the Eurasian steppe: one was derived from Greece and Europe, one was of Middle Eastern origin, another was Indian, and the last was Chinese.

Following that era, Miller noted, Europeans migrated to the Americas driven by several factors, including:

- A population explosion in Europe,
- Development of resistance to diseases of the New World,
- The advent of capitalism, and
- The availability of affordable long distance travel.

Despite the fact that this influx of Eastern Europeans at the end of the nineteenth and beginning of the twentieth centuries led to the emergence of the United States as a world power, American suspicion of the "foreign born" greatly restricted immigration between World War I and the 1960s.[4,5]

A "new age of migration" began in the 1970s, when longstanding migration patterns reversed, rendering Europe a destination for immigrants. Concurrently, Latin America became a net source of new migrants to the United States, and immigration from Asia and Africa also increased. Today, as a result of what Miller called the single most important relationship in the New Age of Migration, approximately 10 percent of Mexico's population resides in the United States, and Mexicans comprise about 5 percent of the U.S. workforce. These circumstances are "emblematic of the increasing impact of migration around the globe," he concluded.

Miller predicted that as the global population grows unevenly—faster in developing countries, more slowly and even negatively in developed countries—migration will increase (see also Gushulak and MacPherson in Chapter 1). "Thirty years ago there were two Europeans for every African," he noted, citing United

[4]The first major wave of immigration to the United States, between 1820 and 1860, largely involved English, Scotch, Irish, and Germans. The second wave included eastern Europeans (which encompasses many different ethnic groups including Russian and Polish Jews, people from the Balkans, and southern Italians), and in much smaller numbers Chinese, Korean, and Japanese, as well as Mexicans from the south.

[5]The passage of the quota systems described in the Immigration Act (Johnson-Reed Act, 43 Statutes-at-Large 153) was in 1924; it was rescinded by the Immigration and Nationality Act (Hart-Cellar Act, P.L. 89-236) of 1965.

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Nations population estimates. "Today there are about equal numbers of Africans and Europeans. In 30 years, there will be twice as many Africans as Europeans." These differences are likely to produce a world of regions that differ greatly from each other, he continued, with "fundamental differences separating the rich countries from the poor countries."

*Population Mobility and Public Health*

While migration issues have become increasingly salient in politics and diplomacy, Miller observed that relatively little attention has been paid to the relationship between migration and health.[6] Yet as speaker Brian Gushulak, of the Canadian Immigration Department Health Branch, explained, this link is becoming increasingly crucial, as the widening economic gap separating countries and regions both contributes to, and results from, health disparities.

"It is possible to look at migration and population mobility as a metaphor for the evolution of public health and public health security," Gushulak remarked, as he traced the history of public health through the various means advanced against introduced diseases (see Gushulak and MacPherson in Chapter 1). Echoing Miller's conclusion that we have reached a new age of unprecedented migration, Gushulak noted that in the mid-1990s, approximately 200 million people—a population exceeding that of all except the worlds' four largest nations—fit the United Nation's definition of "migrant."

Several major changes to immigration ushered in the current era:

- Post-colonial population flows;
- Refugee movements and displacements associated with humanitarian emergencies and conflicts;
- The development of the concept of human capital and employment of international temporary workers; and
- The increasing ease and declining cost of international transportation.

Together, these factors have produced unprecedented demographic changes in receiving countries, rendering disease control processes and policies based on historical patterns of migration irrelevant, according to Gushulak. "We simply can't keep up on a policy level as fast as the ground is changing underneath our feet," he said.

Modern human movements and migration practices have also become increasingly difficult to characterize, due to the diverse origins of migrants,

[6]There is a wealth of medical historical literature on the topic. See Fairchild (2003), Kraut (1995), and Markel (1997, 2004). There have also been dozens of immigrant health articles in the *Journal of the American Medical Association*, *New England Journal of Medicine*, and other prominent medical journals in the recent past, including recent outbreaks of cholera among migrants.

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their often complex journeys, the variety of their experiences upon arrival and resettlement, and the frequency with which many migrants return to their countries of origins for varying lengths of time. Moreover, in addition to migration in the traditional sense (the one-way movement of people from one homeland to another), nonmigratory human travel and trade[7] provide pathogens with a wealth of possibilities for relocation. Gushulak employed the more encompassing term "mobility" to describe this collection of processes, all of which contribute to the phenomenon of globalization.

Since pathogens readily cross geopolitical borders, only "functional disease-based borders" matter, Gushulak argued. These boundaries occur between regions that differ not only in terms of disease epidemiology, but also reflect general health disparities due to socioeconomic factors such as poverty, education, housing, nutrition, and access to care (see Figure WO-1). Mobile people (as well as animals and plants) serve as biological bridges between such disparate regions, thwarting attempts to confine infectious diseases within—or exclude them from—national borders. Controlling the spread of infectious diseases across such functional borders will require international cooperation in surveillance and reporting, Gushulak concluded, and mitigation or intervention strategies that focus on mobility as a determinant of global public health, rather than on the containment of specific diseases.

## Travel, Conflict, Trade, and Disease

In discussions that focused on the rapid acceleration and expansion of international travel and trade as a catalyst of pathogen movements, workshop participants considered various ways in which the movement of people and goods influences the transmission dynamics of infectious diseases, and how these influences might be better understood in order to reduce the global burden of emerging infectious disease. Workshop presentations examined the role of the traveler as a sentinel—as well as a vector—for disease; the role of armed conflict in increasing infectious disease risks; the complex and multifaceted relationship between trade and disease; and the numerous and diverse risks associated with a globalized food supply.

### *Traveling Pathogens*

Figures WO-2, WO-3, and WO-4 provide graphic illustrations of the current state of global connectivity afforded by planes and ships (as well as cars, trucks, and trains) that transport infected travelers, goods, and disease vectors rapidly across vast distances. They also allow adventurous travelers to enter new

[7]Including the exchange of animal- and plant-based items such as bush meat and homeopathic medicines between migrants and family members or friends residing in their country of origin.

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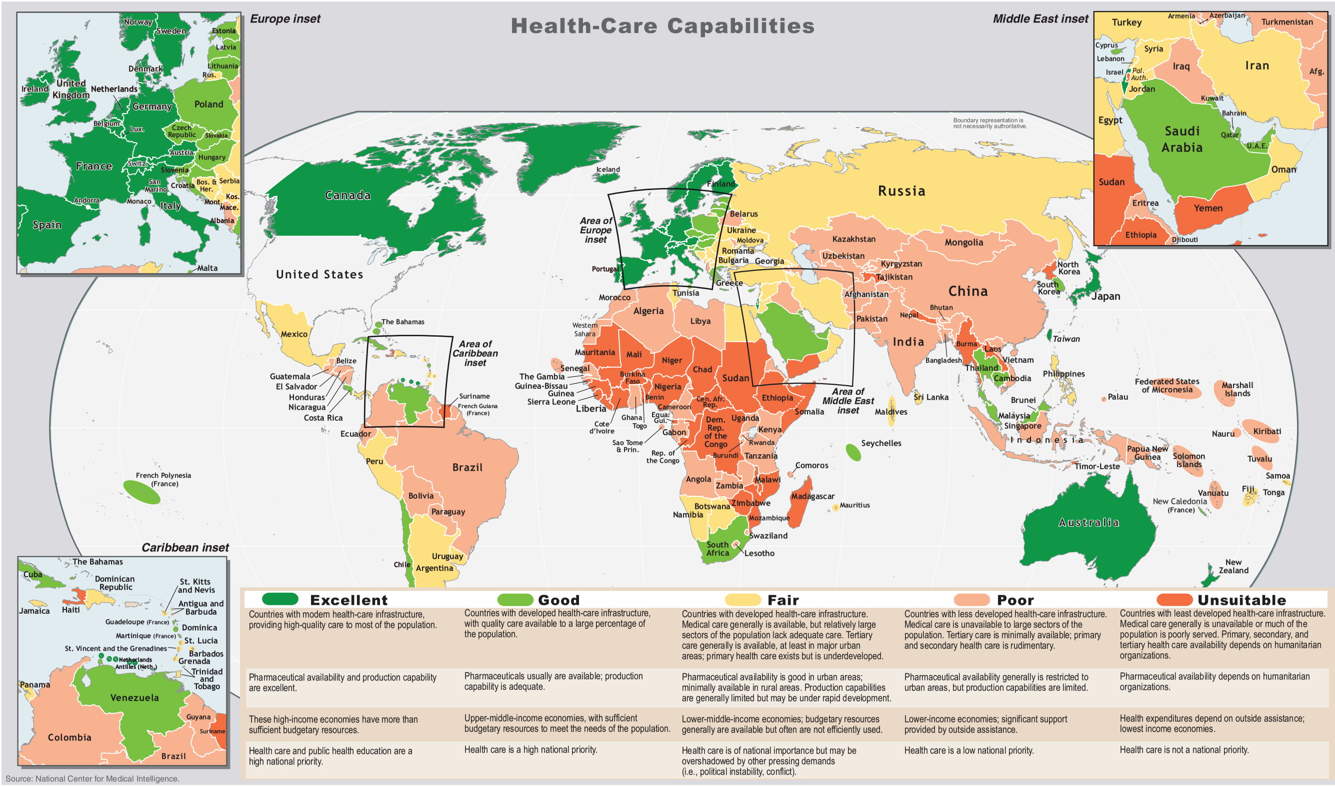


**FIGURE WO-1** Typology of countries by health care status.
SOURCE: NIC (2008b).

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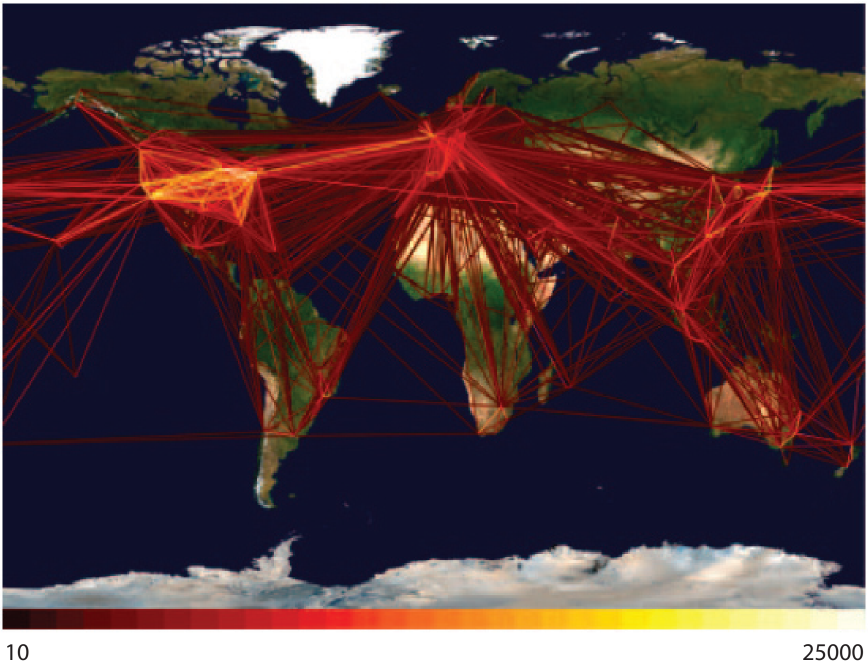


**FIGURE WO-2** The rate of globalization has accelerated to the point where we are connected as never before via globalized travel and trade networks.
SOURCE: Reprinted with permission from Hufnagel et al. (2004).

ecosystems and pick up new pathogens, which may then return with the traveler to a new environment and, under appropriate circumstances, persist and spread through new host populations.

The mobility of the global biota is one among many interacting factors that contribute to infectious disease emergence: growing populations of humans and food animals living in increasingly close proximity to each other, climate change and extreme weather events, and changes in land use (IOM, 2003). This upheaval occurs against a backdrop of microbial evolution, remarked Mary Wilson of Harvard University, whose presentation explored the influence of human travel on the geography of infectious diseases, as well as the role of the traveler as a disease sentinel (see Wilson in Chapter 2). She noted that, in addition to enabling pathogens to span vast distances through direct transmission, travel also introduces antimicrobial resistance genes to new populations.

Some pathogens spread quickly upon introduction to a new environment, while others do not survive the transition for lack of an appropriate environment, vector, or host, Wilson observed. Introduced pathogens may meet with vulnerable

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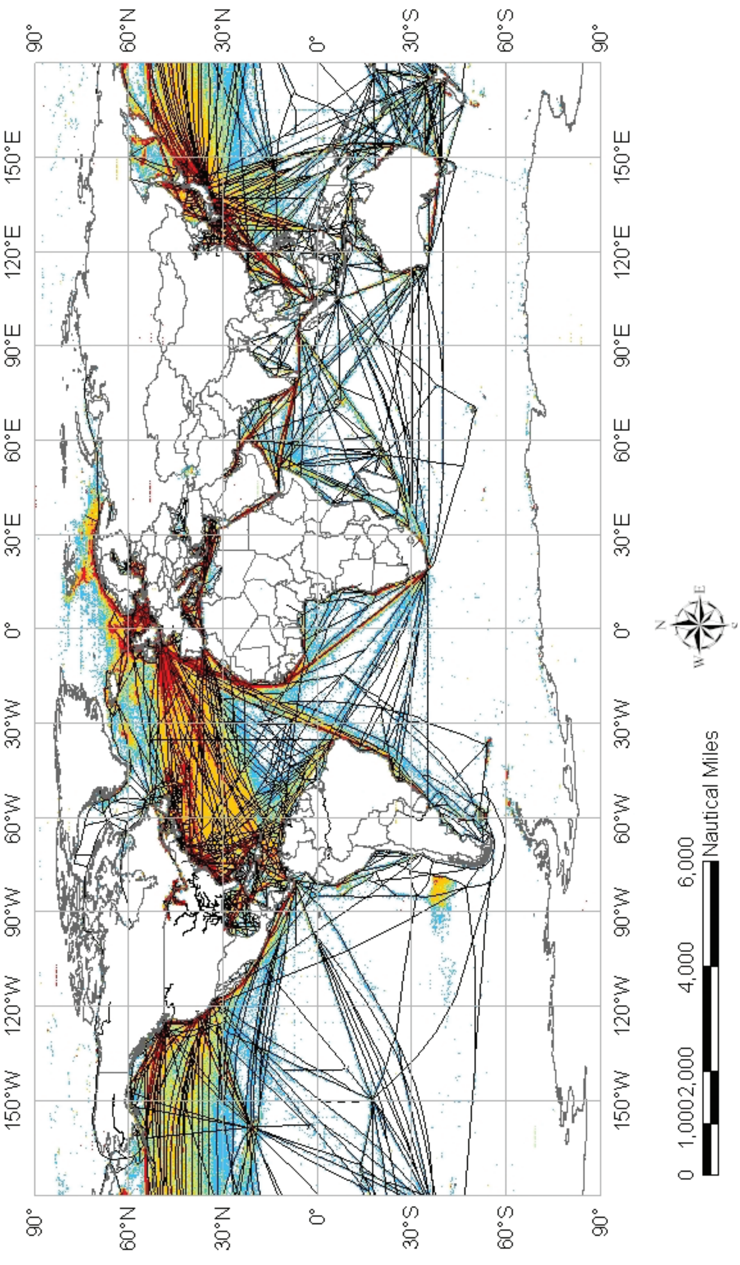


**FIGURE WO-3** World waterways network.
SOURCE: Figure derived from the Ship Traffic, Energy, and Environment Model (STEEM) developed at the University of Delaware (Wang, 2006; Wang et al., 2007).

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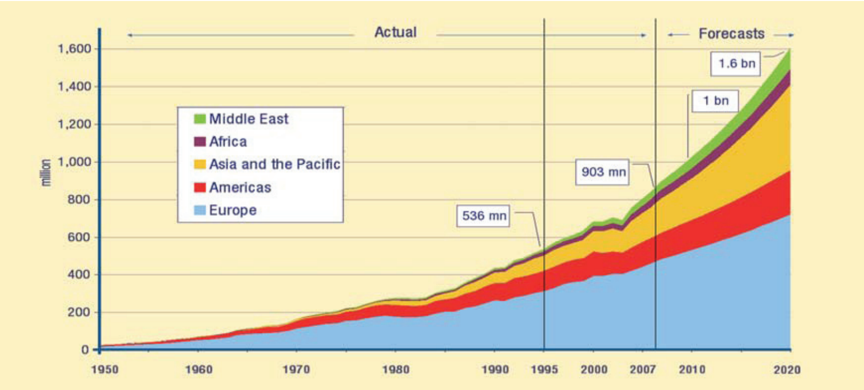


**FIGURE WO-4** International tourist arrivals by region (in millions), 1950-2020.
SOURCE: Reprinted with permission from the UNWTO (2008).

hosts—for example, people with low levels of immunity to the pathogen, or those who live in a community with poor housing, water quality, and sanitation—or with resilient ones. If an introduced pathogen produces an epidemic, it may or may not be easy to control. The ease with which spread of infection can be interrupted is determined, to a large extent, by the proportion of transmission that occurs before the onset of symptoms or during asymptomatic infection (Fraser et al., 2004). For this reason, Wilson explained, SARS was relatively easy to control, while HIV/AIDS continues to spread, unabated, as a "silent" pandemic.[8]

Vector-borne pathogens can travel with relative ease in the blood of viremic hosts, such as human travelers, and upon introduction to a new environment with competent vectors, spread quickly through a new host population, Wilson said. This scenario appears to have occurred in the recent emergence of chikungunya fever in new geographic areas and the expanding distribution of dengue viruses in tropical and subtropical areas. A recent study of trends in emerging infectious diseases finds that emergent events involving vector-borne diseases are occurring with increasing frequency (Figure WO-5; Jones et al., 2008).

*Travelers as Sentinels*

Travelers represent an important sentinel population for disease emergence, according to Wilson, who added that several surveillance networks have been developed to monitor infectious diseases in travelers. She is involved in the decade-old

[8]AIDS is thought of as a "silent pandemic" because the symptoms of illness are not readily apparent until the "end stage" of illness.

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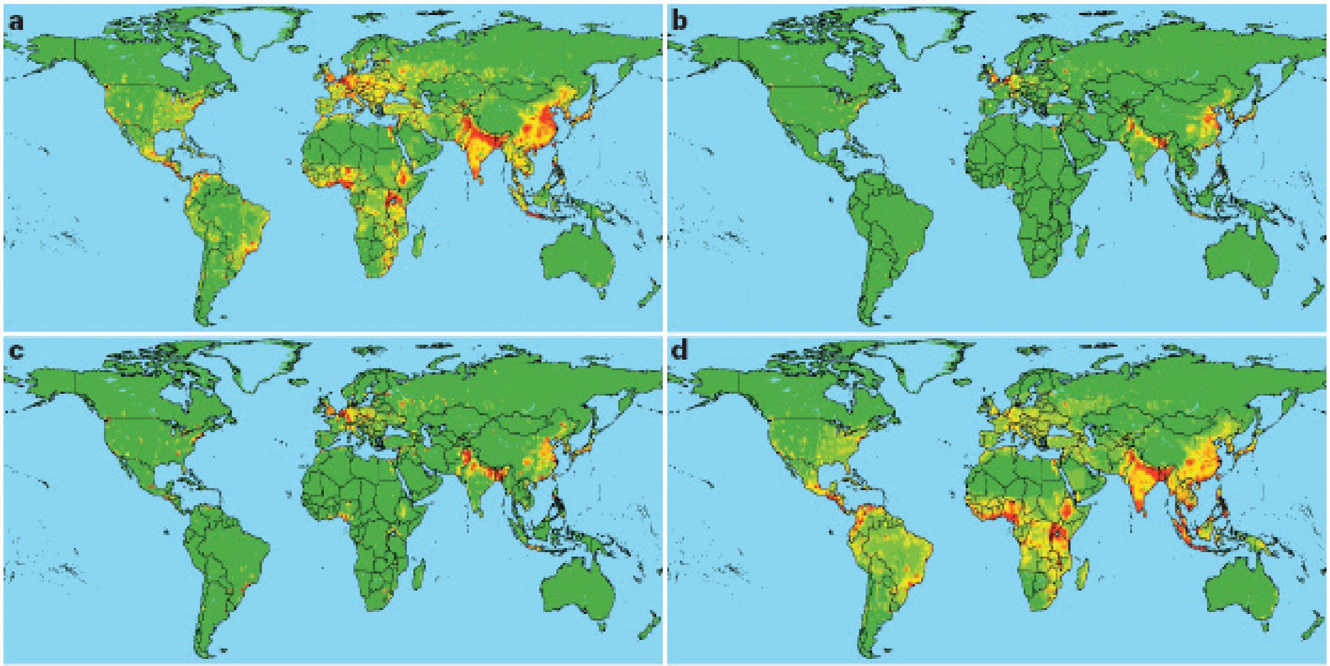


**FIGURE WO-5** Global distribution of relative risk of an emerging infectious disease (EID) event. Maps are derived for EID events caused by (a) zoonotic pathogens from wildlife, (b) zoonotic pathogens from nonwildlife, (c) drug-resistant pathogens, and (d) vector-borne pathogens.
SOURCE: Reprinted from Jones et al. (2008) with permission from Macmillan Publishers Ltd. Copyright 2008.

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GeoSentinel Surveillance Network, which gathers information on ill international travelers and migrants from 42 travel and tropical medicine clinics on six continents, in order to provide early alerts about unusual infections or infections in unusual locations or populations. Much as Gushulak (see previous section and Gushulak and MacPherson in Chapter 1) noted that contemporary human migrations may be complicated by return visits and exchanges of goods, Wilson recognized that travel frequently consists of multiple stages, each of which—including time in transit—has potential significance to infectious disease transmission. And like Gushulak, Wilson emphasized dramatic differences in the incidences of many infectious diseases (Gushulak referred to these differences as "functional disease-based borders") between countries and regions. For example, Wilson said, tuberculosis incidence differs by more than 100-fold between some areas of the world. "If we are regularly traveling from one area to another, it becomes very easy to share some of these [infectious diseases]," she observed. Controlling them will require looking beyond local outbreaks to regional and global patterns of transmission, she concluded.

### *Armed Conflict and Infectious Disease*

In wars and other armed conflicts, public health is compromised, increasing the burden of illness, disability, and death. Studies of mortality during the recent civil war in the Democratic Republic of the Congo found that most deaths during that war were due to the breakdown of health-supporting infrastructure of society, including medical care, supply of safe food and water, sanitation and sewage systems, power generation, transportation, and communication (Coghlan et al., 2007; Van Herp et al., 2003).

Certain categories of infectious diseases tend to increase during war, according to speaker Barry Levy of Tufts University, including diarrheal diseases, acute respiratory infections, and tuberculosis (see Levy in Chapter 2). He described the following major causes of wartime infectious diseases:

- Adverse effects on medical care and public health services,
- Damage to the health-supporting infrastructure and the environment,
- Forced migration, and
- Diversion of resources from health care and health-supporting services.

Measures can be implemented to reduce the frequency of infectious disease during armed conflict. The elimination of infectious disease during armed conflict, however, will require the elimination of armed conflict—the creation of a world without war.

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*Trading Pathogens*

Like travel, globalized trade is vast, rapid, increasing, and a significant risk factor for infectious disease emergence. In her book *Risky Trade: Infectious Disease in the Era of Global Trade* (2006), speaker Ann Marie Kimball, of the University of Washington, concluded that "market forces in the globalized world are misaligned for microbial safety." Using examples of diseases including avian influenza, the use of antibiotics in farm animals, and the growing practice of xenotransplantation,[9] she demonstrated the profound influence of trade on infectious disease emergence, and vice versa (see Kimball and Hodges in Chapter 2).

**Poultry production and H5N1 influenza** The rapid expansion of intensive poultry farming[10] in Asia, shown in Figure WO-6, immediately preceded the H5N1 outbreak of 2003, which Kimball characterized as an "ecological tipping point," as well as an economic disaster. Based on this experience, she remarked, "one could question, and certainly should carefully research, whether intensive poultry agriculture is actually safe at all."

On the other hand, Forum member Michael Osterholm, of the University of Minnesota, argued that in his experience "the best and the safest poultry production in the world right now is occurring in . . . very large facilities, where biosecurity is actually very high." In India, 70 percent of all poultry is produced by a single company, which has high standards for biosecurity and an excellent safety record, he asserted. "Our experience, in Asia in particular, has been that all the H5N1, and even the low-pathogenicity [influenza] viruses, have . . . [been limited to] backyard range production." This is also true in the United States, Osterholm continued. Migratory birds bring in most influenza viruses, and "we see very, very, very little influenza virus activity in our poultry production, where we have high biosecurity [as] required in large facilities."[11]

Kimball responded that, while replacing backyard poultry farming with industrialized poultry production in impoverished areas of Asia might lead to gains in biosecurity, it would compromise the access of poor people to poultry protein because the pricing of poultry from industry is unaffordable compared to the gate price of backyard poultry.

Therefore, she said, she would prefer to better understand how the introduction of intensive poultry facilities into areas with backyard farms contributed to the emergence of H5N1 in humans, and thereby mitigate future risks. Osterholm

[9]Any procedure that involves the transplantation, implantation, or infusion into a human recipient of either (a) live cells, tissues, or organs from a nonhuman animal source, or (b) human body fluids, cells, tissues, or organs that have had *ex vivo* contact with live nonhuman animal cells, tissues, or organs (FDA, 2009).

[10]Intensive farming is a system of raising crops and animals, usually on small parcels of land, where a comparatively large amount of production inputs or labor are used per acre (USDA, 2009).

[11]This assertion is contradicted by Graham et al. (2008).

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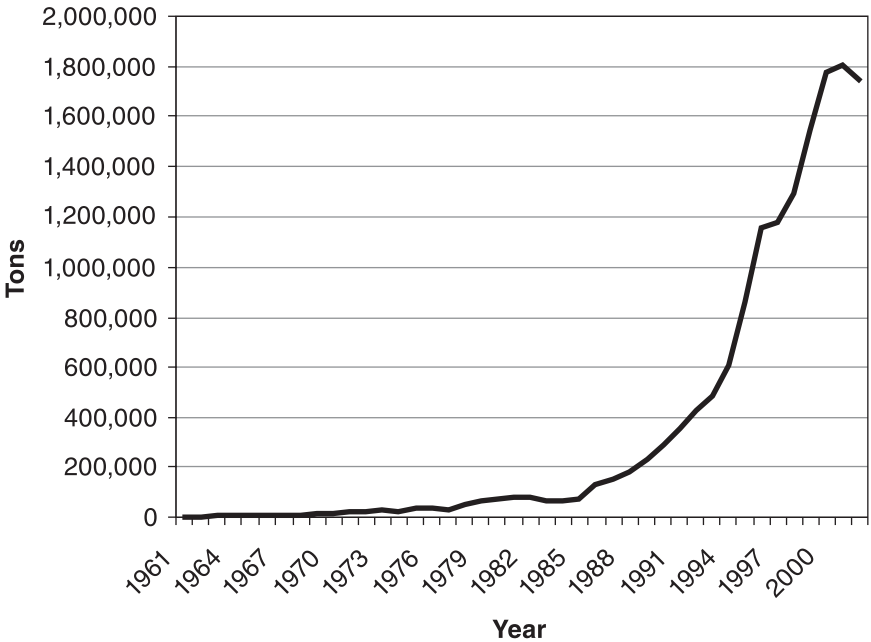


**FIGURE WO-6** Poultry exports from Far East Asian countries from 1961 through 2002.
SOURCE: Based on data in FAOSTAT 2003 and reprinted from Kimball (2006) with permission from Ashgate Publishing.

agreed with the importance of such research, in which he participates, but warned that controlling H5N1 in backyard flocks is extraordinarily difficult.

**Trade in beef and prion diseases** The emergence of two prion diseases, bovine spongiform encephalopathy (BSE) and new-variant Creutzfeldt-Jakob disease (NvCJD), following the entry of the United Kingdom (UK) into the World Trade Organization (WTO), illustrates a similar, but more complex, dynamic relationship between trade and disease. Entry into the WTO required the UK to abandon certain protective tariffs for its beef producers who, due to their resulting need to lower prices, shifted to a less-expensive rendering process that did not deactivate prions. Contrary to popular belief, the practice of feeding sheep offal to cattle as a protein source had been practiced in the UK for decades without incident, Kimball explained. The problems began when processors changed from a batch-rendering process that deactivated prions, to a lower-temperature, continuous vacuum-extraction process that did not. Meat and bone meal produced in this way was used to make animal feed, the vehicle through which prions spread around the world.

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While researchers are still discussing the validity of the prion hypothesis and whether prion disease in cattle can be transmitted to beef-eating humans, those debates have long been settled among consumers and commercial interests, Kimball observed. As a result, in 1996, when case-control studies suggested a possible link between BSE and British beef, UK beef exports declined precipitously.

**Trade in risky therapies** Market forces favoring medical tourism[12] and xenotransplantation are also raising the risks for disease emergence, according to Wilson and Kimball. Kimball noted that organ transplantation is becoming increasingly common, and the pig has become a popular, relatively low-cost source for islet cells (to reverse type 1 diabetes that cannot be managed with insulin therapy) and, occasionally, kidneys as well. Kimball noted that in the United States, only heart valves from pigs may be legally transplanted into humans; in India, porcine islet cells and other organs are also transplanted, as well as precursor stem cells from rabbits.

Concern that endogenous animal retroviruses will be introduced into humans through xenotransplantation prompted the World Health Assembly to pass a 2004 resolution urging member states "to allow xenogeneic transplantation only when effective national regulatory control and surveillance mechanisms overseen by national health authorities are in place" (WHA, 2004). Kimball noted that researchers are attempting to address these risks by breeding endogenous retroviruses out of pigs (Scobie and Takeuchi, 2009) and by encapsulating transplanted porcine islet cells within human cells prior to transplantation (Thanos and Elliott, 2009). However, Kimball observed that it would be difficult to find a transplant site so remote (i.e., South Asia) that complications of porcine transplants done at that site will never be seen in U.S. hospitals or clinics.

### *Responses to Risky Trade*

**Securing the globalized U.S. food supply** A detailed description of infectious disease threats associated with the globalization of the U.S. food supply appears in a recent Forum workshop summary, *Addressing Foodborne Theats to Health* (IOM, 2006), which featured remarks and a contributed paper from Forum member David Acheson, of the U.S. Food and Drug Administration (FDA). In his presentation to this workshop, Acheson noted several examples of imported threats to food and drug safety recently encountered by the FDA (see Acheson in Chapter 2).

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[12]Worldwide, two million to three million people travel outside their home country seeking medical treatment each year, including an estimated 750,000 Americans. The top destinations include Singapore, Thailand, and India. For more information, see Deloitte Center for Health Solutions (2008) and Tutton (2009).

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"American consumers want all kinds of food, and they expect it to be available year-round," Acheson observed. Approximately 15 percent of all food consumed in this country is imported, and food safety standards in many importing nations are far less stringent than in the United States, he reported. Recent experiences, including the 2008 outbreak of *Salmonella* Saintpaul (and the laborious process by which it was traced to Serrano peppers grown in Mexico), as well as the deliberate contamination of wheat gluten with melamine for economic purposes in China, have compelled the FDA to take a more proactive stance in addressing foodborne threats, Acheson explained. Rather than continue to focus its efforts on reacting after the fact to the importation of tainted raw and processed food items, the FDA is now becoming much more proactive by seeking to understand foodborne threats at the point of origin, to anticipate their potential to spread globally, and to use risk-based inspections to detect these contamination events prior to an outbreak occurring in the United States. In his contribution to Chapter 2, Acheson describes efforts under way to increase the agency's presence in foreign countries, to develop model systems for risk-based inspections, and to make use of inspection and testing data generated by industry or other "third parties" to increase the breadth and depth of their surveillance.

**Partnering with the private sector** "The globalization of health . . . has lagged behind economic globalization and business globalization and commerce globalization, because [the latter processes] . . . are market-driven and [public health] is not," Kimball observed. To address this gap, she advocated inclusion of the private sector in efforts to improve the exchange of information on infectious disease threats at all levels, from local to global (see the final section of this summary and Bell in Chapter 5 for further discussion of this topic). Kimball's work with the Asia Pacific Economic Cooperation (APEC) exemplifies such a private-public partnership.

As part of their effort over the past 14 years to create a "community of interest in health" involving the 21 nations comprising APEC, Kimball and her colleagues have sought to create a platform for rapid communications among member nations as a way to develop working relationships focused on health. The Emerging Infections Network (EINET) affords APEC members enhanced communications, opportunities for collaboration, and improved preparedness for infectious disease events. In so doing, Kimball says, APEC hopes to apply lessons learned from SARS to the threat of avian influenza.

### Mobile Animals and Disease

As discussed in the previous section and in a previous workshop summary report of the IOM's Forum on Microbial Threats—*Addressing Foodborne Threats to Health* (IOM, 2006)—trade in livestock, poultry, and foodstuffs made from animals has hastened the emergence of several important zoonotic diseases,

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including H5N1 influenza and BSE. Here, we consider additional mobile animals, such as pets, wildlife, research animals, and insect vectors (with and without their various hosts). They are also sources and sinks for introducing novel diseases into naïve ecosystems—or changing ecosystems in ways that alter transmission dynamics of existing infectious diseases. Workshop presentations and discussions provided examples of infectious diseases associated with various types of mobile animals, as well as the regulatory and research responses to these evolving threats.

*Recognition and Response: The CDC Perspective*

According to U.S. Fish and Wildlife Service data, more than 136,000 live mammals (including 29 different species of rodents) were legally imported into the United States in 2006, as well as 243,000 birds, 1.3 million reptiles, 4.6 million amphibians, and 222 million fish (personal communication between Nina Marano, CDC, and Kevin Garlick, U.S. Fish and Wildlife Service, July 10, 2008). Since 2000, more than half a million shipments containing in excess of 1.48 billion live animals have been imported by the United States (Smith et al., 2009). Exotic pets[13] are readily available in the United States and other wealthy countries, and their popularity is growing, according to speaker Nina Marano, of the Centers for Disease Control and Prevention (CDC). Animals imported into the United States can be purchased online for home delivery, or bought at local "swap meets," Marano explained.

Four U.S. government agencies, including the CDC, regulate the importation of animals based on their risk for zoonotic disease; the others are the Department of Homeland Security (Customs and Border Protection), the Department of Agriculture (Animal and Plant Health Inspection Service), and the Department of the Interior (Fish and Wildlife Service). Marano described the CDC's response in recent years to a series of novel animal disease threats (see Marano et al. in Chapter 3). This effort has included the following:

- The development of the agency's non-human primate program in response to an outbreak of Ebola hemorrhagic fever among monkeys destined for

[13]There is not a single definition of "exotic pets" and those that do exist are evolving. In this report, we define exotic pets as rare and/or unusual animals being kept as pets which are not usually considered pets. These would include animals such as the giant Gambian pouch rat that was the carrier of monkeypox that entered the United States in 2003, or exotic birds that might carry Newcastle disease or influenzas. Large cats and primates are kept as pets as well as some wild African species with dangerous internal and external parasites in addition to diseases such as rinderpest, tuberculosis, and other foreign animal diseases that could not only be zoonotic but could result in new animal disease epidemics that would be very costly to our livestock and poultry. Thanks to Lonnie King, DVM, Dean of the College of Veterinary Medicine, Ohio State University, and member of the Forum on Microbial Threats, for providing perspective on this definition.

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medical research that were housed in a quarantine facility in Reston, Virginia, in 1989 (CDC, 1990). This program instituted new requirements for the importation of primates, specifically requiring that the importers isolate and quarantine imported animals in a CDC-approved facility for 31 days upon entering the United States.

- The prohibition of interstate transportation, sale, distribution, or release into the environment of native prairie dogs and six species of African rodents implicated in a multistate outbreak of monkeypox[14] in 2003 (CDC, 2003). This was a joint order issued by the CDC and the FDA; the FDA lifted the ban on interstate movement of prairie dogs in September 2008.
- Enhanced surveillance and analysis to address the importation of bushmeat,[15] a potential source of zoonotic viruses including the human immunodeficiency virus (HIV), simian immunodeficiency virus (SIV), and the Ebola virus.
- The embargo of birds imported from countries with H5N1 influenza.

To date, the CDC's regulatory actions to address disease threats from imported animals "have been very reactive . . . species-specific and very pathogen-specific," Marano said. Much like the FDA as described by Acheson (see previous section and Chapter 2), the CDC is moving toward more proactive regulation of imports, according to Marano. The agency seeks broader restrictions, such as those proposed in a recent bill introduced in the House of Representatives entitled the Non-native Wildlife Invasion Prevention Act (U.S. Congress, House, 2008). Should this legislation become law it would require that every nonnative wildlife species proposed for importation into the United States receive a risk assessment, including identification to the species level, geographic source, and likelihood that importation could harm other species and habitats in the United States.

"For public health purposes we need a risk-based, proactive approach to preventing the importation of animals and vectors that pose a zoonotic disease risk," Marano and coauthors conclude in their contribution to Chapter 3. "The risk-based approach should include systematic and targeted surveillance of high-risk animals and animal products and vectors in the countries of origin. Emphasis should be placed on restricting the importation of animals and vectors of diseases not already present in the United States."

[14]Monkeypox is caused by *Monkeypox virus*, which belongs to the orthopoxvirus group. It is a rare viral disease that occurs mainly in the rain forest countries of Central and West Africa. The disease was first discovered in laboratory monkeys in 1958. Blood tests of animals in Africa later found evidence of monkeypox infection in a number of African rodents. Laboratory studies showed that the virus also could infect mice, rats, and rabbits. In 1970, monkeypox was reported in humans for the first time. In June 2003, monkeypox was reported in prairie dogs and humans in the United States (CDC, 2008b).

[15]Wildlife species which are hunted in the "bush," or forests (WCS, 2009).

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### *Mosquitoes on the Move*

As is noted in the summary of a recent Forum workshop, *Vector-Borne Diseases: Understanding the Environmental, Human Health, and Ecological Connections* (IOM, 2008a), the rapid expansion of global trade and transportation has been associated with the spread of mosquitoes and mosquito-borne diseases such as dengue and chikungunya. Thanks to today's globalized economy, these vector-borne diseases—once considered well controlled in industrialized countries—are poised for resurgence, while others, such as West Nile viral fever and chikungunya, have significantly expanded their geographic range (IOM, 2008b).

Speaker Paul Reiter, of the Institut Pasteur, described the distribution pathway that followed from the first U.S. detection of *Aedes albopictus*, the Asian tiger mosquito, which he captured in Memphis, Tennessee, to his discovery, three years later, that these mosquitoes were being shipped all over the world in used tires (see Reiter in Chapter 3). "There was a world trade in used tires, tens of thousands of used tires being shipped all over the world from Japan particularly," he recalled. "Japan was shipping at that time to137 different countries." As a result, he continued, *Ae. albopictus* is now well established in the United States as far north as Chicago, as well as in 13 European countries, and several African countries. In Africa, Reiter reported, this species has been implicated in the transmission of yellow fever and chikungunya.

These and other diseases described by Reiter in his contribution to Chapter 3 have expanded their geographic range thanks to traveling hosts, vectors, and ease of shipping and transportation. Yellow fever spread to the Americas upon the arrival of slave ships bearing both infected travelers and a highly competent vector, *Ae. aegypti*, that bred in barrels of potable water, Reiter noted (Crosby, 2006). Chikungunya arrived in Italy—where its vector *Ae. albopictus* was already present in the environment—in the guise of a viremic traveler from India who visited family members in the small northern town of Castaglione (see Box WO-2). The ensuing outbreak resulted in 205 confirmed cases of the disease (Rezza et al., 2007).

"There has been a quantum leap in the movement of vectors and the movement of pathogens," Reiter concluded, noting the recent emergence of vector-borne diseases ranging from dengue fever in Hawaii (a small outbreak in a small, relatively isolated community of globe-trotting surfers), to trypanosomiasis in France (brought in by camels), to the arrival of bluetongue virus in Europe (in midges blown in from Africa [IOM, 2008b; Osburn, 2008]), which he predicted would herald "a major tragedy in European agriculture."

### *Invasive Species*

Introduced animals, plants, and microbes can disrupt ecosystems in ways that increase the potential for infectious disease outbreaks. The term "invasive species" is widely used to describe plants and animals that, when introduced to and

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**BOX WO-2**
**The Travels of Chikungunya**

The chikungunya virus, an alphavirus of family *Togaviridae*, was originally isolated in Tanzania in 1953. The virus circulates among monkey populations in the forests of that country. It is transmitted by mosquitoes of the genus *Aedes*, particularly *Aedes aegyptii* (which is widely distributed in the Americas today) and *Aedes albopictus*. Nosocomial transmission of chikungunya by needle stick has been reported.

Chikungunya received relatively little attention until a recent series of explosive outbreaks began in African coastal cities in 2004, and afterward in islands in the Indian Ocean, in mainland India, elsewhere in Asia (most recently, in Thailand and Malaysia), and in Italy (Figure WO-7). There have been thousands of chikungunya infections in travelers, most notably an Indian man whose visit to family members in Castaglione, Italy, in 2007, ignited a localized outbreak of chickungunya fever. The vector in this case was *Ae. albopictus*, which was introduced to Italy in used tires imported from the United States, which in turn received the species in used tires imported from Japan.

Symptoms of chikungunya infection include rash, myalgia,[a] headache, arthralgia[b] (which tends to be severe, incapacitating, and persistent), and fever. The virus has a high attack rate, so it can disable entire populations upon its introduction. An apparently recent mutation in the chikungunya virus improved its efficiency of transmission by *Ae. albopictus*; this may explain the explosiveness of recent outbreaks (Tsetsarkin et al., 2007).

Although many cases of chikungunya have been imported to the Americas, to date none of these have resulted in transmission. However, a recent study found that *Ae. aegyptii* and *albopictus* strains present in the United States could be infected with, and could subsequently transmit, recent outbreak strains of the virus (Reiskind et al., 2008; Vazeille et al., 2007).

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[a]Muscle pain.
[b]Joint pain.

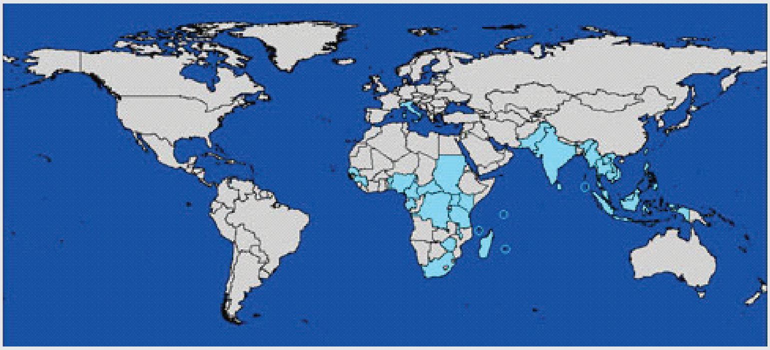

**FIGURE WO-7** Approximate global distribution of chikungunya virus, 2008.
SOURCE: Modified from Powers and Logue (2007); reprinted from CDC (2008a).

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established in new environments, spread aggressively (Dybas, 2004). Ecologists, including speaker Andrew Dobson of Princeton University, apply the concept of biological invasion to describe pathogen transmission and persistence at the population level.

Dobson's presentation considered several pathogen-host relationships in this context. A typical invasive species, the European green crab (Figure WO-8), found few of its own host-specific pathogens in its new home on the west coast of the United States, and so can grow to many times the size of its native-born brethren. An atypical invader, the house finch, at first expanded rapidly across the United States in ever-larger flocks; however, flocks that encountered conjunctivitis-causing mycoplasmas in their travels experienced massive, density-dependent population crashes. In general, Dobson said, invasive host species have a major advantage over native ones because the invaders have escaped their parasites (Torchin et al., 2003).

Examining the relative success of various invasive plant species in California, Dobson and colleagues determined that "the things that come in and cause you the biggest problems are going to be similar to the things that are already there" (Seabloom et al., 2006). Applying this principle to emerging diseases, he expressed

**FIGURE WO-8** Size comparison of largest green crabs caught from a parasitized population in the crab's native range (left) and unparasitized population in the crab's introduced range (right).
SOURCE: Reprinted with permission from the Ecological Society of America from Torchin and Mitchell (2004). Photo credit: Jeff Goddard.

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great concern regarding diseases that resemble measles, such as the Nipah and Hendra viruses, for which bats provide a reservoir (see Dobson and Cleaveland in Chapter 3). Because "anything that is like measles that gets into humans [is likely to] stay," Dobson and colleagues are creating mathematical models that describe Nipah virus behavior at the level of host populations, identifying patterns that could be used to provide early warning of an outbreak.

Dobson also described efforts by his group to apply ecological insights from other biological invasions to predict outbreak risks for the H5N1 influenza A virus. By examining influenza outbreaks in European duck populations, they discovered that the ducks migrate ahead of cold fronts, aggregating in larger and larger groups (in which, presumably, disease could spread quickly) as the weather becomes colder. He also noted that complex models, involving two or more duck species, consistently show that when several possible hosts are available to a pathogen, it becomes persistent (endemic) and relatively stable. An important way to build resilience against zoonoses and non-host-specific infectious diseases, according to Dobson, is to make diverse and abundant host species available to pathogens. For example, Dobson said, if he found himself in one of the several locations in India where 99 percent of mosquito bites occur in cattle, he "would much rather go buy a cow than have a malaria vaccine."

Some participants questioned the general applicability of Dobson's influenza model, based on their own research findings. Osterholm remarked that his data from Asia would not suggest that H5N1 outbreaks were associated with cold fronts; instead, he has noticed that feeding opportunities, such as crab breeding seasons, often drive bird crowding. Osterholm warned against the tendency of models to obscure such complexity with "precision and graphic clarity." Dobson argued that models such as his help researchers to examine problems in an appropriate spatial and temporal scale. "To get at the complexity [of disease emergence] you have got to look at the community level . . . [and] at the interaction with climate, and on a big enough geographic scale to understand processes on the scale at which they work," he insisted. "To me the power of the models isn't what they tell you, it is what they tell you to go and look at next."

To create more and better predictive population dynamic models of infectious disease emergence, "we need to spend much more money on data collection and surveillance" and in training scientists to analyze the results, Dobson declared. "There are more knee surgeons than we have mathematical epidemiologists who understand how to do these analyses," he complained, adding that "there is no longer any NIH funding for [the study of] population dynamics in infectious diseases."

Predicting the consequences of movements of agents, vectors, or pathogens, and preventing the most harmful among them, is likely to require a variety of approaches, observed Forum Chair David Relman, of Stanford University, at the close of the discussion that followed Dobson's presentation. Progress toward this goal can be made by applying a wide range of scientific tools, drawn from a variety

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of disciplines, he added; these include both modeling and measurement in order to acquire "better ground truth data."

### Global Public Health Governance and the Revised IHR

As globalization renders national and geographic boundaries increasingly porous and from an infectious disease standpoint practically meaningless, infectious disease control demands international cooperation and coordination. This became abundantly clear in 2003 when SARS emerged in China and rapidly spread to North America.

The public health response to SARS demonstrated the effectiveness of recently established global information and response networks (see Heymann in Chapter 4). While yet unnamed, SARS was identified in Asia by the Global Public Health Information Network (GPHIN) and other networks such as ProMed; within a week, members of the Global Outbreak Alert and Response Network (GOARN) in 26 institutions and 17 countries, as well as field teams, were exchanging information about the outbreak in real time. Their findings were used by the WHO to make timely travel recommendations in order to contain the global spread of SARS, and recommendations on best practice for clinical management.

The SARS event provided a powerful rationale and catalyst for global public health governance, according to presenter David Heymann, of the World Health Organization (WHO).[16] In the months following this workshop, the emergence of swine origin influenza A (H1N1) virus prompted the WHO to take actions authorized under the IHR for the first time since their revision in 2005 and underscored the value of global coordination of infectious disease control (see Chapter 4).

#### *The IHR 2005: A New Era in Global Governance*[17]

Heymann explained that the emergence of SARS in 2003 was a major catalyst toward a fundamental revision of the IHR that had begun in 1995; that process was completed in 2005 and the regulations took effect in 2007. The original IHR, established in 1969, were preceded by a long history of multinational public health measures designed to control the spread of infectious diseases across national borders (see also Gushulak and MacPherson in Chapter 1). The IHR 1969 were intended to monitor and control six diseases—cholera, plague,

[16]At the time of this workshop in December 2008, Dr. Heymann was Assistant Director-General for Health Security Environment and Representative of the Director-General for Polio Eradication at the World Health Organization. In April 2009, he became Chair of the Health Protection Agency, UK, and head of the Global Health Security Programme at Chatham House, London.

[17]Global health governance involves the use of formal and informal institutions, rules, and processes by States, international organizations, and non-State actors to deal with challenges to health that require collective action to address effectively (personal communication with David P. Fidler, Indiana University Maurer School of Law, October 16, 2009).

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smallpox, relapsing fever, typhus, and yellow fever—whose occurrence required WHO notification (WHO, 2005). Following revisions in 1973 and 1981, only three "notifiable" diseases remained: cholera, plague, and yellow fever.

By the mid-1990s, the IHR 1969 appeared obsolete. A vast number of global microbial threats had emerged and reemerged, including many diseases that were not deemed "notifiable," such as Ebola hemorrhagic fever (IOM, 2007; WHO, 2005). There was also concern that the IHR dependence on "official" country notification, along with a lack of a formal, internationally coordinated mechanism to contain the international spread of disease, might fail to contain a disease with pandemic potential (WHO, 2005). Several resolutions passed by the World Health Assembly (in 1995, 2001, and 2003) encouraged revision of the IHR; the final resolution—WHA58.3—formally adopting IHR 2005, passed on May 23, 2005.

As of June 15, 2007, when revisions to the IHR came into force, member nations of the WHO are required to report all new and reemerging diseases with epidemic or pandemic potential, as well as chemical, radiological, and food-related threats, irrespective of their origin or source (WHO, 2008). Speaker May Chu of the WHO noted that the IHR 2005 provides a specific decision instrument for this purpose, based on the following four questions:

- Is the public health impact of the event serious?
- Is the event unusual or unexpected?
- Is there a significant risk of international spread?
- Is there a significant risk of international travel or trade restrictions?

If the answer to any two questions is "yes," the member nation is compelled to notify the WHO of the event, Chu explained. Upon investigation of such a report, the WHO may declare such an event to be a "public health emergency of international concern (PHEIC)," triggering a specific response (see Chu et al. in Chapter 4). This occurred for the first time on April 25, 2009, in the case of swine-origin influenza A (H1N1) virus (see contributions by Chu and Fidler in Chapter 4).

Chu also discussed the second key obligation of signatories to the IHR 2005: to develop the capacity to detect, assess, notify, and report a possible PHEIC. Member nations are required to assess their disease surveillance capacity and develop national action plans by 2009. By 2012, member states must meet standards for national surveillance and response systems, as well as for designated airports, ports, and ground crossings (extensions may be obtained, however).

Chu observed that instructions with regard to capacity-building within the IHR 2005 were flexible, enabling its 194 member nations to build or access (via outsourcing) disease surveillance and investigational capacity. However, she added, the IHR 2005 provide an insufficient basis for evaluating some crucial areas, such as laboratory requirements (e.g., quality assurance). Members of the

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public health community, including several workshop participants, have contended that the IHR 2005 insufficiently address economic barriers to reporting infectious outbreaks, and cannot succeed unless supported by funding for public health capacity-building in developing countries (Fidler and Gostin, 2006).

*Challenges to IHR 2005*

Although preceded by more than a century and a half of international sanitary conventions (Stern and Markel, 2004), the IHR 2005 represent a "radical departure from all previous uses of international law for public health purposes," according to speaker David Fidler, of Indiana University (Fidler and Gostin, 2007; see also Fidler in Chapter 4). He noted five attributes that set the IHR 2005 apart from their predecessors:

- Significant expansion of epidemiological and political scope,
- Obligations for member states to develop and maintain minimum core capabilities for surveillance and response,
- Empowerment of WHO to collect and use information from non-governmental sources,
- Authorization of the WHO Director-General to declare a public health emergency of international concern, and
- Incorporation of human rights concepts and principles requiring that WHO member states apply public health powers according to principles of international human rights law.

However, Fidler observed, "the mere existence of radical changes in the IHR 2005 does not guarantee that the IHR 2005 will radically change global health." He noted that global crises—including energy, food, climate change, and most recently, the precipitous downturn of worldwide financial markets—have overshadowed the threat of infectious diseases, causing the effort to implement the IHR 2005 to lose momentum. The emergence of the swine-origin influenza A (H1N1) pandemic briefly raised the priority of health issues in foreign policy, but as Fidler observed in his contribution to Chapter 4, when the outbreak began to resemble seasonal flu rather than the 1918-1919 pandemic, global health faded quickly from political prominence.[18] This event and other recent experiences in global health governance, including but not limited to the worldwide campaign to eradicate polio, the issue of "viral sovereignty," and the global responses to the

[18]Although the furor over the spread of the 2009-H1N1 influenza A virus waned in the months following its being declared as a level 6 pandemic by the WHO, in the ensuing months domestic and international attention has increased as the virus spread from the Northern Hemisphere to the Southern Hemisphere and back again. For further information, please see Bertozzi et al. (2009) and PCAST (2009) .

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swine-origin influenza A (H1N1) virus, described below, highlight the limitations of the IHR 2005 as an instrument for international cooperation and coordination, while revealing the crucial role of global governance instruments in addressing infectious disease threats.

**Polio eradication** Between 1988 and 2003, efforts to control polio reduced its presence from 125 to only 6 countries, according to Heymann (see Chapter 4). This progress was halted, and then partially reversed, when politicians in northern Nigeria used an Internet rumor that polio vaccine sterilized young girls as a basis for suspension of polio vaccination programs. Heymann described a range of approaches undertaken by the WHO to remedy this situation, including testing vaccines for impurities or hormones that could cause sterility and discussions with a wide range of political, medical, and religious persons and groups of influence, without success. Only after press reports of World Health Assembly resolutions strongly condemning the Nigerian government for suspending polio immunization reached the country's citizens did their president agree to "do everything humanly possible to ensure that polio is finally and totally eradicated from Nigeria." Thereafter, polio vaccination programs were resumed in northern Nigeria.

When polio eradication is achieved, the IHR 2005 could be used to ensure the simultaneous, global cessation of oral polio vaccinations, so that no country is put at risk, Heymann said. However, when this measure was recently proposed to the World Health Assembly, it was not accepted, nor was a proposal to address the destruction or consolidation in secure laboratories of wild polioviruses under the IHR. Thus, Heymann observed, although the IHR 2005 were negotiated and established as an international convention, "there is still hesitancy to use these regulations as many in public health had hoped they would be used."

**Viral sovereignty** In 2006, Indonesia refused to share samples of the H5N1 avian influenza virus, collected within the country, with the WHO's H5N1 influenza surveillance team (see contributions by Fidler and Heymann in Chapter 4). Instead, Indonesia claimed "viral sovereignty" over these samples, and announced that it would not share them until the WHO and developed countries established an equitable means of sharing the benefits (e.g., vaccine) derived from viruses collected within its borders. "Indonesia argued that it took these actions because it, and other developing countries, was not gaining benefits in terms of response capabilities from sharing of virus samples for purposes of global surveillance," Fidler said. Indonesia criticized WHO's practice of distributing influenza viruses it received for surveillance to pharmaceutical companies, which would make patented vaccines from such samples—vaccines that were often too costly for developing countries to purchase.

Proposals to use IHR 2005 as a means to force Indonesia to share H5N1 virus samples for global surveillance purposes failed, because the IHR 2005 do not require such sharing or address inequitable access to the benefits derived

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from such samples, Fidler observed. Instead, all 194 member countries passed a resolution at the World Health Assembly in 2007 to initiate a series of intergovernmental meetings to discuss, debate, and develop a new framework for the sharing of influenza viruses, a move that marginalized the IHR 2005 both legally and politically, Fidler asserted.

**Influenza A (H1N1)** The emergence of pandemic influenza subsequent to this workshop has highlighted the costs, as well as the benefits, of global information-sharing under the auspices of the IHR 2005. Mexico and the United States complied with their obligations to report outbreaks to the WHO, which declared a PHEIC within 48 hours of laboratory confirmation that the Mexican and U.S. viruses represented a new strain (Condon and Sinha, 2009).

However, despite WHO recommendations to the contrary, a significant number of countries imposed travel and trade restrictions as a result of the outbreak that produced severe economic repercussions, particularly in Mexico (Condon and Sinha, 2009; Editorial, 2009; Gostin, 2009). As Condon and Sinha (2009) observe, the "disproportionate response of several countries to Mexico's response may well discourage other countries from acting so quickly, effectively and transparently in future disease outbreaks, to the detriment of all countries. The lack of any effective recourse under either the IHR (2005) or the WTO compounds the problem of disproportionate and asymmetrical travel and trade restrictions and creates disincentives to report outbreaks and deal with them in a transparent and decisive manner."

*Intent Versus Reality*

The intent of the IHR 2005—to raise the importance of global health as a foreign policy issue and to transform global health governance—contrasts starkly with the reality of multiple barriers to its implementation, several workshop participants observed. They noted that the virus-sharing controversy highlighted several important inequities in public health capacity that exist between developed and developing countries that are not adequately addressed by the IHR 2005. Most daunting among these appears to be the previously mentioned "surveillance gap" that separates global surveillance needs and the resources available to support the development of capacity in resource-poor countries (Fidler and Gostin, 2007).

Divisions between developed and developing countries are further exacerbated by the lack of mechanisms to ensure global equity in response to infectious disease threats. After posing the rhetorical question as to whether a developed country's national vaccine, antiviral, or antibiotic stockpile will be shared with developing countries in the event of a disease emergency, Fidler and Gostin (2007) observe that despite attempts by the WHO to create global stockpiles of such resources, intervention strategies are largely limited to—and by—national

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governments. This situation contributes to the view that the IHR 2005 offer little to developing countries.

"A large proportion of policy makers in resource-constrained countries perceive that the emphasis of the IHR 2005 on the international spread of disease evinces little concern regarding the burden of infectious diseases on the nations in which they occur," said speaker Oyewale Tomori, of Redeemer's University in Nigeria (see Tomori in Chapter 4). He added that this perception "is fueled by a longstanding history of selective application and implementation of global health policies in order to support the interests of countries in the developed world," such as disproportionate international reaction to outbreaks that occur in industrialized countries.

These perceptions can only add to the significant disincentives to reporting infectious disease outbreaks. As speaker David Bell, of the CDC, noted in his contribution to Chapter 5, "countries may perceive substantial economic disincentives to reporting and responding to public health threats as required by the IHR. Economic harm to tourism or export industries could result from public health measures such as travel advisories, quarantine, seizure of hazardous products, or culling of infected livestock—or simply from unjustified public fears. Mounting an emergency response will challenge the health budget of many developing countries, yet the IHR include no provision for financial support or compensation."

## Global Disease Surveillance and Response: Challenges and Opportunities

The IHR 2005, a landmark in the development of a global governance mechanism to respond to global health threats, demonstrate both the promise and the peril of global health governance and, more specifically, of global infectious disease surveillance. Fidler, who characterized surveillance as the "'center of gravity' for public health governance," noted that efforts toward global governance are unlikely to succeed unless the benefits afforded by surveillance are equitably distributed. Workshop participants discussed a range of approaches to support global disease surveillance and response efforts both within and beyond the purview of the IHR 2005.

### *Addressing Present and Future Challenges to the IHR*

In addition to the previously described roadblocks to implementing the IHR 2005—inequity in sharing its costs and benefits, lack of funding for surveillance in developing countries, overcoming sovereignty issues, competition with health and other global agendas—Fidler considered the following four out of five global trends, identified in a recent report from the National Intelligence Council (NIC, 2008a):

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- Overall risks to human life and health are expanding and accelerating,
- Incentives for political disagreement are increasing,
- Limitations on governance mechanisms are increasingly apparent, and
- Vulnerabilities of societies to "pathogen politics"[19] are deepening.

While these realities present significant challenges to the implementation and impact of IHR 2005, Fidler said, other international governance mechanisms have proven comparatively weak and ineffective in addressing the many and various drivers of infectious disease emergence and spread (e.g., migration, environmental and climate change, antimicrobial resistance, armed conflict). These failures reinforce the importance of the IHR 2005 to the future of global health, he concluded.

Greater recognition of the potential of the IHR 2005 to promote global security is key to their effective implementation, Heymann added. In the face of the current global recession, he offered two arguments to dissuade those who might favor reducing support for IHR 2005 implementation: its importance to public health security and therefore, to overall global security; and to preserve the foundation of health for economic development and redevelopment.

Bell's presentation, entitled "Global Trade Security Depends on Implementation of the IHR," echoed Heymann's arguments, and explored how trade and tourism stakeholders (e.g., international corporations, industry and trade associations, ministries of trade and tourism) might support various aspects of the implementation of IHR 2005 (see Bell in Chapter 5). For example, Bell envisioned that an international scheme to compensate individuals or countries for economic hardships resulting from infectious disease outbreaks could be created as a public-private partnership involving trade and tourism stakeholders, and structured as a trust fund or insurance product.

"Business, trade, and tourism stakeholders, and those who support them, such as the insurance industry, have a strong vested interest in working with public health authorities to promote global health security," according to Bell (2008). "The IHR also promote global trade security, which may be provisionally defined as maintenance of a stable trade environment by promotion of safe and unhindered travel and transport, stability of supply and distribution chains, continuity of business operations, and safety of imports and exports. . . . For businesses, industry associations, and international trade organizations and their member states, promoting IHR implementation is good risk management, since the risk of business and trade disruption is reduced in countries where the IHR are implemented."

Speaking informally with business leaders, Bell found that most had never

[19]Dr. Fidler defines pathogen politics as the exercise of political power, the convergence and divergence of political interests, and the use of political processes in national and international responses to threats posed by pathogenic microbes.

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heard of the IHR. However, he added, "they immediately understood its importance to them once the issues were explained. Their question was, what exactly do you want us to do, what might the next steps be?" although their interest was subsequently diverted by the global recession. Revision of the IHR was one of the highest global health priorities of the U.S. government, but it risks sitting on the shelf because support for its global implementation is lacking.

*One World, One Health®*[20]

Recognizing the importance of zoonoses as emerging diseases and the economic impact of animal diseases, several workshop participants advocated expanding the purview of surveillance under IHR 2005 by linking its human infectious disease networks with those focused on animal diseases. A similar argument was made to integrate infectious and foodborne disease surveillance by speaker David Nabarro of the United Nations (UN), among others. Nabarro, who serves as the UN's coordinator for avian and human influenza, as well as for global food security, applauded the advent of such an integrated strategy, known as One World, One Health®, which he characterized as seeking "new ways of aligning action to better address diseases that emerge at the interface between animals and humans in different ecosystems" (Schnirring, 2008).

Speaker Ottorino Cosivi of the WHO described the development of the One World, One Health® strategic framework, which evolved from lessons learned in efforts to address the threat of pandemic avian influenza. Partners in this framework currently include the WHO, the Food and Agriculture Organization of the UN (FAO), the World Organisation for Animal Health (OIE), the UN Children's Fund (UNICEF), and the World Bank. The concept of One World, One Health® is embodied in projects such as the Global Early Warning and Response System for Major Animal Diseases, Including Zoonoses (GLEWS), which is jointly operated by the FAO, OIE, and the WHO (WHO, 2009a).

**Role of the OIE** Further alignment of human and animal disease surveillance efforts appears promising based on comparisons between surveillance as

[20]One World, One Health® is a registered trademark of the Wildlife Conservation Society. Health experts from around the world met on September 29, 2004, for a symposium focused on the current and potential movements of diseases among human, domestic animal, and wildlife populations organized by the Wildlife Conservation Society and hosted by The Rockefeller University. Using case studies on Ebola, avian influenza, and chronic wasting disease as examples, the assembled expert panelists delineated priorities for an international, interdisciplinary approach for combating threats to the health of life on Earth. The product—called the "Manhattan Principles" by the organizers of the "One World, One Health®" event—lists 12 recommendations for establishing a more holistic approach to preventing epidemic/epizootic disease and for maintaining ecosystem integrity for the benefit of humans, their domesticated animals, and the foundational biodiversity that supports us all. For more information, see http://www.oneworldonehealth.org/ (accessed July 16, 2009).

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conducted under the IHR 2005, and through the OIE's World Animal Health Information System (WAHIS), by speaker Alejandro Thiermann of the OIE (see Chapter 5). He described that organization's efforts to address animal disease to ensure animal health worldwide, food safety and safeguard global trade, which parallel those of the WHO. Member countries are bound to report cases that meet any of the following criteria to the WAHIS: diseases with potential for international spread, apparent emerging diseases, diseases with zoonotic potential, and diseases that show significant spread in naïve populations. OIE reviews and immediately publishes such reports on its World Animal Health Information Database (WAHID), accessible by all member countries. When appropriate, OIE also issues early warnings on a webpage.

Unlike IHR 2005, WAHIS can only publish official information, submitted by its delegates (the chief veterinary officers of its member countries), Thiermann explained. Nevertheless, he added, through collaborations with other surveillance networks, including those operated by the WHO, the OIE searches non-official sources of information for indications of "notifiable" disease events. When evidence of such an event is detected, the information is submitted to that country's delegate for immediate confirmation or denial. In some cases, the OIE has posted alerts based on such information in the absence of official confirmation, Thiermann said. For example, when Chinese officials did not confirm unofficial reports indicating the presence of avian influenza in ducks in southern China, the OIE nevertheless proceeded to notify its members. Official confirmation was forthcoming from China, but not until 24 hours after this information was posted.

Thiermann noted that when a disease event occurs at the interface of animal and human health, ministries of health and agriculture within the same country often respond differently; in such cases, only the WHO, or only the OIE, may be notified. These situations are best managed through "a close collaboration" that enables the exchange of information between the two organizations, and a joint response to zoonotic threats, he said. Organizations with surveillance and response functions for zoonotic diseases—particularly OIE, FAO, and WHO—need to continually share and collaborate, he concluded.

**Role of the WHO** A variety of interagency collaborations promote the early detection and control of disease at the animal-human interface, according to Cosivi (see Chapter 5). He described a series of such formal agreements and joint programs involving the WHO, and frequently, the OIE and the FAO as well, dating back to 1948. In addition to the previously described GLEWS and GOARN, these include the following:

- The International Food Safety Authorities Network (INFOSAN), which disseminates information and fosters international collaboration on food safety (WHO, 2007);

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- Global Salm-Surv, which promotes integrated laboratory- and epidemiology-based foodborne disease surveillance (WHO, 2009c); and
- The Mediterranean Zoonoses Control Program, which supports the prevention, surveillance, and control of zoonoses and foodborne diseases and serves as a platform for interagency collaboration for country-level capacity building to address these diseases (WHO, 2009b).

Cosivi described the development of the "One World, One Health®" strategy as a paradigm shift in public health, from the "response and rehabilitation mode" characterized by initial attempts to address avian influenza, to prevention and preparedness for all emerging infectious diseases. "To prevent human diseases," he concluded, "we need to increase attention to prevention, surveillance, and control in wild and domestic animal health, animal production and food systems, and the environment."

### *Building Capacity and Trust*

In order to build on the foundation provided by the IHR 2005 and the "One World, One Health®" strategic framework, according to Nabarro the following three challenges must be resolved (see Chapter 5):

1. Implementing adequate systems and capacities to conduct global surveillance and respond to global public health emergencies (e.g., animal surveillance for H5N1 influenza);
2. The need to engage all stakeholders, and particularly the private sector, in global disease surveillance and response, recognizing that some key groups do not perceive such action to be in their best interest; and
3. Most importantly, to create the most important incentive for participation in global health initiatives: trust.

**Building capacity** In addition to previously described workshop discussions that addressed Nabarro's first point, regarding the need for capacity-building (and for funding to support it), Tomori advocated equal emphasis on the national and international spread of diseases. "The practice of 'dangling the carrot' of international resources for responding to a disease outbreak (e.g., vaccines, funding, and foreign expertise) as an incentive for reporting such an outbreak may undermine the determination of resource-constrained countries to develop, strengthen, and maintain national core surveillance and response capabilities," he contended (see Tomori in Chapter 4). "Moreover, it is far more efficient to contain disease outbreaks than to respond to full-blown epidemics." Making a similar argument from a global perspective, Forum member Terence Taylor, of the International Council for the Life Sciences, observed that in an age of mobile populations such as those described by Gushulak (see Chapter 1), border

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biosecurity "is less important than building . . . national core infectious disease surveillance capacity."

Tomori stated that countries should be encouraged to develop the capacities to report, detect, and investigate suspected disease outbreaks and thus prevent sporadic cases from escalating to epidemics, and that more resources be provided for establishing and maintaining disease surveillance systems at the national level. He described the establishment of the acute flaccid paralysis (AFP) surveillance system, backed by an African region-wide laboratory network, as a model for such national surveillance systems.

The only way to make progress on global health governance is to empower countries to develop their own surveillance capacities, Nabarro said. Developing countries must be encouraged to work with other countries in their subregions to develop networking and common approaches across nearby borders, but such efforts have to originate within countries, he insisted.

**Engaging all stakeholders** Nabarro, whose remarks focused on the issue of conducting effective global disease surveillance and response in an atmosphere of increasing suspicion toward the value of globalized initiatives, recalled that, for a time, the threat of pandemic avian influenza generated "unity of purpose and synergy of action." Although occasional discord arose, coordination between donors, foundations, national governments, regional bodies, and international nongovernmental groups was strong.

"What was the incentive that brought so many disparate groups to work together as if in a strong magnetic field, and not to lose their separateness? Answer: It certainly wasn't cash," Nabarro said, because although money was available, it moved slowly, and little of it made it to those organizations that were working in concert. Instead, he observed, these groups were motivated to join a global movement. "They found it both attractive and at the same time comforting . . . to be coherent, to be together, to be joint stakeholders within a movement," he concluded, adding that the same force has motivated recent collaborations to address HIV/AIDS, and to eradicate polio (as described by Heymann; see Chapter 1). "I believe that the best incentive for working together on surveillance, on reporting, on response, is the creation of a movement that is open enough, strong enough, inclusive enough, to enable hundreds of different stakeholders to feel at home inside it," he concluded.

Two Forum members—Gail Cassell, of Eli Lilly, and Phil Hosbach, of Sanofi Pasteur—urged that such collaborations include another stakeholder in global disease control not mentioned specifically by Nabarro: the pharmaceutical industry. For example, Hosbach said, pharmaceutical companies represent the solution to one of the critical challenges to influenza surveillance. "The benefits-sharing that these countries are looking for is . . . [protection] from influenza, and what better way to do that than with vaccine?" he asked. Heymann agreed that industry had served as "a faithful partner in the influenza pandemic and vaccine

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production," but he maintained that pharmaceutical companies have not "brought to the table any solutions to make vaccines available." Resolving this impasse would require dialogue between global public health and industry groups, focused on solving this critical problem, he observed.

**Building trust** "You can't get results on control of H5N1 or other diseases through compulsion," Nabarro continued. "If you compel, then people start to hide, they fail to explain, they don't involve themselves. So it is absolutely essential to build the necessary trust so that the work can progress." Moreover, he said, mistrust among stakeholders in a common enterprise, such as global disease surveillance and response, must be anticipated, insured against, and addressed as soon as it arises.

The United States has been the strongest and most consistent leader in promoting global collaborations to address H5N1 influenza over the past three years, Nabarro said. While he encouraged the United States to continue this leadership, despite the risks involved, he also encouraged inclusiveness. Likening the role of the United States as the builder of a tent to be occupied by a host of stakeholders in global health, he advised the country to "make the tent so it is big enough, but also so that it is open enough . . . [and] exciting enough to bring people in."

*Toward Resilience*

Workshop participants were compelled to discuss the unfolding worldwide economic crisis and its possible repercussions for global public health. Nabarro suggested that any among a range of potential shocks—including pandemic disease, climate change, food crisis, and recession—would have similar effects on a given community or individual household, depending upon its overall resilience. "The stronger, most resilient households will survive," he said, and "in many cases . . . resilience can be surprising." Less resilient households, particularly those that have recently moved from a subsistence into the market economy, will not be so fortunate, he continued, and are likely to decline into subsistence; this will be especially likely for women-headed households and those in which a breadwinner becomes ill or disabled.

Therefore, in the context of global recession, and in order to prepare people, communities, and countries to withstand any of the various threats looming on the horizon, Nabarro advocated the promotion of resilience. He noted that the World Bank has taken a leadership role in this effort, but this effort will require a multifaceted approach that includes public health. He also advocated continued support, led by the United States, for development assistance "geared toward efficient action, leverage, and [the] empowerment of local communities to do more for themselves."

Reflecting on workshop presentations and discussions that encompassed history, public health policy, ecology, and medical science, Relman considered the

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relationship between diversity and resilience. "Is there an aspect of diversity that predicts resistance to perturbation?" he asked. "One might look for this feature in patterns of diversity amongst susceptible host species or in diversity amongst local response mechanisms, or both, to mention a few possibilities."

"It sounds to me as though many people are suggesting that there is no one global fix for the kinds of problems we are talking about," Relman continued. Rather, he concluded, we are presented with a set of possible local solutions, based on common principles, which can be adapted and strengthened to support specific ecosystems, communities, and public health capacities.

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# 1

# Migration, Mobility, and Health

## OVERVIEW

Opening presentations by Mark Miller of the University of Delaware and Brian Gushulak of the Canadian Immigration Department Health Branch set the context for this workshop by exploring the history and ongoing political and public health significance of human migration and mobility. Their contributions to this chapter establish a firm foundation for those that follow, providing both a wealth of detail and an overarching view of the changing picture of human migration through the ages, and particularly during the recent decades.

Miller's essay reviews human migratory history, focusing on the contemporary "Age of Migration" that began around 1970. This era "has witnessed major developments in human mobility affecting all areas of the world," Miller writes. "Understanding this still evolving global migratory context bears importantly upon comprehension of contemporary microbial threats." Conversely, he notes the importance of health issues to the study of migration and security, particularly in recent years.

Miller examines the geopolitical origins of the present Age of Migration and examines its defining features. These he characterizes as the globalization, acceleration, differentiation, politicization, feminization, and proliferation of migration in the traditional sense (the one-way movement of people from one homeland to another); the advent of formal mechanisms supporting "circular" migrations such as guestworker programs; and the growth of international tourism. Reflecting on the future of migration and development, and recognizing that "the chief threats to U.S. security since the 1970s arose from failed states and the abysmal living conditions of average people in much of the world," Miller advocates a



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stronger commitment on the part of the United States to development in Africa, the Middle East, and other developing countries, including increased admissions of permanent residents from these regions.

In his subsequent contribution, Gushulak, along with his colleague Douglas MacPherson, of McMaster University and Migration Health Consultants, Inc., presents a comprehensive history of migration-associated disease and disease control policies. The authors characterize "modern migration"—the mechanism that drives Miller's "Age of Migration"—in terms of its departure from traditional migratory patterns, and explore the challenges it presents for global health, and particularly for the control of infectious diseases.

In order to "shift the paradigm" of disease control away from policies focused on geopolitical borders and individual infectious diseases, Gushulak and MacPherson introduce the concept of "population mobility" to replace traditional considerations of migration. "Considering mobility as a global health determinant provides a model upon which we can integrate disease management policies, processes for prevention, knowledge of disparate prevalence environments, and a rigorous health threat to risk assessment ability," the authors write, and they suggest several approaches to the control of mobility-related disease to support this model.

## INTERNATIONAL MIGRATION PAST, PRESENT, AND FUTURE[1]

*Mark J. Miller, Ph.D.*[2]
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Public health has been importantly influenced by human mobility patterns since time immemorial. A rich, but frequently overlooked, tradition of scholarship attests to the significance of understanding human mobility for comprehension of events involving plagues and spatial diffusion of illnesses (Diamond, 1997; McNeill, 1977). Many students of world politics and international relations have distinguished themselves by their neglect of health questions in explanations of wars and conquests (Koslowski, 2000). Nevertheless, no effort will be made here to reprise that literature. Rather, the focus will be upon sketching what Stephen Castles[3] and I call *The Age of Migration*, the contemporary migratory epoch that

[1]This essay builds on a paper prepared for the International Organization for Migration/Center for Migration Studies, Conference on International Migration and Development: Continuing the Dialogue—Legal and Policy Perspectives convened in New York City January 17-18, 2008. That paper was subsequently published in J. Chamie and L. Dall'Oglio, eds. 2008. *International Migration and Development*. Geneva: ILO and New York: CMS. Pp. 71-78.

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began circa 1970 which has witnessed major developments in human mobility affecting all areas of the world. Understanding this still evolving global migratory context bears importantly upon comprehension of contemporary microbial threats. Health issues comprise a not insignificant dimension of the still emerging field of study of migration and security, a scholarly focus of considerable historical pedigree that reemerged after the Cold War and especially after 9/11 (Castles and Miller, 2009).

### Migrations Past: International Migration in the Modern Age

To paraphrase Kemal Karpat,[4] rarely does migration not figure importantly in the history of humankind. Recent anthropological evidence concerning the late Iron Age in Europe suggests that distinctive societies were much more interconnected and fluid than once thought (Wells, 2001). The prosperity and goods of ancient Greece and Rome fostered trade and myriad other interactions just as the military might of Greece and Rome posed a perceived grave threat to tribes and peoples on the periphery, forcing them to adapt, change, and define their identities. The extensive Viking migrations of the eighth to eleventh centuries gave rise to plunder and violence. But those migrations also involved trade and commerce. Medieval migration of Jews in Europe often was linked to rulers' efforts to spur economic development and to generate greater tax revenues. Much the same could be said about medieval German migrations eastward (Miller, 2008).

The term international migration, which the United Nations (UN) defines as occurring when a citizen or national of one state moves to another state for a period of at least one year, presupposes the existence of an international system of states. Many students of international relations trace the emergence of the contemporary international or Westphalian system to seventeenth-century Europe and the end of the Thirty Years War[5] brought about by the treaties of Westphalia. This embryonic nation-state system then diffused to the rest of the world through processes of colonization and imperialism followed by decolonization and the embrace of the sovereign national state system born of Europe after World War II.

Voyages of discovery, conquest, and trade by Europeans marked the advent of the Modern Age. European domination of the New World ensued as many indigenous people succumbed to European-borne diseases, although European populations also were adversely affected by diseases contracted in non-European areas for which Europeans possessed insufficient or little immunity. In general, with the major exception of the 400-year-long African slave trade, which involved over 15 million Africans, population transfers initially were

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quite limited (Curtin, 1997). The cost of maritime travel was prohibitive except for the wealthy and, in an age of Mercantilism, European rulers viewed their subjects as valued possessions, especially for military conscription. The anti-migration norm began to erode only after 1800.

A number of developments set the stage for the first era of mass migration, which mainly involved Europeans. The French Revolution gave birth to a new norm, a human right to emigrate. Technological innovations and other factors began to make transatlantic travel economically possible for larger segments of the European population. Many of the former colonies comprising the newly founded American Republic welcomed and encouraged settlement by Europeans. Population growth, particularly in Great Britain and Ireland, which can partially be attributed to improvements in public health, particularly in cities, also constituted a factor.

The growth of the Irish population figured centrally. Ireland had been incorporated into Great Britain in 1801, resulting in growing migration of Irish to England in particular. The poverty of many of the Irish migrants and their Roman Catholicism caused alarm. Soon local governments discovered it was less expensive to help transfer the Irish to Canada and the United States than to provide for them *in situ*. By the 1820s, the mercantilist anti-emigration norm had eroded (Zolberg, 2006).

Between 1820 and 1939, roughly 60 million Europeans immigrated to the New World, which included Argentina and other areas in Latin America, Australia, and New Zealand as well as the United States and Canada (Hatton and Williamson, 1998, 2005). However, the composition of the migration flows changed over time, especially after abolishment of serfdom in the Czarist Empire. By the late-nineteenth century, many areas in western and northern Europe had become zones of immigration, particularly France which, in the interwar period, had become the world's premier land of immigration.

In the United States by the 1880s and 1890s, concerns over the effects of immigration had increased. The first federal commission to study immigration, thereby inaugurating migration studies in the United States, suggested reductions in immigration, recommendations that began to be translated into law by 1917. The Quota Acts of 1921 and 1924[6] severely curtailed European migration to the United States. Other New World immigration lands emulated the United States, thereby bringing the first period of mass migration to a virtual end.

After the Great Depression and the long night of World War II, a number of areas reemerged as significant lands of immigration or emigration. The United States admitted several groups of "displaced persons" and continued to admit Mexican temporary workers, which had resumed under a 1942 bilateral accord

[6]These laws instituted the National Origins system of visa allocation that, as subsequently revised, remained in effect until 1965. The system favored visa applicants of northern European background as opposed to applicants from southern and eastern Europe. See Daniels (2004).

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with Mexico.[7] A major reform of U.S. immigration law in 1952[8] somewhat reopened the "Golden Door" which had largely been closed in the 1920s. The resumption of immigration policy was accentuated by the 1965 amendments to the 1952 law, which came into effect in 1968 (Daniels, 2004).

Hatton and Williamson (2005) have identified five developments that precipitated the Age of Migration by 1970. Latin America changed from being a net importer of international migrants to a net exporter. The bulk of Latin American emigrants went to the United States as Latin American economic growth lagged behind that of the United States. Later, and especially after the Cold War, significant flows of Latin Americans would also go to Europe, especially to the Iberian Peninsula and Italy. Western Europe itself also became a major zone of immigration, especially after a large faction of post-World War II guestworkers settled, contrary to expectations, and were joined by family members. The oil-producing areas of the Middle East and North Africa also became major zones of immigration. Unlike during the era of mass European emigration to the New World, areas of Asia and Africa also became significant zones of emigration to other areas of the world, but especially to Western Europe and parts of the New World. Finally, somewhat later, the areas of Eastern Europe, long frozen by Soviet domination, itself an echo of the mercantilist antimigration norm, began to thaw. Ostpolitik[9] and détente[10] began to open the door to emigration. The collapse of Communist governments led to large-scale emigration followed by migration transition; that is, Central and European states simultaneously became lands of emigration and immigration especially after the European Union (EU) enlargements of 2004 and 2007, which brought 12 additional states into the European regional integration framework.

### The Age of Migration

Stephen Castles and I maintain that the current era is defined by six general tendencies:

[7]The agreement instituted what is termed the second bracero period in U.S. immigration history. Bracero means strong-armed one in Spanish and refers to Mexican workers admitted to the United States to perform temporary services of labor, mainly in agriculture. From 1942 to 1964, there were approximately five million Mexican workers admitted under the accord and subsequent U.S.-Mexican arrangements.

[8]The Immigration and Nationality Act (INA) of 1952 as amended remains the basis of U.S. immigration law today. Its major provisions included retention of the National Origins system of visa allocation and the Texas Proviso, which exempted U.S. employers from prosecution for hiring of aliens ineligible to work in the United States. It passed over President Truman's veto.

[9]German term meaning "eastern policy." It generally refers to Germany's normalization of relations with the Eastern bloc countries, including the German Democratic Republic in the early 1970s.

[10]The relaxation of strained relations, particularly relating to the United States and the Soviet Union.

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1. *The globalization of migration:* the tendency for more and more countries to be crucially affected by migratory movements at the same time (Miller, 2008).
2. *The acceleration of migration:* international migration is increasing in all the world's regions. While the percentage of international migrants in the world's population remains roughly constant at between 2 and 3 percent, the world's population continues to grow and will do so for several decades into the future, before peaking at about nine billion persons. Most future growth will occur in Africa and Asia. Nevertheless, growth of international migration is not inexorable. Repatriations, for instance, have significantly reduced some refugee populations (Miller, 2008).
3. *The differentiation of migration:* most countries, states, and governments around the world face increasingly complex challenges in regulating international migration as they encounter, and sometimes precipitate, diverse inflows of migrants (Miller, 2008). Immigration countries tend to receive migrants from a larger number of source countries, so that most immigration lands have entrants from a broad spectrum of social, economic, and cultural backgrounds.
4. *The politicization of migration:* international migration-related issues are becoming increasingly salient in domestic politics, bilateral and regional relations, and at the global level as witnessed by the creation of the Global Commission on International Migration (GCIM) and the convening of a high-level conference on migration and development at the UN in 2006. After consultation with then UN Secretary-General Kofi Anan in 2003, a number of UN member states funded the GCIM to conduct research, promote dialogue, and make recommendations about policies concerning international migration.[11] It mainly stressed the potential benefits of international migration for development. In 2003, the UN General Assembly also decided to hold a high-level dialogue on international migration and development in 2006. The Secretary-General's report on this meeting recommended a forum for UN member states to discuss migration and development issues further. However, the forum was to be purely advisory and was not intended to facilitate negotiations. The first Global Forum on Migration and Development was hosted by the Belgian government in July 2007, with a second in Manila in October 2008.
5. *The feminization of migration:* women have become more salient participants in international migration. Many international flows are comprised mainly of women, such as domestic workers in the Middle East. And women are disproportionally victims of human trafficking (Miller, 2008).
6. *The proliferation of migration transition:* more and more states have experienced migration transition; that is, traditional lands of emigration

[11]The 2005 report of the Geneva-based commission can be accessed at www.gcim.org.

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> have become lands of immigration. States as diverse as Thailand, Turkey, Morocco, Greece, Italy, Spain, the Republic of South Korea, and Mexico have experienced transition during the Age of Migration (Miller, 2008).

Table 1-1 summarizes the evolution of global migration between 1960 and 2005. There is mounting evidence that the worldwide financial and economic crisis of 2008-2009 has disproportionately adversely affected international migrants as has been the pattern in earlier economic crises such as in the mid-1970s.[12]

Other measures of human mobility likewise attest to the growing significance of international migration. Table 1-2 lists the top 10 countries with the highest numbers of international migrants in 1990 and 2005. Spain viewed itself as a land of emigration and as a transit zone as late as 1990. Virtually all of its nearly five million migrants in 2005 had arrived illegally, were legalized, or arrived through family reunification measures.

Table 1-3 indicates that international tourism is surging despite the War on Terrorism. Refugee and asylum-seeker flows, widespread human trafficking and smuggling, short-term highly skilled labor flows, student study abroad, and other forms of international mobility suggest that few human beings today are unaffected by international migration. In 2009, the Organisation for Economic Co-operation and Development (OECD) estimated that approximately five million people cross international borders each year to take up residency in a developed country.

### Thoughts About the Future of Migration and Development[13]

Usually understanding the past serves as the best guide to understanding the future. International migration played a central role in the shaping of the modern, Westphalian world in which we still live. It is likely to continue forging and reforging states and societies in the future.

International migration can foster development in both receiving and sending areas, as attested to by the U.S.-Swedish migratory relationship before 1914.[14] High hopes were attached to the promise of international migration generating sustained socioeconomic and political development in the Asian and African hinterlands of West Europe in the 1960s and 1970s, but those hopes largely proved misplaced.

Nevertheless, a new optimism has arisen over prospects for migration and development through well-managed bilateral and regional policies. This optimism

[12]Postings on the effects of the ongoing crisis for international migrants can be found at www.age-of-migration.com.

[13]The following text comes from Miller (2008).

[14]Hatton and Williamson (2005) observe that Sweden largely closed its development gap with Great Britain and other more advanced European states between 1860 and 1914 when about one-fifth of all Swedes emigrated to the New World and principally to the upper midwest of the United States.

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**TABLE 1-1** Number of International Migrants by Region, 1960-2005 (in millions)

| Region | 1960 | 1970 | 1980 | 1990 | 2000 | 2005 |
|---|---|---|---|---|---|---|
| World | 76 | 81 | 99 | 155 | 177 | 191 |
| More developed regions | 32 | 38 | 48 | 82 | 105 | 115 |
| Less developed regions | 43 | 43 | 52 | 73 | 72 | 75 |
| Africa | 9 | 10 | 14 | 16 | 17 | 17 |
| Asia | 29 | 28 | 32 | 50 | 50 | 53 |
| Europe | 14 | 19 | 22 | 49 | 58 | 64 |
| Latin America & Caribbean | 6 | 6 | 6 | 7 | 6 | 7 |
| Northern America | 13 | 13 | 18 | 28 | 40 | 45 |
| Oceania | 2 | 3 | 4 | 5 | 5 | 5 |

NOTE: The UN defines migrants as persons who have lived outside their country of birth for 12 months or more.
SOURCE: UNDESA (2006).

**TABLE 1-2** The 10 Countries with the Highest Number of International Migrants (in millions)

| Rank | 1990 | | 2005 | |
|---|---|---|---|---|
| 1 | United States of America | 23.3 | United States of America | 38.4 |
| 2 | Russian Federation | 11.5 | Russian Federation | 12.1 |
| 3 | India | 7.4 | India | 10.1 |
| 4 | Ukraine | 7.1 | Ukraine | 6.8 |
| 5 | Pakistan | 6.6 | France | 6.5 |
| 6 | Germany | 5.9 | Saudi Arabia | 6.4 |
| 7 | France | 5.9 | Canada | 6.1 |
| 8 | Saudi Arabia | 4.7 | India | 5.7 |
| 9 | Canada | 4.3 | United Kingdom | 5.4 |
| 10 | Australia | 4.0 | Spain | 4.8 |

SOURCE: Based on data in UNDESA (2006) and reprinted from Koslowski (2008) with permission from the Center for Migration Studies.

is linked to more precise understanding of the vast volume of migrant remittances to homelands.

A number of scholars and policy makers have advocated temporary foreign worker admissions policies in OECD democracies as part of a circular migration strategy to promote mutually beneficial development in sending and receiving states. A certain skepticism about such advocacy appears in order.

The historical track record of temporary foreign worker admissions policies in democratic settings can be termed checkered at best. Guestworker, seasonal

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**TABLE 1-3** International Tourist Arrivals (in millions, ordered in 2006 ranking)

| Rank | | 1995 | 2000 | 2002 | 2003 | 2004 | 2005 | 2006 |
|---|---|---|---|---|---|---|---|---|
| | World | 535.0 | 682.0 | 702.0 | 691.0 | 761.0 | 803.0 | 846.0 |
| 1 | France | 60.0 | 77.2 | n/a | 75.0 | 75.1 | 75.9 | 79.1 |
| 2 | Spain | 34.9 | 47.9 | n/a | 50.8 | 52.4 | 55.9 | 58.5 |
| 3 | US | 43.5 | 51.2 | 43.6 | 41.2 | 46.1 | 49.2 | 51.1 |
| 4 | China | 20.0 | 31.2 | 36.8 | 33.0 | 41.8 | 46.8 | 49.6 |
| 5 | Italy | 31.1 | 41.2 | n/a | 39.6 | 37.1 | 36.5 | 41.1 |
| 6 | UK | 23.5 | 25.2 | n/a | 24.7 | 27.7 | 28.0 | 30.7 |
| 7 | Germany | 14.8 | 19.0 | n/a | 18.4 | 20.1 | 21.5 | 23.6 |
| 8 | Mexico | 20.2 | 20.6 | 19.7 | 18.7 | 20.6 | 21.9 | 21.4 |
| 9 | Austria | 17.2 | 18.0 | n/a | 19.1 | 19.4 | 20.0 | 20.3 |
| 10 | Russia | n/a | n/a | n/a | 20.4 | 19.9 | 19.9 | 20.2 |
| 11 | Turkey | 7.1 | 9.6 | n/a | 13.3 | 16.8 | 20.3 | n/a |

SOURCE: Based on data in UNWTO (2005, 2006, 2007) and reprinted from Koslowski (2008) with permission from the Center for Migration Studies.

worker, and bracero-style policies[15] had problems and unintended consequences for quite well understood reasons. The Swiss reformed their seasonal worker policy in 1964 to allow those workers who worked five consecutive seasons to adjust to resident status under diplomatic pressure from Italy. The volume of seasonal foreign worker admissions also became controversial, leading to the divisive anti-Ueberfremdung[16] campaigns of the 1970s which gave way to similarly unsuccessful referenda campaigns to abolish seasonal foreign worker policies as incompatible with human dignity in the 1990s. Swiss seasonal worker policy was not mismanaged. And as late as the 1973 to 1975 period, many seasonal worker permits were not renewed due to the recession, thereby enabling Switzerland to shift some of the costs of the recession to Italy.

Similarly, German guestworker policies generally were well administered. But there was considerable political sympathy for legally admitted foreign

[15]The lexicon of international migration specialists is replete with terms derived from non-English languages. Guestworker derives from the German *Gastarbeiter*, a word coined after World War II to replace *Fremdarbeiter*, foreign worker, as many foreign workers had died and suffered deprivations under Nazi rule. Seasonal worker derives from the French *saisonnier* and the German *Saisonarbeiter.* It refers to foreign workers who are admitted for periods of less than one year and who are required to repatriate at the end of that circumscribed period. *Bracero* means strong-armed one in Spanish and, in the context of U.S.-Mexico migratory relations, refers to Mexican workers admitted to perform temporary services of labor in the United States from 1917 to 1921 and from 1942 to 1964. Tellingly the once obscure vocabulary of international migration specialists has become the lexicon of diplomacy in the Age of Migration.

[16]A term coined in Swiss German prior to World War I referring to the perceived threat of an excessive presence of foreigners.

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workers by the 1970s. German courts blocked conservative efforts to enforce rotation after 1973 as incompatible with the Federal Republic's legal engagements and responsibilities. This constituted an enormous victory for German postwar democracy that is too little appreciated.

Bracero-policy history between Mexico and the United States does not appear to have yielded much evidence of fostering sustainable development in Mexico. U.S. recruitment of temporary Mexican foreign workers dates back to before World War I. Such recruitment helped set in motion large-scale unauthorized migration to the United States. Significantly more unauthorized Mexican workers were returned to Mexico than legally recruited during the 1942 to 1964 period. The United States unilaterally terminated the policy in a period of growing consciousness and concern about civil rights and the effects temporary foreign worker admissions had upon American farm workers.

The evolution of French seasonal foreign worker admissions after World War II somewhat resembled events in Switzerland. Admissions of seasonal workers mainly for agricultural employment crested at about 250,000 per year in 1968 but were steadily phased out afterward. Significant numbers of seasonal workers became so-called faux saissoniers (or false seasonal workers) and overstayed their visas. Many applied for the recurrent legalizations between 1972 and the 1980s. Seasonal foreign worker admissions continue today but in very small numbers.

Since 1990, a new generation of temporary foreign worker admission policies have emerged in Europe, especially in Southern Europe. The new policies are more narrow-gauged than policies during the guestworker era. The key issue is: Will their outcomes resemble those of the guestworker era? Advocates of circular migration policies take an optimistic view.

Spain's recent bilateral initiatives toward Black African states in Western Africa perhaps best exemplify the optimistic perspective. In return for cooperation with Spain and the EU on management of international migration, including prevention of illegal migration and human trafficking, as well as readmission of citizens illegally entering the European space, Spain will provide for job training and then admit trained and prepared foreign workers for time-bound employment in sectors lacking adequate labor supply such as agriculture.

At first glance, such policies may appear constructive, even progressive. But almost by definition, the legal status of temporary foreign workers is contingent. Usually the foreign workers are tied, as it were, to a particular employer or industry. Of course, there is no incontrovertible way to measure need for additional foreign workers in a given industry, but especially in agriculture. Perceptions of need represent outcomes of political and legal battles usually pitting employers against unions. Usually, employers have their way even with governments of the left, which has been the case in Spain since 2004.

It is important to point out that there are viable policy alternatives to the circular migration model. Spain could also admit more persons from West Africa with permanent alien resident status. Those Africans admitted would be free to

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work throughout Spain. Nothing would constrain these workers to become EU citizens but it would be a possibility. Such legally admitted permanent resident aliens would be free to travel back and forth to their homelands. But many certainly would opt for naturalization.

Herein lies the major advantage of increased admission of permanent resident aliens. Spain and Spaniards would have to accept the likely reality of settlement, giving Spanish society and government a strong incentive to foster immigrant integration. Historically, supposedly temporary foreign worker policies have resulted in significant settlement. But states and societies were unprepared for such unexpected outcomes leading to integration deficits and long-term integration issues.

Preliminary analysis of Spain's temporary foreign worker admissions, the so-called contingents, suggests that the historic pattern of unexpected policy outcomes will continue. Several contingents served as ways to legalize aliens in irregular status rather than to recruit foreign workers from abroad. Perceived unfairness in the administration of the contingents has roiled Spain's relations with Morocco and several other homelands whose governments feel that more of their citizens should be legally admitted under bilateral agreements. Spanish unions and employers often disagree on how large the authorized contingent should be, reminiscent of the annual "headaches" that Swiss cantonal and federal officials spoke of in the 1970s and 1980s.

Further enlargement or deepening of the EU and of other regional integration frameworks worldwide also merits consideration. Canada, the United States, and Mexico could emulate the history of regional integration in Europe. The key problem lies in the dissimilarity between the North American Free Trade Agreement (NAFTA) and the EU. NAFTA does not have a political project, unlike the European Community (EC) and now the EU. The Security and Prosperity Partnership (SPP)[17] agreement announced by the three NAFTA heads of state in 2005 may suggest a move in that direction.

However, within each region and globally one can readily discern a need for greater cooperation between more developed and lesser developed states to promote greater socioeconomic development. The history of European structural funds designed to promote a more even playing ground within the European space deserves careful scrutiny by the NAFTA partners.

Unfortunately, most OECD member states have ducked negotiations over international migration and development issues. The pattern was set at the 1986 OECD-sponsored conference on the future of international migration. The U.S. delegation was instructed to avoid anything resembling North/South dialogue at

[17]The SPP pledged the three states to work more closely and cooperatively on border, international migration, trade, and international security issues, particularly prevention of terrorist attacks.

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that conference. The Reagan Administration adamantly opposed Willy Brandt-style North/South Dialogue.[18]

The U.S. position appears to have evolved little ever since. It would take inspired American leadership for the decades-long migration and development stalemate to change. American leaders of either party simply continue to endorse the benefits of globalization and free trade as evidence mounts that it increases socioeconomic disparities, both within and between states and societies. The circular migration advocacy risks generating false hopes that bilateral and regional cooperation on international migration will result.

A new approach to migration and development would serve U.S. interests. The chief threats to U.S. security since the 1970s arose from failed states and the abysmal living conditions of average people in much of the world (Cooper, 2003). After 9/11, a window of opportunity opened but it has been largely squandered. Nevertheless, successful prosecution of the War on Terrorism requires progress on sustainable development in Africa, the Middle East, and elsewhere within what Thomas Barnett (2004) calls the "non-integrated gap area." The important question revolves around the credibility of options proposed to bring about development. The track records of structural funds in contexts of regional integration and of increased admissions of permanent resident aliens appear preferable to the circular migration model.

## PEOPLE, BORDERS, AND DISEASE—HEALTH DISPARITIES IN A MOBILE WORLD[19]

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### Introduction

The relationships between migration and introduced diseases of epidemic proportions are a recurrent story in human history (Morens et al., 2008). Epi-

[18]In the 1970s and 1980s former German Chancellor Brandt advocated dialogue between developed and lesser developed states to attenuate the socioeconomic gap between the two areas. For more information, see Independent Commission on International Development Issues (1983).

[19]The opinions expressed in this paper are those of the authors alone and do not necessarily represent the position of any government, university, organization, agency, or society to which the authors are or have been affiliated.

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demic events and other scourges of mankind have always traveled along the lines of human population mobility. In this paper, the term *population mobility* will be used when human "migration" extends beyond traditional patterns of the regulated processes of immigration and emigration.[22] This is based on the concept that modern aspects of population mobility between disparate health environments can be more important in the context of health and globalization than the administrative or legal status of the person moving or the geopolitical boundaries that may be crossed.

Disease has frequently followed those pulled to new destinations by opportunity, better conditions, or simple inquisitiveness; or pushed from their homes by events, calamity, or chaos. The ebbs and flows of populations have often involved a connection between different environmental, socioeconomic, genetic, biological, or behavioral conditions that existed between the migrant and host populations (Ampel, 1991). The dynamic interaction of the populations and the determinants of health influenced and changed those who were migrating as well as the populations hosting the migrants.

Experiences involving disease and migration have been woven into humankind's social, cultural, and medical history. Remotely, epidemics of plague, cholera, leprosy, and syphilis, and more recently, HIV/AIDS, viral hemorrhagic fevers, severe acute respiratory syndrome (SARS), and swine influenza H1N1 have defined policy responses to protecting regional interests in economics, trade, security, and health (IOM, 1992). Detailed historical and scientific discourses regarding the origin of disease and its introduction into previously unaffected parts of the world have continued for centuries (Harper et al., 2008). Several of the public health and infectious disease challenges facing today's increasingly integrated and globalizing world have similarities in context to situations involving migration, illness, and disease that have occurred in the past.

Traditionally, the implications and consequences of the relationships between disease, migration, and population mobility are described in terms of individual diseases, time periods, or events. This paper will approach migration and disease control frameworks through a process-related lens that includes several parameters associated with population mobility. Those parameters include population dynamics, differentials in disease or health indicator prevalence, the phases of migration (pre-departure, transit, post-arrival including return travel), and perceived and real risks to the health of the migrant and host populations.

Local, regional, and more recently international disease control strategies have been developed over time in response to the long-felt, but perhaps underappreciated, relationships between human mobility and disease (MacPherson and Gushulak, 2001; Welshman and Bashford, 2006). Frequently, existing immigration health control and mitigation practices reflect integral components from the

[22] *Immigration* is to arrive and take up permanent residence in a country other than one's usual county of residence. *Emigration* is to leave one's usual country of residence to settle in another.

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history of public health. In doing so, they often mirror the perceived nature of the health risk and science of the era in which they were developed. In terms of migration and imported infections, those approaches were commonly based on diseases of topical interest at the time and the sociological, legal, or administrative characteristics (seafarers, crusaders, military personal, humanitarian workers, immigrants, refugees, asylum seekers, migrant workers, smuggled and trafficked persons) of new arrivals.

Examining the evolution of programs to mitigate international disease importation reveals a pattern of reactive public health policies intended to mitigate risks. Over time, changes in transportation technology, migration patterns, and advances in medical science have also changed the nature and perception of risk. Changing perceptions of threat and risk have themselves been associated with corresponding changes in the disease control endeavors (Gill et al., 2001).

Older methods of disease control and mitigation were progressively superseded by approaches designed on the basis of improved capacity or better understanding of the nature of the risks themselves. For example, the nineteenth-century international consultations that were convened in Paris to deal with controlling the spread of cholera (Goodman, 1952), and which began a process that continues to this day through the revision of the International Health Regulations,[23] preceded the germ theory of disease and subsequently evolved with the science of microbiology. This global evolutionary process of change, challenge, and response continues. The interfaces of migration, human mobility, and disease control remain an important aspect of national, regional, and global public health activity.

By its very nature, reactive policy development and implementation will always be tested by new or unanticipated events and processes. When those events occur against a background of low-speed travel and a limited degree of global integration there is often adequate time for policy development to meet a specific disease event. This pattern of specific or situational threat or risk and the response is the traditional model that underlies most migration-associated disease control strategies. The dynamic changes present in situations of high-volume, rapid, and increasingly diverse migration significantly challenge the traditional, situational, or disease-specific event and response paradigm. In this context of decreasing cycle times and prerequisite need for anticipatory planning, policies and practices often need to be more generic and broadly applicable to reflect the evolutionary changes in risk.[24]

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[23]Beginning in Paris in 1851, a series of 14 international conferences began to examine international agreements on the standardization of quarantine and international disease control practices. The last International Sanitary Conference was held in 1938. Following World War II, these efforts eventually merged into activities in the World Health Organization and were adopted as the International Sanitary Regulations in 1951. They were renamed the International Health Regulations in 1969 (Howard-Jones, 1975).

[24]In this document, risk is used as a known harm or benefit related to health. Threat is a credible potential event for which existing outcomes or other measures of proof have not been demonstrated.

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To be effective, programs, practices, and policies must reflect the nature and dynamics of current challenges. Several of the factors that influence and affect migration, disease, and health have recently undergone significant change. In many circumstances those changes have not yet generated corresponding responses in migration health policy or program design. Given the importance and prominence of global infectious disease control in the context of human development, security, economics, and social integration, it is an appropriate and necessary time to consider the health implications of modern migration and population mobility (MacPherson et al., 2007). Examining the international spread of diseases of public health importance as a component of the process of human migration and population mobility can perhaps offer new elements in the approach to global health and disease control.

This paper reviews the history of migration and disease control policies in contrast with the modern health implications of human population mobility. It will also describe the impact that mobility has, and will continue to exert, in a rapidly globalizing world where trade, economics, security, and the environment all are interacting factors with health consequences. The focus of this discussion will be transmissible infectious diseases of global public health significance. The principles presented can equally be applied to any illness or condition associated with inter-regional differentials in prevalence that can be linked by mobile populations (Gushulak and MacPherson, 2006).

### History of Migration and Disease Control Policies

There is an intimate relationship between human mobility, the introduction and spread of infectious diseases, and consequential attempts at control and mitigation of adverse health outcomes (Cunha, 2004; Gellert, 1993). Observations that plagues and epidemic diseases followed the arrival of traders, commercial ventures, travelers, pilgrims, colonists, soldiers, and other migrants have been noted for centuries (Cartwright, 1972; Curtin, 1989). For an equally long period of time, religious orders, cities, states, and nations have implemented disease control policies and practices in what would be recognized today as public health interventions triggered by population mobility and disease events.

Extensive and coordinated attempts were made to mitigate the impact of leprosy in medieval Europe (Miller and Smith-Savage, 2006). The disease is believed by some to have afflicted returning pilgrims and crusading soldiers from the Middle East, although there are suggestions that it was present in Europe before the Crusades (Browne, 1975). Whatever its origin, it was a major health concern of the time (Edmond, 2006). Leprosy control efforts were associated with the development of policies of inspection and isolation enforced by religious and municipal authorities. Facilities and institutions were constructed to house and deal with those believed to have the disease. Once in place, these facilities and practices could be easily applied to other similar situations.

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By the fourteenth century, commerce and trade from the rapidly expanding renaissance city-states and nations had reached intercontinental levels not seen since the height of the Roman Empire. Those extensions to the east reached the Caspian Sea and western Asian areas at the same time as that region was experiencing an epidemic of plague (Herlihy, 1997). The outbreaks of plague in close association with the arrival of vessels carrying individuals who were ill or who became ill shortly after arrival were responsible for the development of organized health responses that became shared between many nations. Civic, municipal, and national policies and instructions were implemented to require vessels, goods, cargo, as well as passengers and crew to be denied port landing in an attempt to prevent disease introduction. Periods of detention sufficient to allow incubating disease to present with clinical illnesses were introduced and the process of quarantine was born. At the same time, municipal and civic health officers and staff were employed to deal with imported disease events.

Quarantine practices accompanied the Europeans during their subsequent colonization activities and were introduced in the Americas and other regions. While originally focused on specific infections of epidemic potential such as plague, cholera, and yellow fever, quarantine became the cornerstone of organized, coordinated attempts to deal with globalization and disease control.

The impacts on commerce associated with the global pandemic of cholera in the nineteenth century precipitated regional responses to regulate the movement of vessels, goods, and individuals in an attempt to reduce imported disease risk (Baldwin, 1999). It is historically notable that at this time international and intercontinental maritime traffic included a large human component of migrants destined from Europe to the opportunities of the "New World" as well as populations banished or transported for criminal or legal reasons, and trafficking in human slaves.

The principles of inspection, isolation, and denial of admission were applied to new arrivals at quarantine stations and ports of entry (Parascandola, 1998). The health policies and practices of traditional border inspection services were created to prevent the introduction of diseases arriving with immigrant populations. Initially organized around the seaports where most immigrants arrived, several immigration-receiving nations later moved the medical assessment of immigrants to the place of departure, further with the intended outcome of reducing the risk of arrival of unwanted diseases.

As major immigration nations began to regulate the process through legislation at the end of the nineteenth century, the medical inspection of newly arriving immigrants became required in nations such as the United States and Canada. The requirement for systematic medical inspection to detect both noninfectious and some infectious diseases resulted in the expansion of port-of-entry medical activities. Extensive inspection station facilities were constructed at large ports such as Ellis Island in New York (Yew, 1980), Angel Island in California (Lucaccini,

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1996), and Grosse Ille in Canada[25] (Montizambert, 1893). Medical inspection at these facilities provided opportunities to identify those with clinical illness. Depending on the situation and disease, individuals could be hospitalized, quarantined, or returned to their place of origin. Similar to modern border-associated processes, the true effectiveness of these activities was influenced by availability of accurate screening processes (Imperato and Imperato, 2008), the failure of inspection to detect those arriving with latent or subclinical illness, the logistical challenges of providing services at multiple ports of entry (Stern and Markel, 1999) and the application of screening based on the status, class of transport (i.e., steerage), or nationality of the arrival (Fairchild, 2004).

An example is provided by the approach to trachoma, a disease that could result in deportation if detected during immigration inspection in the early part of the twentieth century (Dwork, 1999). The denial of admission to those with disease detected on a brief clinical examination may have reduced the burden of disease in North America at the time. However, the ultimate control of trachoma required the development of antibiotic therapy and social and economic improvements that prevented its acquisition (Cook, 2008).

Approaches to infections of public health concern were also influenced by the sociological conditions present during the origin of immigration health policies and practices. Initial port health medical assessment and screening, for example, was often based on the class in which the passenger traveled, and was only required for steerage and third-class passengers. Weaknesses in those screening policies have been appreciated for some time, as noted in 1922:

> The quarantine officers allow first cabin passengers and usually the second cabin passengers coming from abroad to enter with very little or no medical inspection, as if the possession of money to buy better accommodations were a guarantee against various infections. (Copeland, 1922)

The organized screening and health assessment of arriving immigrants and refugees thus undertaken by several nations continues in this basic form to this day (Australian Department of Immigration and Citizenship, 2008; CDC, 2008a; Citizenship and Immigration Canada, 2003; Immigration New Zealand, 2005). The general approach to immigration health remains focused on the screening of certain groups for certain diseases, predominantly transmissible infections. Diseases of great interest in the early twentieth century, such as trachoma and smallpox, are no longer public health issues of concern. Current listings and types of disease to which immigration screening is organized tend to reflect illnesses of public health importance of the mid- to late-twentieth century, such as tuberculosis, sexually transmitted diseases, and some tropical infections. While

[25]The shorter sailing time between northern European ports and Canadian seaports meant that some migrants destined to the United States entered North America via Montreal or Halifax.

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no longer based on the class of passage, foreign nationals may remain subject to health requirements that are not applied to other travelers on the basis of visa or immigration status rather than travel heath-related risk.

### *The Demography and Nature of Modern Migration*

Discussions regarding the demography of migration relevant to health are hampered by the lack of standard definitions concerning the populations of interest (Lemaitre, 2005). These definitional gaps challenge the development of appropriate and effective strategies to deal with the health consequences of migration.

Traditional administrative classifications of immigrants and emigrants in current use frequently do not adequately account for the diversity in the determinants of health and health outcomes of modern international migrants. At the level of individual countries, the issue is frequently complicated by differing approaches to the definition and use of nationality, citizenship, and residence. Depending on location, the same or different terms may be applied to several functionally different populations. For example, the terms *immigrant*, *refugee*, and *migrant* may variously be applied to new legal residents from foreign countries, as well as refugee claimants, asylum seekers, temporary foreign workers, illegal and irregular migrants, and international students. Traditional definitions based on administrative criteria may not include or consider other subpopulations of migrants whose health status is a direct result of their migration experience (The Hague Process on Migration and Refugees and UNESCO, 2008). Examples in this category include those who are trafficked or smuggled, children born to newly arrived migrants, those with dual or multiple citizenship, stateless individuals, and long-staying international visitors.

International attempts to standardize terminology related to migration frequently consider the intent of the individual to change their place of residence or the duration of their stay. Migrants, unlike visitors or travelers, can be considered people changing their usual place of residence to live, work, or study in another nation, either permanently or on a temporary basis. Some international definitions further refine this classification on the basis of time, using a 12-month period to separate migrants from other travelers or international visitors (UN, 1998).

Using those international definitions, it is estimated that there are approximately 200 million international migrants (International Organization for Migration, 2008) living outside of their normal country of residence. About 60 percent of these international migrants reside in the economically advanced regions of the world and 40 percent are found in developing regions. Much of the growth in international migration has taken place within the past decade. If these foreign-born persons were considered a separate national population, international migrants would represent the fifth largest nation in the world (Table 1-4). The magnitude of this migrant population reveals the current global demographic

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**TABLE 1-4** Population by Nation, 2008

| Country | Population (millions) |
|---|---|
| China | 1,325 |
| India | 1,149 |
| United States of America | 305 |
| Indonesia | 240 |
| **International Migrants** | **200** |
| Brazil | 195 |
| Pakistan | 173 |
| Nigeria | 148 |
| Bangladesh | 147 |
| Russia | 142 |
| Japan | 128 |

SOURCE: Adapted with permission from Population Reference Bureau (2008a).

significance of migration. The proportional contribution of the health and disease outcomes of this large mobile population cohort in terms of global health and disease management is also significant.

In addition to its magnitude-derived importance, modern migration is functionally a much different process than the historical patterns of immigration when most immigration-related disease control activities were developed. Recent demographic, social, and geopolitical forces have made the dynamics of international migration subject to a new series of influences. Together those influences have produced major changes in the processes and patterns of modern migration.

Migration is both an integral component and a consequence associated with globalization. International migration is affected and influenced by global population pressures. In spite of slowing rates of growth, total human population is predicted to continue to increase until it exceeds 10 billion individuals (Figure 1-1). These current global population dynamics will influence international population mobility in two ways (Hillebrand, 2007). First, the increasing size of the global population will continue to sustain present volumes and provide a growing pool of current and future migrants. Concurrently, the differential population demographics present between several economically advanced and developing nations related to aging populations and evolving birth rates will affect the need and demand for immigration in low-population-growth nations.

Changes in regional population density and growth rates affect and will continue to influence migration and population mobility (Table 1-5). Patterns of immigration and population flows reflect diverse and emerging demographic, economic, and social pressures, many of which differ from historical immigration trends (World Bank, 2008). The health and disease challenges associated with

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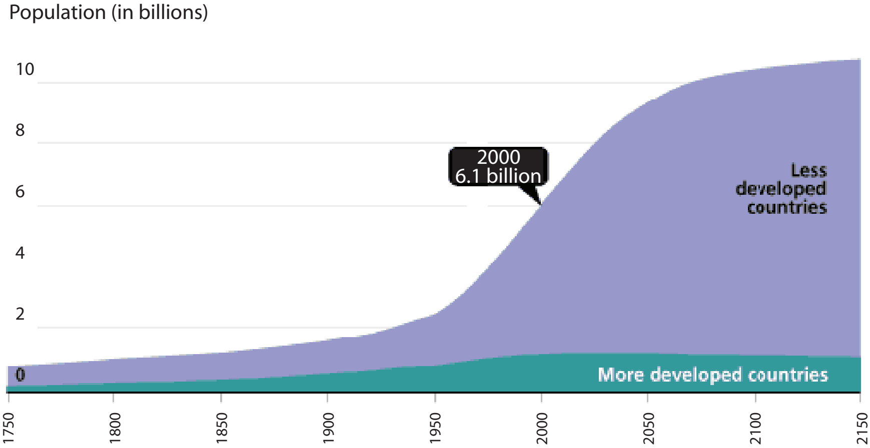


**FIGURE 1-1** World population growth, 1750-2150.
SOURCE: Reprinted with permission from Population Reference Bureau (2008b).

**TABLE 1-5** Country and Region Population with Rate of Growth

| Current Top 10 Countries by Population Size | 1950 Population, in thousands | 2002 Population, in thousands (percent growth per year) | 2025 Projected Population, in thousands (percent growth per year) |
|---|---|---|---|
| China | 554,760 | 1,294,377 (2.56) | 1,470,787 (0.59) |
| India | 357,561 | 1,041,144 (3.68) | 1,351,801 (1.3) |
| United States of America | 157,813 | 288,530 (1.59) | 346,822 (0.88) |
| Russia | 102,702 | 143,752 (0.77) | 125,687 (–0.55) |
| Japan | 83,625 | 127,538 (1.01) | 123,798 (–0.13) |
| Indonesia | 79,538 | 217,534 (3.34) | 272,911 (1.1) |
| Brazil | 53,975 | 174,706 (4.3) | 218,980 (1.1) |
| Bangladesh | 41,783 | 143,364 (4.68) | 210,823 (2.05) |
| Pakistan | 39,659 | 148,721 (5.3) | 250,981 (2.99) |
| Nigeria | 29,790 | 120,047 (5.8) | 202,957 (3) |
| **Selected Regions** | | | |
| Asia (excl. Middle East) | 1,331,636 | 3,493,424 (3.12) | 4,345,549 (1.06) |
| Europe | 548,206 | 725,124 (0.62) | 683,532 (–0.25) |
| Sub-Saharan Africa | 176,775 | 683,782 (5.52) | 1,157,847 (3.01) |
| North America | 171,365 | 319,925 (1.67) | 383,678 (0.87) |
| South America | 112,995 | 355,695 (4.13) | 460,770 (1.28) |
| Oceania | 12,607 | 31,281 (2.85) | 40,020 (1.21) |
| **World** | **2,519,495** | **6,211,082 (2.82)** | **7,936,741 (1.21)** |

SOURCE: Based on data from World Resources Institute (2009).

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these modern movements are reflective of several elements that have developed since traditional immigration health policies were conceived.

In addition to the forces of global population growth, the past five to six decades have been associated with a series of important new factors that have made the current process of migration markedly different than the traditional immigration/emigration pattern that marked most of the previous 200 years (Table 1-6).

At the global level, one of the major political influences affecting historical migration flows has been the process of decolonialization. At the end of World War II, most of Africa, a considerable part of South and Southeast Asia, and much of the Caribbean were colonial components of other nations, primarily in Europe. In 1955, the United Nations had 76 member states; by 1965 that number had risen to 117, and by 1990 there were 159 member states (UN, 2009a). Currently, there are 192 member states (UN, 2009b). Residents of previous colonies could access or avail themselves of residence in the previous colonizing power depending on location, history, and factors related to independence, and post-colonial relations (Gibney and Hansen, 2005). Several resulting post-colonial population flows established connections that changed the nature of immigration, the influences of which continue to be observed (Reynolds, 2001).

Geopolitical influences on migration continued toward the end of the twentieth century, when the dissolution of the former Soviet Union and end of the Cold War produced major changes in migration. Population redistributions that followed the end of the USSR were extensive and extended beyond Europe (Bade, 2003). The rising of the "Iron Curtain" opened new migration and travel pathways that have allowed new routes of access for migrant flows through previously restricted areas.

Another significant factor influencing modern migration that has implications for the mitigation and management of health and disease risk has been the evolution of refugee and displaced persons movements. During the Cold War, many refugee movements had significant political overtones and intercontinental

**TABLE 1-6** Major Influences in Migration Dynamics Since the 1950s

| Influences on Modern Migration |
|---|
| Differential regional population growth |
| Decolonialization |
| Availability, accessibility, and affordability of air travel |
| Speed of travel |
| Magnitude of international mobility |
| Refugee and internally displaced persons producing situations—civil, political, and environmental |
| End of the Soviet Union |
| Evolution of international labor market demands |

SOURCE: Based on data in Gushulak and MacPherson (2006).

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refugee resettlement frequently involved European populations. The geopolitical differences that marked that period of history often made these movements permanent. That dynamic began to evolve in response to the conflicts in Southeast Asia and Central Asia in the 1970s. International activities to deal with the human consequences of conflict and disaster became more internationally coordinated and more often involved the temporary resettlement of large numbers of refugees (Suhrke and Klink, 1987). These movements and resettlement programs often involve the movement of populations between locations of disparate disease epidemiology compared to that of the settlement country. In some cases, for example with the humanitarian evacuation from Kosovo in 1999, the speed of the movement exceeds the capacity of traditional screening programs, necessitating the return to "on arrival holding" and medical screening (CDC, 1999).

Modern migration patterns for refugees are also being affected by geopolitical factors. The political and ideological limits on immigration associated with the "East-West" *entente*[26] often prevented the return travel of refugees to their place of origin and hindered family reunification. Many of those restrictions are no longer relevant and travel is common by previous refugees and subsequent generations of offspring to their country of ancestral origins.

International labor migration has also changed considerably during the past four decades. Globalization and the concept of human capital as a component of an international workforce have produced extensive effects on migration dynamics (ILO, 2009). The rapid growth and contraction of economic sectors produces large flows of migrant labor and populations of temporary workers. Many of these events have occurred in locations that until recently have not been nations of immigration, such as the Middle East or East Asia. Economic opportunity also acts as a "pull" factor for disadvantaged persons seeking employment or improved living conditions. Often these are unregulated or unofficial migrant populations that can be large enough to affect national demographic indicators as seen with population flows into the United States from Mexico and Central America and into Southern Europe from Africa and Asia. Some of the greatest growth in labor demand now occurs in economically emerging nations in Asia (Zlotnik, 2003). Gender aspects of labor migration have also changed in the recent past. Modern labor migration frequently involves migrant women moving internationally or within nations from rural to urban settings.

Finally, another factor in modern migration relevant to disease control activities has been the evolution of international travel. Until the 1950s, intercontinental migration was accomplished primarily by ship. The introduction of commercial jet aircraft in 1958 triggered an abrupt shift in mode of travel (IATA, 2009). Journeys that previously required days of ocean travel could now be made in a few hours (*New York Times*, 1960). At the same time,

[26] *Entente* is an arrangement or understanding between nations regarding affairs of international concern.

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increased aircraft size and efficiency reduced costs and increased access for air travel. Current international and intercontinental movement statistics describe unprecedented levels of human travel. International transportation authorities estimate that 831 million passengers flew internationally and 1.249 billion flew within their own country of residence in 2007 (IATA, 2007). The World Tourism Organization estimated 924 million international tourist arrivals (UNWTO, 2009) in 2008. This explosive growth in air travel over the past five decades and the reduced travel time associated with this growth in volume have greatly compromised the ability of existing policies and practices based on screening and quarantine to control the international spread of infectious diseases (Bitar et al., 2009).

*How Modern Migration Will Functionally Impact on Global Health in the Future*

Activities to mitigate the risks of infectious diseases of public health significance resulting from international migration reflect the characteristics of the migratory process at the time they were developed. Basic components of historical migratory population flows were structured on a traditional linear and primarily unidirectional format based on the great migration patterns of the nineteenth and early twentieth centuries (Figure 1-2).

The characteristics of this historical immigration/emigration pattern of migration included limited or restricted migrant source regions. Most of the current immigration medical activities were developed at the time when population flows originated in Europe and some parts of Asia and ended in Europe, European colonies, or the Americas. The travel undertaken by immigrants was long and often arduous but it tended to be as direct as possible. New migrants were greeted

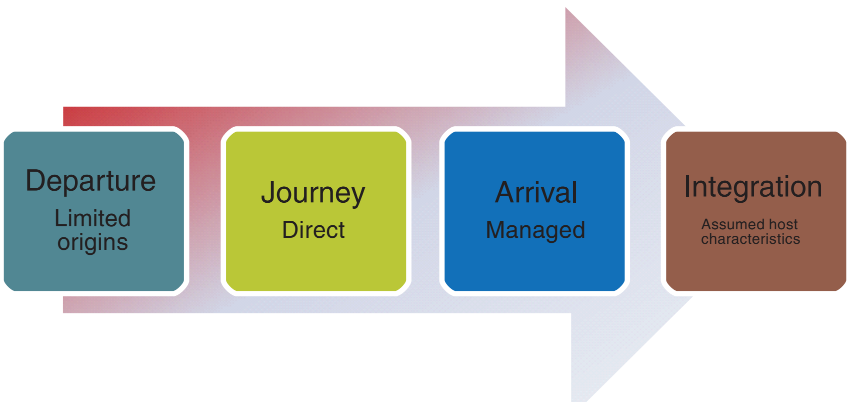


**FIGURE 1-2** Traditional pattern of migration.
SOURCE: Based on data in Gushulak and MacPherson (2004).

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on arrival by an organized system of registration, evaluation, and an assessment that frequently included a medical evaluation. While social and cultural differences present on arrival reflected the migrants' origin, it was often assumed or anticipated that the new arrivals would integrate into the host population and over time would come to reflect the characteristics and determinants of their new home. Return travel to the migrant's place of origin was uncommon either because the cost of such journeys was frequently beyond the economic capacity of the new immigrants, or because political and legal consequences for those who left as refugees prevented it.

In this immigration/emigration paradigm of population mobility, legal and administrative processes and border frontiers played an integral role in the approach to disease control. Following the long-standing approach to quarantine and sea travel, interventions were instigated on the basis of reports of illness or death during travel or the detection of illness or disease on arrival. The duration of the migrants' journey and the time required to unload the vessels and process immigrants was considered to be sufficient to allow for the presentation of significant infectious diseases, which *de facto* represented a differential prevalence risk to public health of the recipient population, to a degree where they could be detected through clinical screening.

Additional carryovers from traditional port-of-entry quarantine included directing inspection and control activities to specific populations based on social or administrative classifications of the migrant. Returning residents, citizens, or passengers traveling in upper-class situations were often exempt from medical evaluation, even if they embarked on the same conveyance and at the same location as the prospective immigrants.

Modern migration, and in particular migration patterns that have developed during the past 50 years, displays a different pattern than that of the historical precedents (Figure 1-3).

Migration in today's globalizing world can be conceptualized as a continuum of related and linked components of pre-departure, transit, and arrival phases including repeated return or onward travel. Each one of these mobility phases is associated with factors that have consequences for health and disease in both migrant and host populations through which the migrant has lived or transited. Traditional disease control processes and policies based on the historical patterns of migration are not robust enough to address the harm or benefit of the modern aspects of continuous and circular migration. The historical bases for these processes are being invalidated by modern circumstances of repetitive, rapid, and high-volume travel between origin and destination locations; varying disparities in the determinants of health between source, transit, and host destinations; and the greater international mobility of migration populations in general. This increased mobility can be observed through the migration continuum and makes the travel patterns and histories of many modern populations of migrants different than those of earlier immigrants and refugees.

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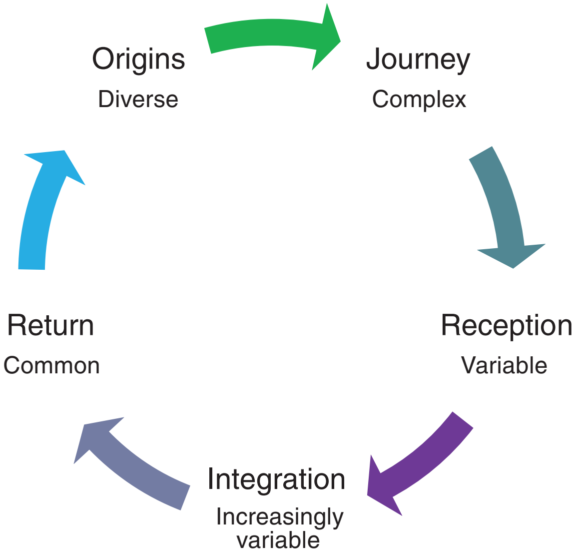


**FIGURE 1-3** Modern patterns of migration.
SOURCE: Based on data in Gushulak and MacPherson (2004).

Different subpopulations of migrants, each with different determinants of health characteristics, are represented as special populations in the numerator of the total migrant populations in the denominator. Examples of special populations include asylum seekers, illegal or irregular migrants, and those with dual or multiple citizenships. The majority of these population-based characteristics were not considered when historical immigration health practices were implemented. Health interventions and disease control practices often remained based in concept and practice on administrative or traditional definitions of immigrants and emigrants and historical linear patterns of movement.

*How Modern Migration Processes Challenge Border Disease Control Policies*

The evolution and characteristics of modern migration dynamics present three sets of challenges in the context of modern border disease control activities. The first set of challenges results from the growth in the volume of migration from increasingly diverse migrant populations, origins, and destinations. This growth has occurred against the background of sustained and in some cases increasing disparity in the health indicators, and disease incidence and prevalence levels between source and recipient regions.

In recent decades, developments in international trade and travel have been implicated in the rapid redistribution of arthropod-borne vectors or the diseases

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they transmit. Examples include extension of the yellow fever vectors in the eighteenth and nineteenth centuries; *Anopheline* mosquito malaria vectors in the 1930s (Soper and Wilson, 1943); *Aedes albopictus* and dengue (Halstead, 2007); the extension of West Nile virus infection into North America (Hayes and Gubler, 2006); and the spread of chikungunya infections in Europe (Simon et al., 2008).

The distribution of known and as yet unrecognized diseases of public health importance remains markedly variable between geographical locations, communities, and populations (Waldvogel, 2004). Some of the epidemiological gradients result from a small number of easily predicable and appreciated factors such as the distribution of vector-borne infections transmitted by geographically defined vectors. Many of the epidemiological disparities observed in other disease distributions are the product of complex relationships of many factors. The major determinants of health (socioeconomic status, genetics and biology, behavioral issues, and the environment) variably affect individual and population-based health status within and between regions and locations. These influences are themselves subject to other global events such as climate change and economic ups and downturns. International migration, by providing a population-based link that bridges those differential zones of health and disease prevalence, affects both inter-regional disease epidemiology and policies (Mackenbach, 2009). Existing policies and programs that owe their basis to the historical premises that migrants or refugees represent homogeneous cohorts will be unable to adequately mitigate the impacts of modern diverse risk profiles.

As an illustration, consider the example of two refugees, one a university lecturer from a metropolitan area, the other a displaced agricultural worker residing in a rural refugee camp, who are both admitted to the same resettlement country. Administratively, both are refugees and present situations where traditional immigration health interventions for "refugees" would be applied in a similar manner. If considered in the context of mobile population health risk assessment, the response and interventions might be different. Policies and programs designed during a time of much simpler immigration formalities may no longer be appropriate for current or future global health needs. Triggers for health interventions or evaluations based on administrative classifications of migrants and other mobile populations will not provide sufficiently robust response mechanisms to deal with the modern diversity and disparity of those populations.

The second challenge to traditional immigration health activities is a product of the technical and social evolution of the transportation industry. The epidemiological and infectious disease consequences of changes in transportation commerce are not limited to human migration but include goods and conveyances as means of moving infectious agents, diseases, and vectors (Tatem et al., 2006). The introduction of commercial jet aircraft saw the speed and volume of international travel increase as access to and affordability of air travel expanded. By the early 1960s, travel by jet aircraft rapidly became the major mode of long-

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distance travel, allowing individuals both a reduction in travel times and easier access to previously isolated locations. Although the public health implications of this revolution in travel were appreciated at the time, the full consequences of the impact of shorter travel times on the procedures and protocols in place to manage the international spread of communicable diseases did not receive great attention until the 1990s. Then, during the initial phases of the revisions to the International Health Regulations in light of the expanding knowledge about emerging and reemerging infectious diseases, the role of the border and frontier in disease control began to be reconsidered. The technical and operational challenges posed by the arrival of international travelers who could now undertake an intercontinental journey within the incubation period of infections posing international public health significance became topics of interest at the international health policy table.

The evolution of air travel also greatly expanded the number of points of international access and ports of entry for migrants and other international travelers. In 1960, for example, nearly half of all air passengers subject to U.S. quarantine inspection arrived at a single airport, Idlewild (now known as JFK Airport) in New York (McKinnon and Remund Smith, 1962). Currently there are more than 100 airports in the United States through which international arrivals can enter the country (DHS, 2003). In 2007, 831 million passengers flew internationally (IATA, 2007) and JFK Airport alone dealt with 21.5 million international passengers (Airports Council International, 2009). Individually assessing the health status of international arrivals without significantly compromising transportation, given the volumes and scope of modern international travel, are functionally and logistically huge challenges.

In the past, a relatively small number of international entry points in any region serviced the majority of new arrivals. These were usually seaports or controlled land crossings. Traditional immigration health practices were concentrated at these limited numbers of ports of entry. Extensive experience in managing the health issues of migrants was acquired by people engaged in those activities. Frequently, ancillary expertise and scientific and diagnostic capacities also became located near major seaports, as reflected in the distribution of institutes of tropical medicine, many of which developed from mariners' hospitals or care institutions.

Quarantine and immigration health practices that were based on the individual examination of new arrivals were developed to deal with the great waves of immigration in the last century. They also included facilities for the routine holding and isolation of those suspected to pose an adverse public health risk, allowing for evaluation over time. Modern patterns of migration and travel have made many of these processes and practices impractical. As the time required to complete international air travel has decreased, it is now possible to embark, complete an international journey, and clear immigration or customs formalities within the incubation period of most infections of public health importance. The

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risks of spreading previously isolated infections through air travel were anticipated and predicted as air transportation technology evolved. Disease control programs to deal with the new threats continued to be focused on international airports as isolated ports of entry. This perpetuated the premise of the national frontier as a structure to prevent disease entry (Findlay, 1946).

When immigration involves travel by ship, the time for presentation and identification of imported disease acquired during the journey has been progressively reduced as the time required to complete travel has decreased. This effect has been elegantly described in studies of measles imported to Fiji (Cliff and Haggett, 2004). The introduction of more rapid steam-driven ocean travel reduced the exposure and infection of susceptible passengers. Disease that historically had run its course prior to arrival became a post-arrival risk (Figure 1-4). This inverse relationship between the incubation period for infections and the time required to complete international travel has a direct impact on the relevance of the border as a limiting factor in disease importation. Further implications were recognized soon after the introduction of intercontinental commercial air travel. For example, this comment on irregular migration in 1949 noted the relationship between high-speed travel and incubation periods: "In view of the fact that the farthest point in the world is now within the incubation period of the major infectious diseases, illegal entry into this country by air creates a grave risk to the public health" (Gartside, 1949).

The relationships between transit time, incubation periods, and disease occurrence described in Figure 1-4 also highlight principles of international disease control. While the speed of travel allows for journeys to be completed within the incubation period of many infections, it also acts to reduce the likelihood of infection acquired during travel. Depending on factors such as transmissibility, virulence, and inoculum size, when passengers do travel while in the communicable period of an infection, the speed of modern air transportation reduces exposure time and the chance of disease acquisition by other travelers during the journey. Together these factors diminish the likelihood that new arrivals will present with clinical disease that was either acquired or developed during the journey.

The challenges posed by travel, migration, and population mobility in the context of global infectious diseases of public health significance are regularly being recognized. Several operational difficulties involved in border health interventions were apparent during the SARS-related events of 2003 (Svoboda et al., 2004). Other operational challenges are noted in contingency planning in the event of a pandemic influenza event or similar disease emergency of enhanced global public health interest (Brahmbhatt, 2005; Epstein et al., 2007; UK Department of Health, 2007; WHO, 2006). As during plague and cholera in the remote past, the Spanish flu in 1918-1920, and SARS in 2003, the implications and consequences of modern population mobility and the limitations of border containment and mitigation strategies to prevent disease importation were again both apparent and noted during the international responses to a novel influenza H1N1

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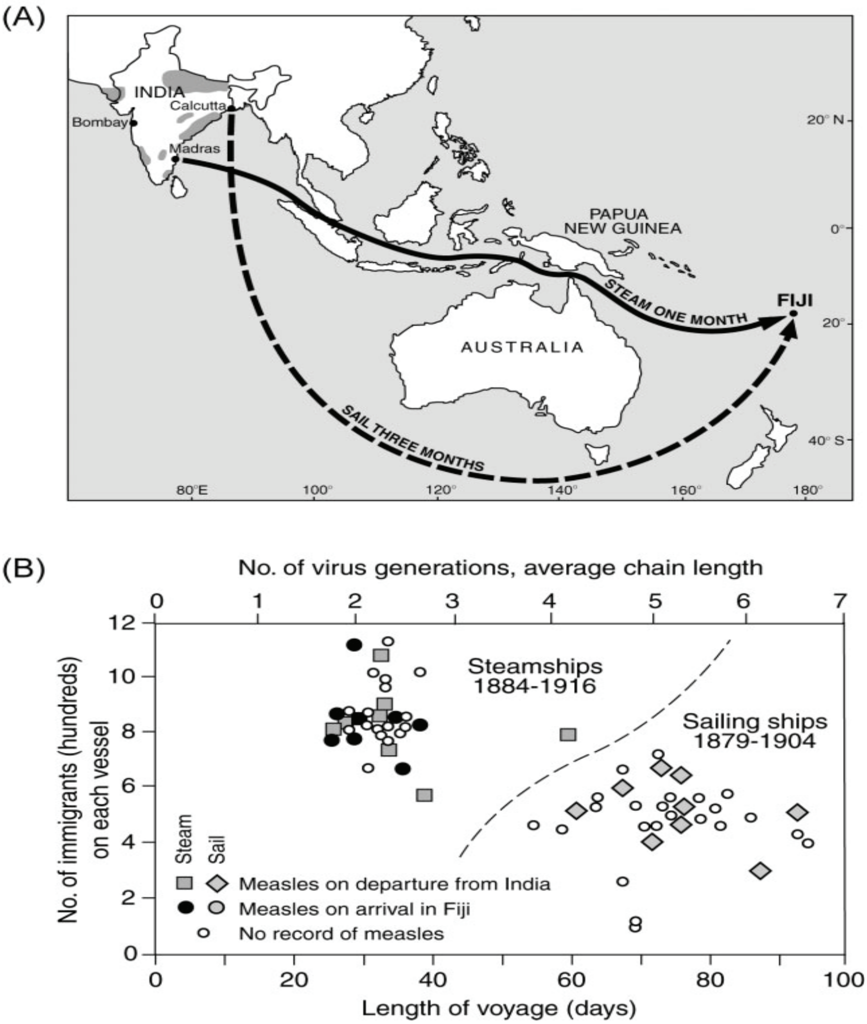


**FIGURE 1-4** Measles outbreaks associated with two modes of international travel.
SOURCE: Reprinted from Cliff and Haggett (2004) with permission from Oxford University Press.

infection detected in North America in March to April of 2009 (Barry, 2009; Khan et al., 2009; WHO, 2009a).

Border-associated technological solutions designed to reduce the introduction of important infections during urgent public health situations have been considered. Some border screening solutions were introduced as components of

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the international SARS control response but analysis of these solutions has not been favorable (Samaan et al., 2004; St. John et al., 2005). In spite of recommendations to the contrary by the World Health Organization (WHO, 2009b), border containment strategies were applied by some nations during the initial phases of the 2009 influenza H1N1 pandemic (SOS International, 2009). At the time of this publication, the cost, impact, and potential effectiveness, or lack thereof, related to these interventions have not been evaluated.

The third aspect of modern migration that exceeds the intent and capacity of traditional immigration and border health policies results from changes in migration patterns themselves. The evolution of migration from a linear, unidirectional pattern to a more continuous and circular pattern of modern population mobility has not been accompanied by policy or programmatic design to accommodate these and future changes. Current social and economic factors facilitate and support the increasingly frequent and recurrent travel by resettled migrants between their new home and other locations, including their place of reference. Their place of reference may be their country of birth, political or faith-based affiliation, education, ancestral migration, spousal or offspring association, or future opportunity. This modern type of travel involves the migrants themselves and other members of their families, including children born to new immigrants after their arrival. The latter movements are known as travel to visit friends or relatives ("VFR travel"); although originally used as an economic measure of travel, trade, and the foreign-born diaspora, it is an area of increasing interest in the travel medicine and global public health sectors (Angell and Cetron, 2005; Leder et al., 2006). The importance of VFR travelers and similar risk-profiled travelers in the context of disease control and mitigation policies and practices for all migrants are the gaps between defining the intent of travel and evaluation of the risk assessment and outcome profiles (Behrens et al., 2007). The completion of administrative and legal immigration formalities brings to an end most immigration health requirements. Some individuals who change their status after arrival or who were noted on immigration screening to have medical concerns may be required to undergo further medical follow-up, but the majority of these cases cease to be subjected to immigration health attention.

Under usual circumstances of post-landing, arriving populations become part of the host population in terms of public health consideration. There is increasing concern that the travel and mobility characteristics of some migrant cohorts differ from those of other components of the domestic population. Interventions and risk mitigation efforts directed at reducing some travel-associated disease risks may be more important in "VFR-like" and other migrant travel situations, but national public health program and policy aspects may not reflect these needs. As populations of recent migrant origin travel more frequently, they may represent mobile populations at differential risks of disease.

Other aspects of the circular and recurrent patterns of migration extend beyond the traditional aspects of migration health. The globalization of com-

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merce, communication, and the immediacy of interconnectiveness that is supported and enhanced by current technology and transportation facilitate the social and cultural continuation of practices, beliefs, and activities. Many of these bridge disparities in health-related events between migrant origin and destination locations. Most of the health implications of these linkages are related to epidemiological differences and disparities between the locations. Relevant disparities in this context go beyond the personal determinants of health and include the control and regulation of food, nutritional, pharmaceutical, and medical products, practices, and activities, in addition to other broader societal, environmental, and behavioral factors.

Modern technology and transportation allow many migrants access to goods and services available outside of their new place of residence. Increasing ease of access provides linkages between divergent systems of international regulation, surveillance, and control standards that vary between locations. Some migrant communities represent markets for the continued importation of traditional foods, pharmaceutical products, and traditional medical practices. Some of these can be associated with the international introduction of infectious diseases or other risks. The international trade in noninspected or nonregulated foodstuffs and traditional therapies is extensive. The acquisition and preparation of bushmeat, for example, may be associated with the exposure to and potential emergence of zoonotic infections (Wolfe et al., 2005). While consumption of the product represents less risk, the importation of bushmeat may also be associated with the importation of human and animal infections. It is estimated that as much as 15,000 pounds of bushmeat may be imported into the United States monthly (Barry, 2007).

Migrants, their families, and other mobile populations may also return to familiar locations to receive medical care and treatment. When those services are provided in locations where infection control, pharmaceutical standards (Primo-Carpenter and McGinnis, 2009), inspections, antibiotic management, and medical and surgical treatment practices may not be regulated or under stringent standards (Yankus, 2006), the risk of acquisition of unusual or resistant infections and subsequent introduction into their new place of residence is present.

### Modern Migration and Global Infectious Disease Surveillance and Control

Attempts to mitigate the impact of migration on the international epidemiology of infectious diseases can be considered in the classic relationships between the host, organism, and environment. Each can pose specific challenges for source, transit, and recipient countries when health outcome determinants have components that arise beyond the national borders where direct control might be exerted.

Pre-departure medical examination and assessment of some classes of immigrants, refugees, or certain cohorts of visitors from designated countries is practiced by nations with long-standing immigration programs, such as

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Australia, Canada, New Zealand, the United Kingdom, and the United States. Other nations may require the routine examination of some migrant or refugee groups after arrival. Depending on the nation and situation, the medical evaluation of migrants may be voluntary. The health assessment approach for nontraditional migrants such as asylum seekers, long-staying visitors, temporary workers, international students, and illegal or irregular migrants is even less well defined or practiced. The result is an international collection of diverse processes, many of which are rooted in old paradigms and protocols of traditional immigration health.

The historical focus of international regulations and disease control has been on a list of specific conditions or microorganisms. This belies the complexity of the nature of transmissible infectious diseases that must include consideration of multiple microbial organism factors, such as incubation period, patency, latency, chronic infection and infectious states, transmissibility, virulence, and infectious and noninfectious sequelae. The characteristics of microbial contagiousness and virulence for human beings, and the availability of effective diagnostic, therapeutic, and specific preventative interventions, such as antibiotics or vaccines, have been more recent considerations in the international disease control approach. System characteristics, such as clinical and public health services for surveillance, detection, confirmation, notification, and the requirement for timely and effective international response further complicate shifting the paradigm from its origin in simple screening of disease for the purpose of preventing the admission of disease.

Medical screening for disease exclusion, supported by national legislation and regulations, on the basis of danger to public health (Gushulak and MacPherson, 2000) is being supplanted in importance and investments by global infectious disease surveillance and emergency preparedness. Interest in infectious disease threats and risks due to potential events such as avian influenza adapting to human hosts, or a globally significant pandemic influenza, have been augmented by concerns regarding new threats. Modern preparedness strategies now include considerations related to novel virulent pathogens occurring in nature or organisms that are malfeasant in design and unleashed on a susceptible population. Most of this interest originates in low prevalence, but threat and risk intolerant countries.

Against a background of endemic outbreaks of largely enteric or respiratory transmitted diseases in economically advanced countries is the risk of imported diseases. Outbreaks of enteric diseases presenting with acute illness, such as salmonellosis or botulism, largely occur due to contaminated food or food products (CDC, 2009a; Sheth et al., 2008; Wachtel et al., 2003). Hepatitis A outbreaks in low-prevalence regions brought in by nonimmune migrants with secondary spread have also been described (Heywood et al., 2007).

Short-incubation respiratory infections that manifest with typical clinical symptoms have grasped international public health attention in the post-SARS and avian-to-human influenza period of the last decade. Equally, the fear of a

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pandemic influenza event has generated global surveillance and emergency preparedness investments of an unprecedented magnitude (Gottschalk et al., 2009). Beginning in April 2009, pandemic influenza preparedness planning was tested in response to what had become, by June, the 2009 H1N1 influenza pandemic (WHO, 2009c). Systems and procedures developed to deal with pandemic influenza were employed and utilized during the recognition phase of the disease and subsequent international surveillance activities as the infection spread locally across the planet (Trifonov et al., 2009). Modern diagnostic and information technologies were extensively utilized as part of or in parallel to these surveillance undertakings allowing for an almost "real-time" monitoring of a developing global infection (Brownstein et al., 2009). Information response resulted in pandemic contingency conceived and developed for more virulent infections and serious disease undergoing evolutionary modification (Miller et al., 2009). At the same time, in spite of the same information base, national responses and interventions at frontiers and borders continued to vary depending on national plans, requirements, and mitigation strategies. "Real-time" pressures within the existing regulatory frameworks precluded deliberate risk assessment discussions within health and between health and other international sectors.

Against this background, "normal" diseases of public health importance, such as vaccine-preventable respiratory viral infections like influenza, mumps (CDC, 2006), and measles (CDC, 2008b), are also regularly reported as imported events with secondary transmission in local populations.

Chronic infections, infections with prolonged latent periods, and infectious with noninfectious consequences are emerging as important phenomena related to migration and may offer unique opportunities for effective mitigation and control. In nations where long-standing public health activities and programs have been effectively implemented and supported, several infectious diseases of previous historical importance are now present in low or very low prevalence levels. Migrants and mobile populations arriving from less-advantaged locations where the prevalence of these infections remain elevated may represent population cohorts posing increased personal and public health risk of disease compared with elements of the domestic or host population (Barnett and Walker, 2008; Falzon and Aït-Belghiti, 2007; Palumbo et al., 2008; Stauffer et al., 2008).

In situations where domestic prevalence disease rates are very low, the sustained arrival of migrant populations from endemic regions will affect the epidemiology of the infection at the destination. Chronic enteric infections, including *Taenia solium* (Schantz et al., 1992), *Strongyloides stercoralis* (Boulware et al., 2007; Robson et al., 2009), and others may take decades to present clinically or only present through detection of secondary transmission (Hotez, 2008; Moore et al., 1995). The changing incidence and disease nature of tuberculosis infections in immigrant-receiving nations is another example of delayed presentations of diseases of public health significance due to chronic states and latency (CDC, 2009b). Similar observations have been made for several other chronic infec-

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tions; hepatitis B (CDC, 2008d), Chagas disease (Milei et al., 2009), malaria (D'Ortenzio et al., 2008), and schistosomiasis (Salvana and King, 2008).

Existing immigration health-related disease control policies with the historical focus on specific infections of acute epidemic potential or acute transmission do not accommodate chronic diseases or the consequences of infectious diseases. In spite of the importance of all of these infections in terms of national and international public health, an accurate measure of the impact of chronic infectious diseases and their consequences can be hard to obtain. Examples include *H. pylori*-related gastric carcinoma (Ohno et al., 2009) and hepatoma resulting from chronic hepatitis infections (Gupta and Altice, 2009; Kim et al., 2008; Umemura et al., 2009) arriving with migrants. The nature of latent or chronic infections is such that the presentation frequently occurs long after the period of travel that brought the infected migrant to the new destination. As a result, the majority of those presenting with clinical disease are individuals who have completed citizenship formalities and, unless diseases are tracked by the patient's place of birth, the relationship to travel and migration may be lost.

For all of these factors, disease surveillance and global public health intelligence alone (WHO, 2009d,e) have been and will continue to be inadequate to control the threat and risk of importation of diseases of public health importance. As advocated by international public health experts, greater inter-regional openness and collaboration are essential to achieve the goals of global emerging infectious disease prevention and control (NIC, 2008). These ideals require shared technical expertise, commonality in definitions, visionary policy approaches that encompass and embrace disparate environments, and an explicit recognition that diverse populations on the move are utilizing multiple processes during relocation that do not follow traditional concepts.

### Shifting the Paradigm: Population Mobility Globalizes Health Disparity

The nature and context of modern migration is currently at the interface of several related determinants of health (socioeconomic, behavioral, genetic and biological, and environmental) and globalization (trade, technology, telecommunications, and travel). Our understanding of the inter-relatedness and dependency of these factors continues to develop since the policies and programs designed to mitigate disease risks in migrants were designed. The majority of those traditional, policy-driven practices have become compromised or operate at the limits of validity.

#### *The Border Is Irrelevant as a Barrier to Disease*

The speed of travel and the volume of human mobility have combined to render political frontiers of marginal use in the context of international disease control. Globalization has seen the trade and commercial sectors work toward

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seamless borders and the greater facilitation of movement and the exchange of goods and services. However, many public health control policies remain nationally focused and sustain principles based on the political or administrative frontier as a disease-limiting tool (Kicman-Gawłowska, 2008).

The demise of the border as a filter for the admission of infectious diseases has in parallel led to a situation where mitigating the risks of imported infections has become shared across the health sector. The fact that imported or travel-associated disease events are now more likely to present away from the border generates new demands on national health services at the very local level. Clinical awareness, diagnostic capacity, treatment, and management capabilities to deal with imported infections are now needed universally. This has implications and consequences for health educators, providers, certification, and regulatory bodies involved in health services. This explicitly requires engagement of policy makers and contingency planners.

As national borders have become less effective limits to the international spread of infectious diseases, an effective public health response assumes greater international importance. Solutions and strategies to prevent and respond to the threats and risks of the spread of diseases between disparate environments must expand beyond national perspectives. Globalization of risks needs to be met with coordinated international responses and preparedness. Increasingly integrated, multipartnered programs and activities have been created to more efficiently deal with global infectious disease risks. Similar approaches are needed to address the current and future pressures of migration and international disease control. The challenge will require a paradigm-shifting reconsideration of the policies and programs based on the historical perception of the role of the political border as a barrier to disease. Critical and comprehensive analysis and evaluation of national and international responses to the 2009 H1N1 influenza pandemic will be essential if important shifts in approaches are to be achieved related to global health considerations and international population mobility.

### *Public Health Challenges Increasingly Arise Beyond the Jurisdiction of Local Control Authorities*

Traditionally public health control activities responded to situations by addressing the current event while acting in a coordinated manner to prevent its recurrence or eliminating its source. Commonly, municipal, civic, and provincial or state programs evolved as part of broader national policies designed to ensure and maintain health standards and reduce levels of risk across the country. Since the mid-eighteenth century, international regulations for disease control were limited in scope to a defined list of specific infectious agents or diseases. The management and control was left to individual nations with the consequence that control activities would vary related to national levels of development, resources and capacities, and perception of risk.

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Disparities in public health capacities are often indirectly proportional to corresponding disease prevalence patterns. The domestic transmission of several historically significant infections has been eliminated in many economically advanced nations. These infections remain at higher prevalence in other locations. Against this growing pattern of disparity in prevalence, globalization and population mobility are actually increasing the risk of international disease transmission (Elefsiniotis et al., 2009; Enserink, 2007; Hinman et al., 2004; Payne and Coulombier, 2009; Stark et al., 2008).

The result often requires that public health agencies invest more resources in the control of local events that are arising beyond the jurisdiction of domestic control authorities. The solution is an integrated response to the globalization of disease risk as standard components of domestic prevention, mitigation, and control strategies. The prudent investment in public health interventions at the source of the event for primary prevention, mitigation, or control may be more effective in terms of both resources and outcomes than secondary control attempts in other locations (Schwartzman et al., 2005). Cost-effective methods that exist for meeting these challenges will require a greater international policy commitment and diversion of program resources away from nationally focused activities toward integrated globally applied interventions.

### *Health Aspects of the Evolution of the Immigration/Emigration Paradigm*

In order to more effectively address the modern nature and scope of global migration, historically based policies and program approaches based on traditional patterns of immigration need to be revised. The dynamics of the flow of individuals and populations across disparities in the determinants of health and outcome measurements are the source of all adverse public health outcomes related to the international spread of infections. Policies, processes, and programs intended to manage these events need to encompass an approach to risk that is wider than the current specific disease or administrative class of migrant models currently in use.

Considering mobility as a determinant of global health provides a model upon which integrated disease management policies, processes for prevention, knowledge of disparate prevalence environments, and a rigorous health threat to risk assessment ability can be designed and implemented. Policies and programs intended to mitigate the risks of disease importation through migration would be more logically based on current factors or future modeling more directly related to risk and undesired health outcomes rather than specific diseases or historical patterns of immigration. The need to increase the flexibility of traditional disease list-based control methodologies to more effectively meet modern approaches to threat-risk assessment is reflected in the 2005 revision of the International Health Regulations that created a greater expectation on national surveillance and international reporting. This approach to public health, of course, is not enough

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without integrating within health and between other sectors of global society including health systems and services, occupational and labor health, security, economics and trade, agriculture and food management, and the environment.

A process of creating more effective tools with the capacity to meet as yet undefined or emerging threats has become a cornerstone of international public health preparedness and response. Extending the process into the sphere of migration health is strongly supported by empirical evidence, recurrent international experience, and projections of the importance of population growth and mobility for the future of global health.

### New Approaches for Migration and Disease Control

It is apparent that human migration will continue to be an important component of global infectious disease distribution. Population migration, disparate health system environments, and gaps in disease prevalence will both continue and probably grow as components of international disease spread over the near and medium term. As migration expands, the need to plan and prepare to deal with the associated infectious and noninfectious disease consequences of population mobility will become interests of more nations and health authorities. Reflecting that growing interest, the health of migrants was the subject of recent EU discussions in Portugal and a resolution at the WHO World Health Assembly in 2008 (WHO, 2008). The convergence of the increasing need to address the issues and the expanding awareness of the importance of health related to global migration provide an opportunity to modernize and revise policies and programs that are no longer effective.

Those revisions will require and benefit from the following undertakings:

- **An integrated approach to migration health threat to risk assessment, analysis, and interpretation.** Global health policies will need to reflect the dynamics, diversity, and disparities that are associated with the demography of modern migration and population mobility. Threat to risk assessment practices need to be more complex and inclusive of outcome determinants rather than being based on administrative migrant class or disease lists. This risk management approach to meeting the disease challenges of migration will better direct resources where benefit can be expected and have the potential to reduce unnecessary practices in low-risk situations. This meets the intent of the International Health Regulations while adhering to standard population and public health principles.

  The United States has recently begun moves in this direction. Centers for Disease Control and Prevention (CDC) guidelines for the immigration medical examinations of foreign nationals have been amended to incorporate more flexible, risk-based approaches based on epidemiological and

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other factors (CDC, 2008c). These changes provide increased capacity to immigration medical screening to be aligned with situations constituting a public health emergency of international concern that require notification to WHO according to the International Health Regulations.

- **Functional approach to borders and boundaries.** The potential for international spread of infectious diseases in association with migration remains a component of a world that contains health disparities and is ever more linked through mobile populations. Political boundaries are increasingly less effective components of control programs and policies. Any new or modern approaches to migration health and infectious disease control will need to address that reality.

  Migration and population mobility globalize risks that have in the past frequently remained isolated. As high-speed travel provides the opportunity for larger numbers of people to move between health disparities, the concept of the global village increasingly extends to the health care sector. While serious acute events of international public health significance are rare, sustained high levels of migration do affect the epidemiology of several infections in those nations transiting or receiving migrants. This has effects on the clinical awareness of health service providers and the need to consider rarely encountered diseases. It also expands the demands for diagnostic and management capacities that historically have been limited in distribution or location.

  The globalization of risk resulting from the fading role of the national boundary will mean that the education and training of health care providers will need to focus more attention on the global aspects of migration health (Boulware et al., 2007). Health services and public health systems must support investigative capacities extending further into the health care delivery sector to support clinical services and international public health.

- **Modeling migration health on other coordinated international actions.** Individual national programs, particularly when they are directed toward threats and risks that originate beyond their areas of jurisdiction, may have some role in dealing with the secondary effects of those risks. In terms of primary prevention, these approaches will be predictably ineffective. Coordinated international efforts are now essential in any attempt to control diseases of global public health significance. Local and national activities must continue but as components of integrated multilateral mitigation strategy. Migration health control activities could easily follow that pattern. National immigration and citizenship legislative and regulatory requirements make it unlikely that nations that require immigration health

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> interventions will reduce or eliminate those requirements. Those policies and programs could be easily integrated into global strategies supporting improved migration-associated disease control (Cattacin and Chimienti, 2007).
>
> Immigration health screening, for example, when it is undertaken by those nations who require it for national legislative purposes, could be integrated into other global health activities. Currently, in excess of two million individuals undergo routine immigration medical evaluation annually for resettlement. While limited to specific infections and certain migrants, the information is presently used only for national immigration requirements. Supporting global tuberculosis activities is an obvious example; the majority of nations who utilize immigration health screening have elements of tuberculosis screening in their programs. The aggregate use of this and similar data could be used in conjunction with other global public health activities. Other potential activities include international collaborative longitudinal studies of migrant health outcomes. Such studies using standardized methodology and definitions could significantly improve knowledge regarding the outcome of chronic or latent infections in migrants.

### Conclusions

Designed to prevent the introduction of a limited list of diseases of historical public health significance that arose beyond national boundaries, most immigration health activities play at best a minimal role in international disease control activities in the modern context. While required by some immigrant-receiving countries' national legislation, they are often based on the historical quarantine-derived strategies of exclusion and isolation, principles that for the most part only represent population-based public health approaches in very limited circumstances. The world public health community remains challenged by a variety of disease threats, several of which are intimately associated with population mobility.

Recent awareness of the implications of local disease events for global health has prompted the revision and reconsideration of some of the basic historical principles behind organized disease control (Cetron and Simone, 2004). Some of the migration-related aspects of that revised regulatory methodology originate from the same historical approaches to disease control and are subject to many of the same weaknesses that prompted the revision of the International Health Regulations in 2005. Migration in its modern mobility-derived context plays an increasingly important role in the global epidemiology of infectious diseases and that role will continue as long as disease disparities exist and populations link high-prevalence to low-prevalence regions through mobility.

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Considering population mobility as a determinant of global health has implications for the systems required for prevention, mitigation, and control of serious events of global public health significance. Addressing the health implications of population mobility will also assist global public health activities through the reduction of population-based health disparities in prevalence. Reducing those primary prevalence differences decreases the likelihood that movement of people between those environments will link the differences.

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# 2

# Travel, Conflict, Trade, and Disease

## OVERVIEW

The essays collected in this chapter examine how travel, armed conflict, and trade move people—as well as animals, plants, and products made from them—and how these movements influence patterns of infectious disease transmission. The discussion begins with an exploration of the role of the global traveler in the emergence of infectious disease by workshop speaker Mary Wilson of Harvard, who illustrates the profound impact of recent increases in the volume, speed, and reach of global travel. "Humans can reach almost any part of the earth today within the incubation period for most microbes that cause disease in humans," Wilson writes. "Travel is also discontinuous, often including many stops and layovers along the way. This means that travelers are part of the dynamic global process of moving biota, along with trade, which moves plants, animals, and other materials." Moreover, she observes, several other trends—including growth in human and food animal populations and urbanization—further contribute to infectious disease emergence.

Travelers can serve as sentinels for disease, and thereby contribute to the global disease surveillance system, as Wilson demonstrates through key findings by the decade-old GeoSentinel Surveillance Network regarding transmission of falciparum malaria and dengue fever. The network gathers information on ill international travelers and migrants from 42 travel and tropical medicine clinics on six continents in order to provide early alerts about unusual infections or infections in unusual locations or populations. Studying travelers can help characterize "global microbial traffic," Wilson concludes.

Travel, migration, and displacement are significant characteristics of armed



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conflict that contribute to increased risk of infectious disease. Certain categories of infectious diseases tend to increase during war, according to workshop speaker Barry Levy of Tufts University; these include diarrheal diseases and acute respiratory infections, as well as measles, malaria, meningococcal disease, and tuberculosis. In the chapter's second paper, Levy discusses major causes—apart from injury—that contribute to the increased incidence of infectious diseases during wartime: reduced availability of health services, environmental damage, and forced migration. Interestingly, Levy notes that whereas one might expect HIV transmission to increase during war due to concomitant increases in several risk factors for its transmission, "several studies have demonstrated that HIV incidence has generally decreased during war—only to increase again after conflict has ended." Moreover, he adds, "there have been many successful HIV/AIDS prevention and treatment programs during armed conflict."

Absent the cessation of armed conflict, the war-related burden of infectious disease can be addressed through attention to specific war-associated risk factors, as well as through a host of measures (e.g., surveillance, preparedness) that apply to any high-risk situation, Levy explains. He also notes the importance of protecting health care workers and preserving health-supporting infrastructure, which may be supported by maintaining their neutrality both during war and in its aftermath.

Like travel, globalized trade is vast, rapid, on the rise, and a significant risk factor for infectious disease emergence. In the chapter's third essay, workshop speaker Ann Marie Kimball, of the University of Washington, and co-author Jill Hodges present case studies of several emerging infectious diseases, including H5N1 influenza and bovine spongiform encephalopathy (BSE), and their relationship to "risky" trade practices in food production and medicine. "While microbial risks have been globalized along with commerce, the corresponding health and protective measures for the most part have not," the authors observe. The International Health Regulations (IHR) 2005 "provides some important safeguards to help limit the international spread of infectious disease," they note, but these regulations require support for both capacity building and community building if their intent is to be fulfilled.

Responding to some of the disease threats described in the previous three essays is the daunting task taken on by workshop speaker David Acheson of the Food and Drug Administration (FDA). He describes the agency's response to two recent challenges to the security of the U.S. food supply—the 2008 outbreak of *Salmonella* Saintpaul and the deliberate contamination of imported wheat gluten with melamine—in his contribution to this chapter. He also discusses changes in FDA's food security efforts to respond to such threats by seeking to understand where and when they arise, to anticipate their potential to spread globally, and to use risk-based inspections to detect them before an outbreak occurs in the United States; these include efforts under way to increase the FDA's presence in foreign countries, to develop model systems for risk-based inspections, and to make use

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of inspection and testing data generated by industry or other "third parties" to increase the breadth and depth of their surveillance.

## GLOBAL TRAVEL AND EMERGING INFECTIONS

*Mary E. Wilson, M.D., F.A.C.P., F.I.S.D.A.*[1]
Harvard University

Humans travel in numbers and at speeds unprecedented in history (IOM, 2003; Wilson and Chen, 2008). Travelers visit remote areas as well as major population centers. Humans may be displaced because of social, economic, or political upheavals or extreme events and environmental disasters (IOM, 2008). The elimination of spatial and temporal barriers, especially by long-distance air transport, means that humans can reach almost any part of the Earth today within the incubation period for most microbes that cause disease in humans. Travel is also discontinuous, often including many stops and layovers along the way. This means that travelers are part of the dynamic global process of moving biota, along with trade, which moves plants, animals, and other materials (Wilson, 1995b). Natural movement of animals via migration, and transport of seeds, microbes, and other materials via water and air currents, is the backdrop against which massive travel and trade are occurring in today's world (Wilson, 1995a). One consequence of this movement is the juxtaposition of species that have never before had physical proximity. The contact between microbes, humans, and animals may result in infection, which may or may not be expressed in disease or death.

Another potential consequence of the movement of species, such as arthropods, mammals and other animals, and plants, whether intentional or inadvertent, is the establishment of species in new geographic areas (Tatem et al., 2006). These introductions may cause major changes in the existing ecosystem, including marine ecosystems. Many examples exist of the harmful effects of invasive species, though many species of well-regarded plants and animals in the Americas were not native to the Americas (Crosby, 1972).

### Characteristics of Global Travel

Global travel has increased as reflected in Figure 2-1, showing numbers of international tourist arrivals from 1950 though 2005 and the projections until 2020. In addition to the marked increase in the overall number, there has also been a shift in areas visited by travelers, especially to areas in Asia. The 2006 figures from the World Tourism Organization showed the most rapid relative increase was to sub-Saharan Africa (UNWTO, 2008b). Travel between regions

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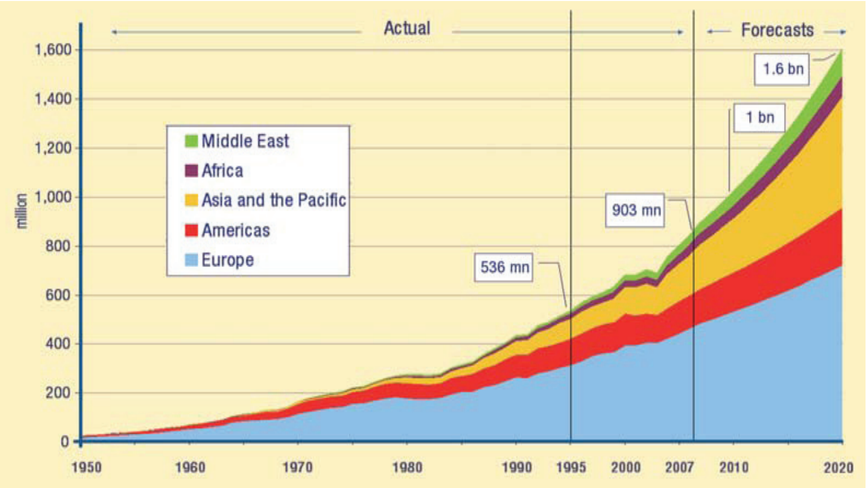


**FIGURE 2-1** International tourist arrivals by region (in millions), 1950-2020.
SOURCE: Reprinted with permission from UNWTO (2008a).

was increasing faster than travel within regions, and air transport was growing at a faster pace than ground and water transport. Figure 2-2 shows the breakdown by means of transport, with air travel accounting for 46 percent of transport (UNWTO, 2008). The shifts in destination mean more people will be traveling to low-latitude countries—areas with greater species richness (Guernier et al., 2004) and often characterized by poor sanitation and limited infrastructure, a milieu where risk for exposure to common and previously unidentified microbes may be higher. In looking ahead, it is unclear to what extent the current dramatic changes in the global economy will affect numbers of travelers or favored destinations. Political instability and disease outbreaks can also influence travel destinations, sometimes abruptly.

A vivid example of the rapid increase in travel is the outline of lifetime tracks by David Bradley (1989; figure also reproduced in Cliff and Haggett, 2004), who recorded the life travel over four male generations in his own family (Figure 2-3). The linear scale for the spatial movement increases by a factor of 10 for each generation (Cliff and Haggett, 2004). Similar findings were noted in a study which showed that spatial mobility, taking into account all forms of transportation, of the French population between 1800 and 2000 increased 1,000-fold (Grubler and Nakicenovic, 1991). Using numbers from the U.S. Census Bureau and the United Nations World Tourism Organization (UNWTO, 2008c), one can calculate that the world population between 1950 and 2007 increased 2.6-fold, whereas the international tourist arrivals increased 35-fold. Although individuals

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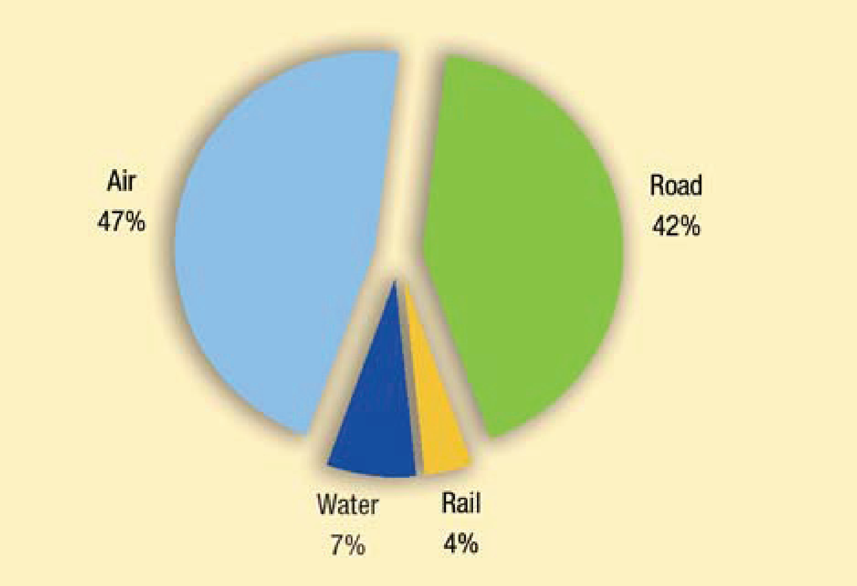


**FIGURE 2-2** Inbound tourism by means of transport.
SOURCE: Reprinted with permission from UNWTO (2008a).

on average are traveling much greater distances, González and colleagues found that individual human trajectories showed high degrees of temporal and spatial regularity, with individuals returning to a few highly frequented locations (González et al., 2008).

*Population Size, Density, Location, and Proximity to Animals*

This increase in human movement is not occurring as an isolated event. Today, the global human population is the largest ever recorded—and so is the population of food animals. About half of the people on Earth live in urban areas, the largest fraction ever (Wilcox et al., 2008). These human hosts provide expanded opportunities for viral replication and mutation events. Most of the population and projected growth are in low-latitude urban areas—regions that are home to sprawling megacities, many surrounded by vast slum areas that lack clean water and sanitary facilities (Figure 2-4). Animals such as dogs, chickens, cows, and rats live in and near human living quarters, which have been assembled from whatever materials can be found. Individuals who inhabit these areas often work in major metropolitan areas, so they have regular contact with large, dense human populations in high-rise buildings and other built environments. Residents

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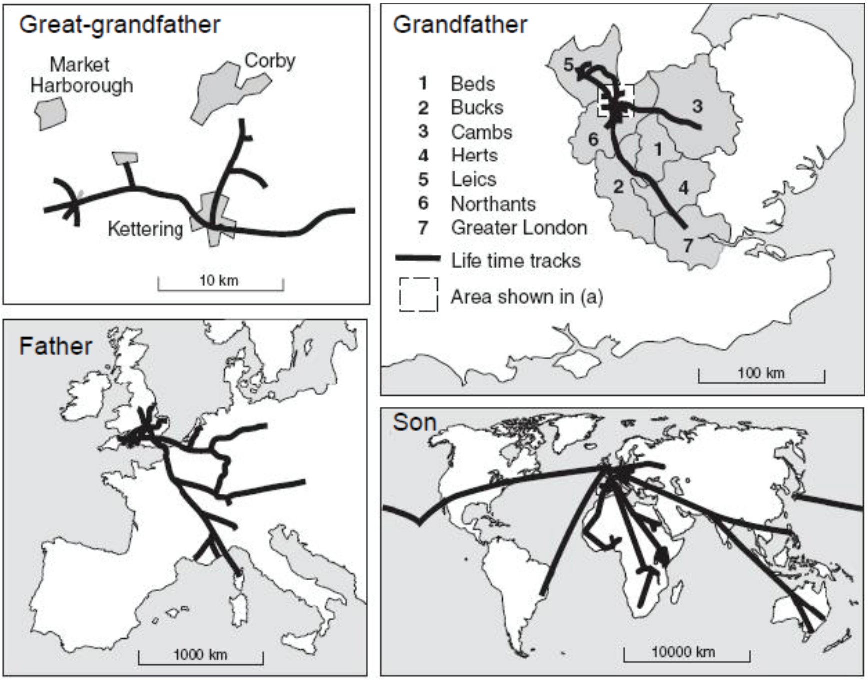


**FIGURE 2-3** Life travel over four male generations in the same family.
SOURCE: Adapted from Bradley (1989) and reprinted from Cliff and Haggett (2004) with permission from Oxford University Press.

of periurban slums may also visit family in rural areas, thus potentially providing a link from rural to urban populations and to the rest of the world. Changes in the environment, including extreme weather events, can favor the appearance of some infections and can also displace populations (IOM, 2008).

Animals have been the origin of many of the recently identified emerging infectious diseases, including HIV/AIDS, H5N1 avian influenza, severe acute respiratory syndrome (SARS) (Jones et al., 2008; Wang et al., 2008), and swine-origin H1N1 influenza A (Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team, 2009; Smith et al., 2009a). Populations of animals have expanded rapidly, in large part to accommodate the desire for more animal protein in the diet, which has coincided with the economic resources to buy it. In China, for example, at the time of the 1968 influenza pandemic, the size of the human population was 790 million, the pig population 5.2 million, and the poultry population 12.3 million. By 2005, while the human population in China increased less than two-fold, the pig population increased about 100-fold to 503 million and the poultry population increased 1,000-fold to 13 billion (Osterholm, 2005).

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**FIGURE 2-4** Juxtaposition of urban slums and modern buildings in São Paulo, Brazil.
SOURCE: Image courtesy of Zema Fontoura.

Concentrated animal feeding operations, where large numbers of genetically similar animals are raised in concentrated areas—so-called factory farms—are becoming increasingly common in the United States and other countries (Pew Commission, 2008). Unfortunately, little systematic surveillance of influenza and other potential pathogens in swine populations is routinely done, a shortcoming highlighted by the emergence and spread of a reassortant influenza in 2009 (Smith et al., 2009a).

*Roles of the Traveler*

Human travelers can easily carry person-to-person transmitted infections to any part of the world. An example is the human immunodeficiency virus (HIV), which was introduced to all areas of the world almost exclusively by travelers (Perrin et al., 2003). Recently, swine-origin H1N1 has spread globally, its movement hastened by global air travel. Although drug-resistant forms of tuberculosis can emerge in settings with inadequate and inappropriate treatment regimens, humans also transport and transmit tuberculosis, including multidrug resistant (MDR) and now extensively resistant (XDR) forms of tuberculosis, in geographic areas far from the point of acquisition (Jassal and Bishai, 2009; Oeltmann et al., 2008). Although tuberculosis is an old disease and is present worldwide,

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the incidence of infection and the levels of drug resistance vary enormously by population and geographic area. In 2008, the overall incidence of tuberculosis in the United States was 4.2 cases per 100,000 population (CDC, 2009). The rate in persons who were foreign born was 10 times higher than the rate in persons who were U.S. born, reflecting the vast differences in rates of tuberculosis around the world. A number of countries have annual incidence rates exceeding 300 per 100,000. Figure 2-5 displays the geographic spread of XDR tuberculosis between December 2006 and June 2008.

The traveler can serve in many roles (Wilson, 2003). Nonimmune travelers are at risk for a number of infections that exist primarily in tropical areas. Vaccines and drugs are available today to reduce the risk for many of these infections, such as yellow fever and malaria. Travelers were important historically in the spread of infections and remain so today, perhaps to an even greater extent (Colizza et al., 2006). They can also carry microbes with resistance genes, even if they are unaware of it. Travelers today continue to spark outbreaks of measles in populations that do not have high levels of immunity. It is easy to see how travelers could play a key role in the global epidemiology of infections that are transmitted from person to person, such as HIV, SARS, tuberculosis, influenza, and measles (Hufnagel et al., 2004), but they are also important in the spread of some vector-borne infections, as will be discussed below.

*Receptivity to Introductions*

Geographic areas and populations vary in their receptivity to introductions of potential pathogens that can cause human disease. Multiple factors are in play. The physicochemical environment may preclude the presence of a necessary mosquito vector or essential intermediate host. The physical environment may also influence transmission dynamics. For example, influenza has a strong seasonal pattern, especially in temperate regions. This seasonality is influenced by the humidity; recent studies suggest that absolute humidity is a more useful measure than relative humidity. The absolute humidity affects influenza virus transmission and virus survival. Absolute humidity can explain 90 percent of the variability of influenza virus survival, whereas relative humidity can explain only 36 percent of variation (Shaman and Kohn, 2009). Hence, travelers with influenza returning to temperate areas during hot, humid months are unlikely to spark epidemic spread (Lowen et al., 2008), though focal outbreaks in contained, air-conditioned spaces (e.g., air-conditioned nursing homes and barges) have been reported during hot, humid weather. Influenza outbreaks in the Southern Hemisphere occur during hot-weather months in the Northern Hemisphere; in the tropics influenza can circulate throughout the year. Analysis of H3N2 epidemics worldwide between 2002 and 2007, including those in temperate regions, suggested that they were seeded annually by viruses that had first appeared in East and Southeast Asia (Russell et al., 2008). These viral strains appeared to have evolved from other Asian strains.

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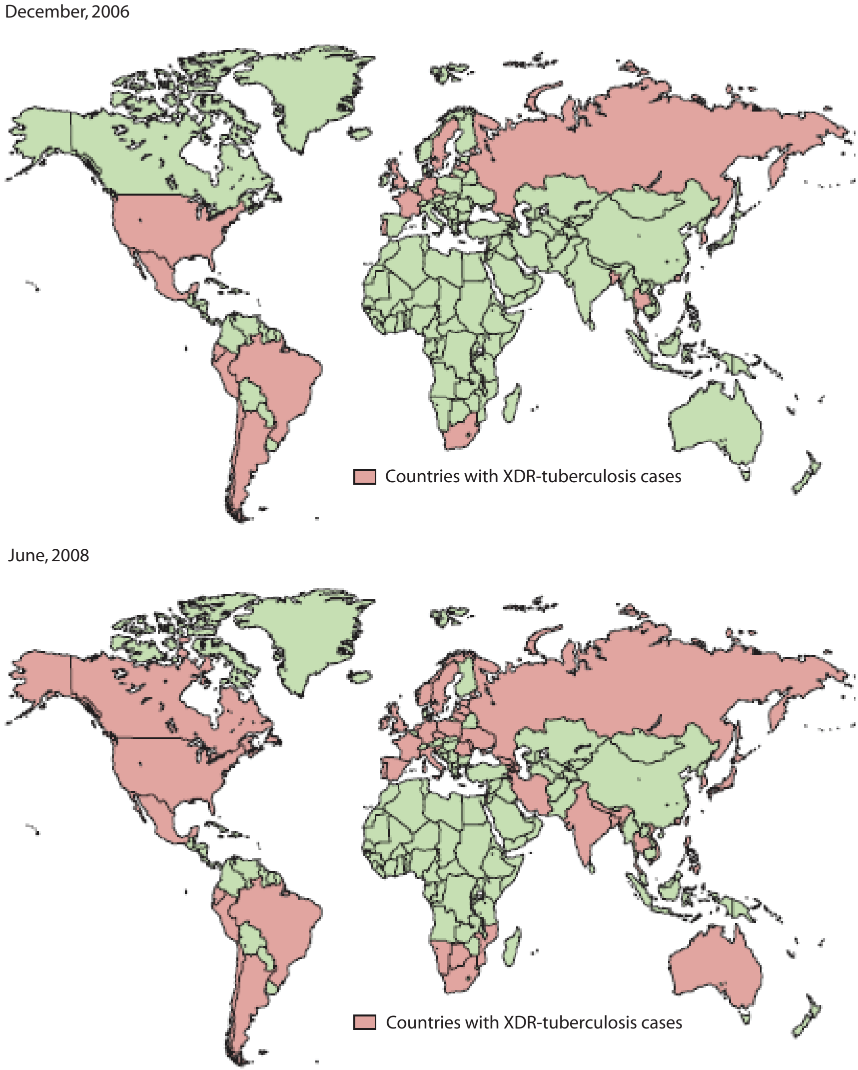


**FIGURE 2-5** Countries with XDR tuberculosis cases in December 2006 and June 2008.
SOURCE: Reprinted from *Lancet Infectious Diseases*, Jassal and Bishai (2009), with permission from Elsevier. Copyright 2009.

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Other local factors that affect the receptivity of individuals and a population to introduction of a new infection include housing, sanitation, and living conditions. Good nutrition can reduce the vulnerability to some infections or diminish their severity. Populations may be immune because of vaccination or prior infection. Human behavior and activities influence exposure to a number of infections (e.g., sexually transmitted infections). And finally, good surveillance and wider access to good medical care may reduce the burden of an infection in a population and allow it to be brought under control.

In addressing the question of how controllable an infection is that is directly transmitted from person to person, a key factor is the proportion of transmission that occurs before onset of symptoms or during asymptomatic infection (Fraser et al., 2004). Public health measures are most likely to be effective when little or no infection is transmitted during asymptomatic infection. Figure 2-6 displays four

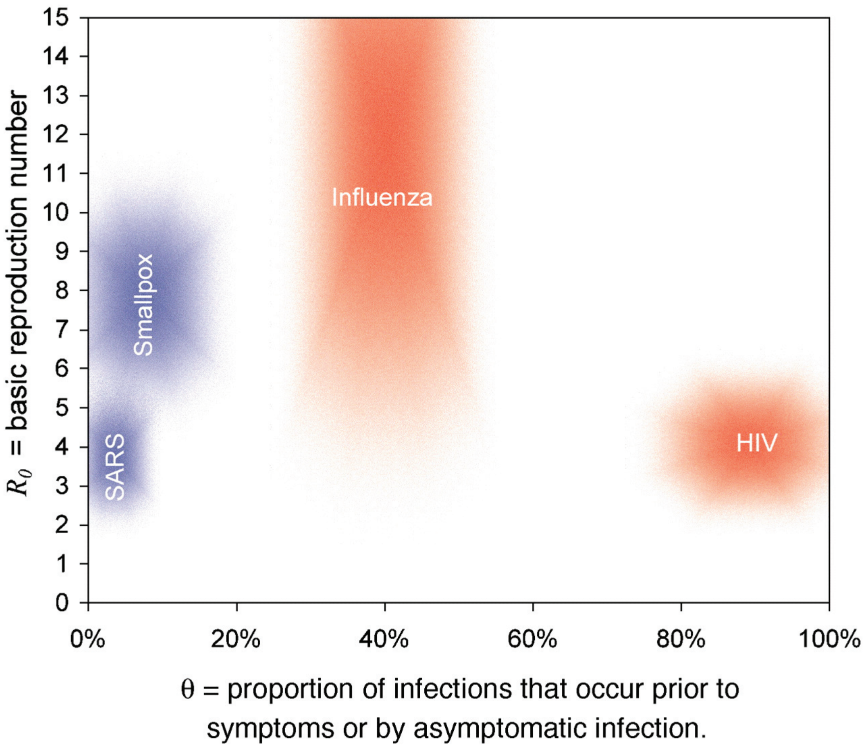


**FIGURE 2-6** How controllable is an infection? Plausible ranges for the key parameters $R_0$ and $\theta$ for four viral infections of public concern are shown as shaded regions. The size of the shaded area reflects the uncertainties in the parameter estimates.
SOURCE: Fraser et al. (2004).

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infections that are transmitted from person to person: SARS, smallpox, influenza, and HIV. Fortunately, the fever caused by infection with the SARS coronavirus preceded onset of transmissibility, meaning that with strict surveillance for symptoms and isolation of those with symptoms, it became possible to interrupt the transmission of this infection. Influenza, on the other hand, is more difficult to contain because transmission may begin before onset of symptoms, and infected patients may have little or no fever. Based on epidemiological analyses, Fraser et al. (2009) estimated the basic reproductive number of the swine-origin H1N1 influenza A virus in the range of 1.4 to 1.6.

### Vector-borne Infections

Vector-borne infections can also be introduced into new geographic areas by travelers, though the vulnerable areas are restricted to those with competent mosquito or other arthropod vectors. Because important vectors, such as *Aedes aegypti* and *Aedes albopictus*, can be dispersed by trade (especially via ships), more human-inhabited areas of the world are infested with these potential vectors than ever before (Tatem et al., 2006). *Aedes aegypti* thrives in an urban environment, and today about 2.5 to 3 billion people live in tropical and subtropical areas infested with this mosquito.

Two vector-borne infections, dengue fever and chikungunya infection, which have expanded in distribution in recent years, illustrate multiple contributions to this dynamic process and spread. Dengue virus is causing more infections, including more cases of severe and complicated dengue fever, than ever before (Wilder-Smith and Gubler, 2008). Although multiple factors contribute, three forces described above are especially important: urbanization with major expansion of populations living in tropical and subtropical areas; population size; and rapid, frequent travel of viremic humans to areas infested with competent vectors. Lax vector control programs and urban settings that lack piped water (so residents must store water in their homes) and are littered with used tires, discarded plastic cups, and other trash with standing water that allow breeding of mosquito vectors exacerbate the problem. Today, the dengue viruses have a much larger host population in which to replicate, recombine, and mutate than ever before, given the size of the human population. Zanotto and colleagues (1996) found that the number of dengue lineages has increased roughly in parallel with the size of the human population over the past 200 years (Figure 2-7). More urban areas in tropical and subtropical regions now have a population size large enough (estimated to be between 150,000 and 1 million) to allow the ongoing circulation of dengue viruses. An increasing number of geographic areas are experiencing cocirculation of more than one dengue serotype, setting the stage for secondary infections and more severe disease.

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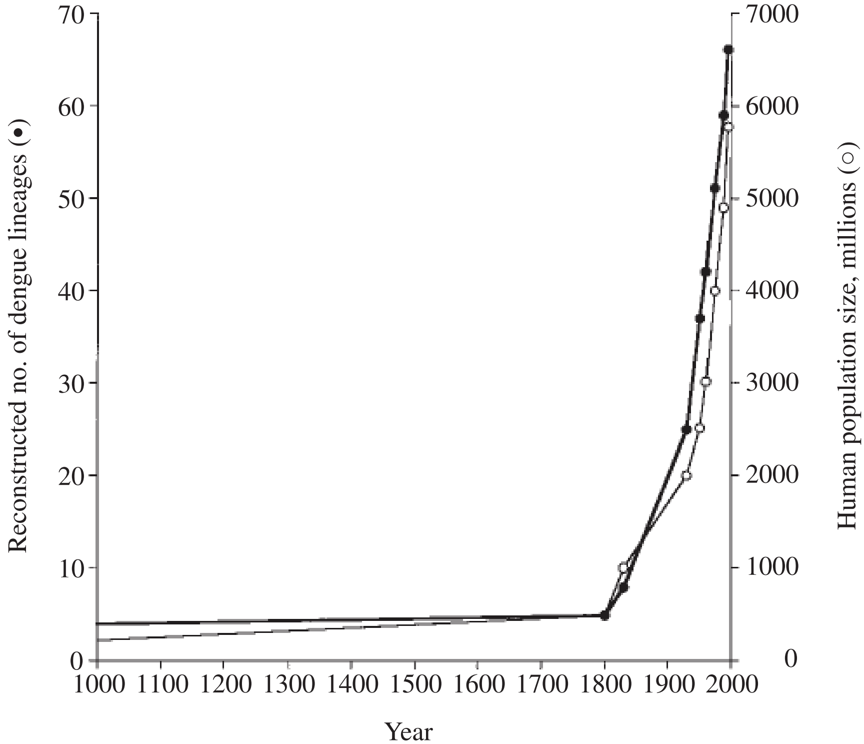


**FIGURE 2-7** Global population size and lineages of dengue virus over time.
SOURCE: Zanotto et al. (1996).

*Spread of Chikungunya Virus Infections*

Although the mosquito-transmitted alphavirus, chikungunya[2] (family Togaviridae), was first identified as a cause of outbreaks in Africa in 1953 (Lumsden, 1955) and has caused outbreaks at irregular intervals since then in Africa and Asia, the virus has caused multiple outbreaks in new geographic areas since 2004. Outbreaks in coastal Kenya in 2004 were followed by multiple explosive outbreaks on the islands of the Indian Ocean beginning in 2005 (Charrel et al., 2007; Josseran et al., 2006; Renault et al., 2007; Sergon et al., 2008). Subsequent outbreaks occurred in India, Thailand, Indonesia, Malaysia, and other Asian countries (AbuBakar et al., 2007; Mavalankar et al., 2008). In India alone, more than a million cases were reported. In some areas, extremely

[2]Chikungunya is a term from the local language that means "that which bends up" or "stooped walk" because of the joint pains.

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high attack rates of infection were observed, affecting more than half of the population (Sergon et al., 2008). Because the virus causes a severe, frequently incapacitating polyarthralgia[3] as part of the illness, the infection has been devastating in areas with high attack rates (Simon et al., 2008). Unlike dengue fever, another acute febrile illness, chikungunya infection is frequently followed by persistent joint symptoms that can continue for months or even years.

More than 1,000 cases have occurred in travelers who have returned to non-endemic regions (Hochedez et al., 2006; Panning et al., 2007; Parola et al., 2006; Simon et al., 2008). A high number of travelers with chikungunya fever have been diagnosed in Europe, reflecting frequent travel destinations in Indian Ocean islands. Chikungunya fever has always been considered a disease of the tropics, but in the summer of 2007, 175 cases were laboratory confirmed as the cause of an outbreak of an acute illness in two villages in northeastern Italy (Rezza et al., 2007). The clinical attack rate increased with increasing age in this outbreak, as has been observed in other outbreaks as well. Investigation identified a visitor from India as the index case. Transmission occurred during the hottest months of the year and stopped when temperatures cooled. Chikungunya virus was found in *Aedes albopictus*, the presumed mosquito vector in this outbreak.

Textbooks describe chikungunya fever as a self-limited illness with fever, polyarthralgia, headache, and rash, but in the recent outbreaks excess mortality was also reported (Figure 2-8; Mavalankar et al., 2008). Deaths have been concentrated in older persons.

Because virus is present in high concentration in the blood of infected humans (may exceed $10^9$ RNA copies/mL of plasma), potential risk exists for nosocomial transmission. At least one instance is described of transmission to a health care provider in France after blood exposure (Parola et al., 2006). The virus could also be transmitted by transfusion of blood donated during the period of viremia. Investigators have modeled the potential risk for transfusion in an area with an outbreak (Brouard et al., 2008). In Reunion, where a massive outbreak occurred in 2005-2007, blood collection was interrupted for several months during the epidemic. Based on sentinel surveillance, knowledge of the duration of viremia in chikungunya infections, and the frequency of asymptomatic infections, the authors estimated that the risk of viremic blood donation was 1,500 per 100,000 donations during the peak of the epidemic and was a mean of 132 per 100,000 donations over the entire course of the outbreak. Returning travelers who donated blood during asymptomatic viremia could also be a potential source of infection in new geographic areas.

A mutation in the chikungunya virus may partially explain the intensity of recent outbreaks (Schuffenecker et al., 2006). *Ae. albopictus*, originally found in Asia, has become widely dispersed beyond Asia and is now found in many parts of the Americas, Europe, Africa, and the Pacific Islands. Although in the past the

[3]Pain in multiple joints.

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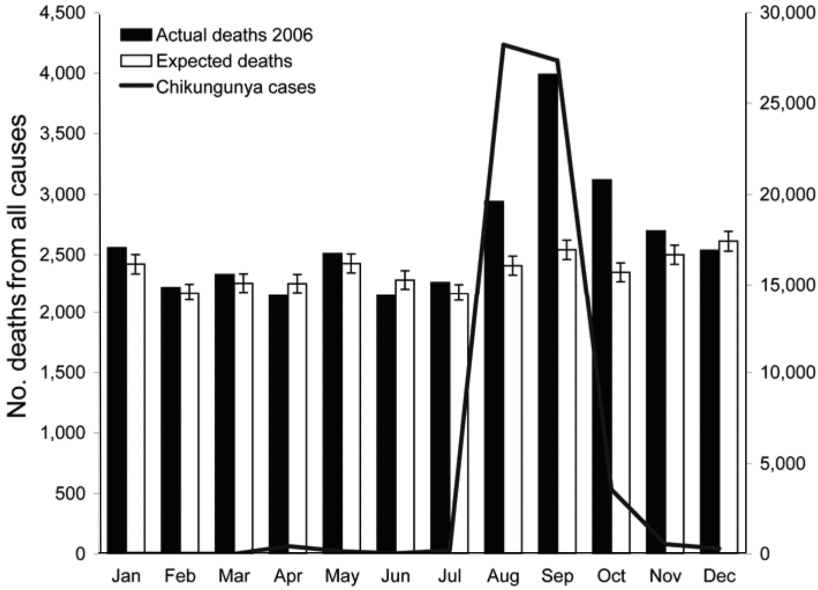


**FIGURE 2-8** Increased mortality associated with chikungunya outbreak, India.
SOURCE: Mavalankar et al. (2008).

mosquito had not been considered a particularly efficient vector, it was identified as the primary vector in some of the recent chikungunya virus outbreaks (Reiter et al., 2006). A mutation has been identified in a viral gene encoding the envelope protein of the virus (A226V) and was found in more than 90 percent of viral isolates in the latter part of the outbreak in Reunion and in isolates from the outbreak in Italy. Of note, presence of the mutation is associated with enhanced susceptibility of *Ae. albopictus* to infection with chikungunya virus and to more rapid dissemination into the mosquito salivary glands. This means that a mosquito can become infected when exposed to a lower level of viremia, which may give the mutant virus enhanced survival benefit (Tsetsarkin et al., 2007). Mosquitoes vary in their susceptibility to infection and competence to transmit viruses (Tesh et al., 1976). Recent studies of *Ae. aegypti* and *Ae. albopictus* strains from Florida, using a chikungunya virus isolate from the Reunion outbreak, demonstrated that the mosquitoes were susceptible to infection and capable of transmitting the virus (Reiskind et al., 2008). Large areas of the Americas are infested with *Ae. albopictus* and *Ae. aegypti*. The potential for introduction of chikungunya virus is greatest in areas with high temperatures, abundant mosquitoes, housing or work places that allow mosquito-human contact (e.g., absence of window screens and air conditioning), and large volumes of travelers arriving from areas of Africa or Asia experiencing outbreaks (Charrel et al., 2008; Wilson, 2009).

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### Other Routes of Transmission

Dengue infection (which can lead to dengue hemorrhagic fever) can also be transmitted by blood transfusion (Tambayh et al., 2008) and by blood exposures in health care settings (Chen and Wilson, 2004, 2005). This may occur more frequently than is documented because occasional events of nosocomial and transfusion-related transmission could be difficult to distinguish from background infections in areas where infection is endemic and epidemic. Such events are more likely to be documented in nonendemic regions (Chuang et al., 2008). Recent studies have identified dengue RNA in blood donated by residents in Puerto Rico, Brazil, and Honduras (Linnen et al., 2008; Mohammed et al., 2008).

### Medical Tourism

A reason for travel that is cited by increasing numbers of international travelers is medical treatment abroad (Reed, 2008). An estimated four million people travel internationally each year for medical care that often involves surgical procedures. A few countries attract the bulk of these travelers. Thailand, for example, currently receives about a million patients per year, and India, Singapore, and Malaysia are expected to attract similar numbers by 2012 (Smith et al., 2009b).Those who seek medical treatment abroad often undergo major procedures, such as heart bypass graft surgery, heart valve replacement, hip replacements, and bone marrow and liver transplantation, procedures that frequently require support by transfusions of blood and blood products. Some international institutions are seeking accreditation by the Joint Commission International[4] to increase patient confidence in the quality of care. Still, in addition to ethical and legal issues, there are concerns about unrecognized risks to these medical tourists because of geographic differences in disease risks. Even if locally donated blood is tested for any evidence of infection, as would be carried out in the United States, other risks may exist in these areas, such as locally endemic and epidemic diseases, like dengue and chikungunya (Wilder-Smith et al., 2009). At present, blood donated in these regions is not screened for these infections.

### Travelers as Sentinels

Travelers can serve as sentinels and couriers and should be an integral part of the global surveillance system (Wilson, 2003). Although travelers to an area do not experience all of the same infections seen in a local population, their infections reflect those present in the area. Returned ill travelers often have access to

[4]The Joint Commission (formerly the Joint Commission on Accreditation of Healthcare Organizations) is a private sector U.S.-based organization that strives to improve health care through provision of health care accreditation and related services. An international offshoot, the Joint Commission International, was founded in 1997.

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medical care in facilities where diagnoses can be confirmed, bacteria cultured, malaria species identified, viruses isolated, specific serologic tests carried out, and sensitivity testing done. Under some circumstances, sequencing of an organism or molecular studies carried out in a research laboratory can yield insights that can be helpful in the understanding, prevention, control, or treatment of the disease in the area where it was acquired. Infections in travelers can also provide a global alert about infections in an unexpected location or with an unusual resistance pattern. In some instances, the diagnosis of an infection in a returned traveler can be the first indication of the presence of an infection in a particular geographic area or at a specific site. During their visits, travelers sample the biome of an area simply by staying in the area, and they can be a courier in which the microbes survive, replicate, and can later be sampled and examined.

Study of infections in travelers has also provided new insights about transmission mechanisms that might not have been identified in endemic areas where laboratory support is less robust. Examples have been documented of transmission of dengue to health care workers by exposure to blood of infected travelers in temperate areas where dengue is not endemic (Chen and Wilson, 2004).

The GeoSentinel Surveillance Network,[5] a worldwide communication and data collection network of travel and tropical medicine clinics started more than a decade ago, systematically gathers information on ill international travelers and migrants and has been able to provide early alerts about unusual infections or infections in unusual locations or populations. This global network includes staff at 42 travel and tropical medicine clinics with sites on all six continents. As of early 2009, data from more than 100,000 clinical visits had been entered into the database. Despite the limitations of data gathered by this type of surveillance network (Leder et al., 2008), analyses have yielded useful insights, including showing how the spectrum of disease varies depending on the place of exposure among ill returned travelers (Freedman et al., 2006).

Falciparum malaria infections in travelers returned from the Dominican Republic signaled the reappearance of malaria in parts of the island and led to changes in recommendations for chemoprophylaxis (CDC, 2005). The increasing resistance of salmonellae to quinolones documented in returned travelers with typhoid fever has influenced initial treatment choices in patients with severe typhoid fever. An index case of schistosomiasis in a traveler returning to Israel from a luxury safari trip to Tanzania prompted an investigation leading to the identification of 22 cases of acute schistosomiasis (Leshem et al., 2008). Subsequent investigation revealed that 81 percent of those exposed at a specific site became infected. Early diagnosis of the index case enabled clinicians to study the usefulness of different diagnostic tests and observe the clinical course of acute schistosomiasis in nonimmune persons who had been infected during a single short (mean duration, 40 minutes) exposure to an unchlorinated, freshwater pond.

[5]See http://www.istm.org/geosentinel/main.html.

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Dissemination of information about the outbreak through electronic networks (ProMED and GeoSentinel) made it possible to inform the global community about the outbreak more than a year before a paper about the outbreak appeared in a peer-reviewed medical journal.

Analysis of dengue cases from the GeoSentinel database over a 10-year period revealed that a surge in dengue infections in returned travelers could herald an increase in dengue-endemic countries in identified regions (Schwartz et al., 2008). In 2002, an increase in cases led GeoSentinel staff to post an alert on ProMed (Freedman et al., 2002). In several instances, an increase had been evident before official surveillance data were available from specific countries, which reinforces the importance of sentinel surveillance in travelers.

A different kind of network, the Boston Area Travel Medicine Network (BATMN), is in the early stages of collecting serum samples on selected travelers before and after travel to begin to assess exposures to infections in different geographic regions.

### Conclusion

Travelers play a critical role in the movement of microbes globally. In an increasingly interconnected world with a growing, increasingly urban population in low-latitude areas, new risks exist and disease-causing microbes and resistance genes can move even more rapidly than in past decades. Travelers can also serve as an important sentinel population. Studying them can help to characterize the global microbial traffic.

## ARMED CONFLICT AND INFECTIOUS DISEASE

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This paper is designed to stimulate discussion on a complex set of issues associated with armed conflict (war), infectious disease, and public health—what we, as a society, do collectively to ensure the conditions in which people can be healthy (IOM, 1988).

The health consequences of war include:

- War-related injuries and diseases,
- Adverse effects on medical care and public health services,
- Damage to health-supporting infrastructure and the environment,
- Forced migration,

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- Violation of human rights,
- Diversion of resources, and
- Promotion of violence (Levy and Sidel, 2008).

Certain categories of infectious diseases are increased in war and other complex emergencies, including diarrheal diseases, acute respiratory infections, measles, malaria, meningococcal disease, and tuberculosis. Two studies from the recent civil war in the Democratic Republic of Congo demonstrated that infectious diseases are frequent causes of death during wartime. One study found that diarrhea, respiratory infections, and suspected malaria were among the most frequent causes of death (Van Herp et al., 2003), and the other study found that fever/malaria and diarrhea were among the most frequent causes of death in young children (Table 2-1; Coghlan et al., 2007).

### Causes of Infectious Diseases Due to War

Among the major causes of infectious diseases due to war are:

- Adverse effects on medical care and public health services,
- Damage to the health-supporting infrastructure and the environment,
- Forced migration,
- Diversion of resources, and
- Biological weapons.

Each of these causes deserves further discussion.

*Adverse Effects on Medical Care and Public Health Services*

During war, a variety of factors adversely affect medical care and public health services. Physicians, nurses, and other health workers are injured or killed

**TABLE 2-1** Causes of Death in Young Children (0-4 Years of Age), Western Democratic Republic of Congo, January 2006-April 2007

| | |
|---|---|
| Fever/malaria | 35% |
| Neonatal death | 13% |
| Diarrhea | 13% |
| Anemia | 7% |
| Acute respiratory tract infections | 7% |
| Measles | 5% |
| Meningitis | 5% |
| Malnutrition | 5% |

SOURCE: Based on data in Coghlan et al. (2007).

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or they flee. Clinics and hospitals may be damaged. Public health services are curtailed. Supplies of medications and vaccines are reduced.

*Damage to the Health-Supporting Infrastructure and the Environment*

During war and in the immediate aftermath of war, damage to the health-supporting infrastructure is often the main reason for poor health and excessive numbers of deaths. Food safety and supply, sewage treatment, water safety and supply, electrical power, transportation, and communication may be adversely affected. In addition, there may be extensive damage to the physical environment that may, in turn, adversely affect health; for example, bomb craters in Vietnam subsequently filled with stagnant water and became prime breeding sites for malaria-carrying mosquitoes.

Damage to the health-supporting infrastructure and the environment promotes diarrheal disease due to contamination of food and water supplies and inadequate sewage treatment and disposal. It also promotes acute diarrheal disease due to overcrowding, air contamination from indoor fires, and inadequate shelter. Tuberculosis (TB) often increases during war. For example, a study of 36 conflicts found that the TB notification rate before conflicts was 81.9 per 100,000 and after conflicts was 105.1 per 100,000. It also found that the risk of presenting with TB 2.5 years after the outbreak of conflict was the same as that 2.5 years before the conflict, indicating improvement in the post-conflict period (Drobniewski and Verlander, 2000).

Another study found that, in the war in Afghanistan during the 1980s, TB occurrence increased because TB control activities ceased. After the war, the situation improved, but even by 1999 the incidence of active TB cases there was still high (278 per 100,000) and only 10 percent of TB patients received directly observed therapy (Kahn and Laaser, 2002).

A study during the civil war in Guinea-Bissau in 1998 found that those TB patients who received irregular or no treatment had a three-fold increase in mortality, and that HIV-positive patients had an eight-fold increase in mortality (Gustafson et al., 2001).

A study in East Timor found that successful restoration of TB services during the five years after the end of conflict was primarily due to the structure and experience of a local nongovernmental organization, and the commitment and flexibility of local personnel and international advisors (Martins et al., 2006).

HIV transmission could increase during war for a variety of reasons, including increased risk-taking behavior, sexual violence, inadequate access to condoms, untreated sexually transmitted infections, commercial sex, HIV-contaminated blood, and inadequate use of universal precautions. However, several studies have demonstrated that HIV incidence has generally decreased during war—only to increase again after conflict has ended. For example, a study of seven countries with long-term civil disorders or wars in sub-Saharan Africa found that

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HIV prevalence was relatively low during war. In Sierra Leone and Somalia, adult HIV prevalence was less than 1 percent. In the Democratic Republic of Congo, prevalence stabilized during civil war and disorder after 1991. In Angola and Liberia, there was apparently low HIV prevalence during wartime. And in Mozambique, HIV prevalence was approximately 1 percent immediately after civil war (although there was a dramatic increase in HIV prevalence after the war; Gisselquist, 2004).

There have been many successful HIV/AIDS prevention and treatment programs during armed conflict. In Côte d'Ivoire, this success occurred largely due to the importance of nongovernmental organizations working with regional and international organizations and United Nations agencies (Betsi et al., 2006). In the Democratic Republic of Congo, major factors in successful prevention and treatment of HIV/AIDS were adequate human resources, secure drug storage, decentralization of care, and integration of services (Culbert et al., 2007).

Violation of human rights of women and children adds to vulnerability to HIV infection during wartime. For example, a study in northern Uganda found that mass abduction of children into the resistance army led to increased vulnerability to HIV infection, with boy soldiers being coerced to use rape as a weapon and girls forced to become sexual slaves. It also found that in camps for internally displaced persons in northern Uganda, women were raped and driven to provide sex for money, thus increasing their vulnerability to HIV infection (Westerhaus et al., 2007).

### *Forced Migration*

There are approximately 12 million refugees and 22 to 25 million internally displaced persons globally. They suffer from loss of sociocultural support systems and reduced access to safe food and water, inadequate medical care and public health services, and inadequate clothing and shelter, and they are at increased risk for many infectious diseases. For example, in 1980 at a camp for Cambodians in Thailand, the leading diagnoses in the emergency ward of a 1,000-bed field hospital were predominantly infectious diseases (Table 2-2). In 1994, approximately

**TABLE 2-2** Leading Diagnoses, Emergency Ward, Khao-I-Dang Camp for Cambodians, Thailand, 1980

| | |
|---|---|
| Upper respiratory infection and pneumonia | 25% |
| Gastroenteritis/diarrhea | 13% |
| Measles | 8% |
| Otitis media | 5% |
| Trauma | 5% |
| Fever of unknown origin | 4% |
| Meningitis | 4% |
| Malaria | 2% |

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**TABLE 2-3** Cause-Specific Mortality Among Internally Displaced Persons in Camps, South Darfur, May-June 2005

| | |
|---|---|
| Diarrhea | 25% |
| Injuries | 14% |
| Acute respiratory infections | 7% |
| Malnutrition | 5% |
| Tetanus | 5% |
| Malaria | 5% |
| Meningitis | 2% |
| Measles | 2% |
| Maternal mortality | 2% |
| Other causes of death | 33% |

SOURCE: Reprinted from World Health Organization and Federal Ministry of Health, Sudan (2005) with permission from WHO/EMRO.

1 million refugees from Rwanda fled to Zaire in less than one month; many of them died from cholera or dysentery soon after arrival in refugee camps there. In 2005, mortality among internally displaced persons and others in Darfur, Sudan, was mainly due to infectious diseases (Table 2-3; World Health Organization and Federal Ministry of Health, Sudan, 2005).

### *Diversion of Resources*

War and the preparation for war cause extensive diversion of human and financial resources. For example, in 1990, per capita military expenditures in Ethiopia were $16 compared to $1 per capita for all health expenditures, per capita military expenditures in Sudan were $25 compared to per capita health expenditures of $1, and per capita military expenditures in Angola were $114 compared to per capita health expenditures of $8. Diversion of resources also occurs in developed countries during war and preparation for war. As one relatively small example, the $107 million spent by taxpayers in the District of Columbia for U.S. nuclear weapons programs for fiscal year 2009 could have funded health care for 34,000 children for one year (National Priorities Project, 2008).

### *Biological Weapons*

There is a long history of the sporadic use of biological weapons during war or preparation for war. Examples have included contaminating drinking water with microorganisms, hurling of plague victims into a walled city, infecting blankets with smallpox virus, placing dead animals in water sources, infecting horses with glanders bacteria, and testing anthrax bombs on a deserted island (Metcalf,

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2002). In the 1950s and the 1960s, the United States and the Soviet Union each developed a large infrastructure for research and development of both offensive and defensive biological weapons. In 1972, the Biological Weapons Convention was signed, which banned the development, production, stockpiling, or acquisition of biological weapons and their means of delivery, except for peaceful purposes. Although there is no formal verification regime for the Convention, 162 nations have now signed or ratified it.

The Centers for Disease Control and Prevention has developed three categories of diseases caused by biological agents, based on the severity of these diseases and the presumed likelihood that they could be caused by bioweapons. Category A includes anthrax, botulism, plague, smallpox, tularemia, and viral hemorrhagic fevers; category B includes brucellosis, disease caused by epsilon toxin of *Clostridium perfringens*, food safety threats, glanders, melioidosis, psittacosis, Q fever, ricin toxin, staphylococcal enterotoxin B, typhus fever, viral encephalitis, and water safety threats; and Category C includes emerging infectious diseases, such as those caused by Nipah virus and hantavirus.

Preparedness for bioterrorism should be placed more appropriately among U.S. national priorities for prevention and control of infectious diseases. Table 2-4 shows the incidence and mortality for selected causes of infectious disease in the United States from 2001 to 2004, demonstrating that the numbers of incident cases and deaths for AIDS, hepatitis C, and hospital-associated infections were much higher than those for bioterrorism.

The U.S. National Counterterrorism Center Report for 2007 reported on approximately 14,000 terrorist attacks worldwide, accounting for approximately 22,000 deaths and approximately 44,000 wounded people. Armed attacks and bombings accounted for the vast majority of fatalities. However, none of these reported attacks were due to biological agents (U.S. National Counterterrorism Center Report, 2008).

**TABLE 2-4** Incidence and Mortality for Selected Causes, United States, 2001-2004

| | Incident Cases | Deaths |
|---|---|---|
| Bioterrorism | 23 | 5 |
| AIDS | 157,468[a] | 68,802 |
| Hepatitis C | 107,000 | 36,000 |
| Hospital-associated infections | 6,800,000[b] | 395,948[b] |

[a]Based on 35 areas with confidential name-based HIV infection reporting.

[b]Based on estimates for 2002.

SOURCES: Based on data in CDC (2005), Klevens et al. (2007), Page et al. (2002), and Wasley et al. (2008).

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### What Needs to Be Done

The following measures need to be better designed and implemented to address the problems related to armed conflict and infectious disease:

1. Surveillance for infectious diseases, and also for factors that are known to increase the risk of armed conflict;
2. Evaluation of prevention and control measures for infectious diseases related to war, and for measures to help prevent armed conflict;
3. Protection of medical care and public health services and maintenance of their neutrality during war and the aftermath of war;
4. Elimination, or the prevention of increases, of disease vectors during war and the aftermath of war;
5. Epidemic preparedness and responsiveness to outbreaks, especially in less-developed countries;
6. Diagnosis, treatment, and prevention of infectious disease;
7. Protection of the health-supporting infrastructure and the environment during war and the immediate aftermath of war;
8. Reduction of forced migration during war and its aftermath, and meeting of the basic needs of refugees and internally displaced persons and protection of their human rights;
9. Control of biological agents and strengthening of the Biological Weapons Convention; and
10. Creation of a world without war by addressing the underlying causes of war, controlling weapons, and strengthening the infrastructure for peace.

Ultimately, eliminating infectious disease caused by armed conflict will require the elimination of armed conflict.

## RISKY TRADE AND EMERGING INFECTIONS

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University of Washington

*Jill Hodges, M.P.H., M.S.L.*

Global commerce is rapidly globalizing our food supply, our supply of pharmaceuticals, even our supply of biological sources. It has been well demonstrated that this process entails new microbial threats (Kimball, 2006). The recent outbreak and global spread of a new strain of influenza A (H1N1) that originated in

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Mexico provides a compelling illustration of how the dynamics of globalization can contribute to the emergence and spread of microbial disease. As of this writing, the investigation into the source of the H1N1 virus is still under way. But the virus, a blend of strains appearing in wild birds, pigs, and now humans, illustrates the type of reassortment enabled by the intensive farming practices developed to meet the demands of global commerce. These industrial-scale farms, with thousands of animals confined in close quarters, offer ripe breeding grounds for new agents (Weuthrich, 2003). And in the event that these agents jump from animals to humans, nearby population centers present the opportunity for these agents to spread. Indeed, within six weeks of the initial detection of the virus in Mexico in February 2009, the virus had spread to more than 2,000 people in 23 countries across the globe (WHO, 2009) via international travel.

Concern over the spread of the virus virtually shut down Mexico City and led to flight cancellations, school closures, and airport screenings around the globe (Carroll and Branigan, 2009).

Fortunately, the recent H1N1 strain has proven thus far to be relatively mild and the outbreak modest in scale. But it is just one of a growing number of cases that demonstrate how the pressures and incentives of global trade and travel can threaten the biosecurity of the global population. The following discussion will focus on other recent examples that highlight some of the areas of greatest concern, specifically food production, processing, and distribution; the use of antimicrobials in food animals; and xenotransplantation. After examining the risks, this discussion will explore potential solutions. In short, there's an urgent need to employ a multisector, global approach to enhance the safety web to meet the threats global trade poses for the emergence and spread of microbial diseases.

### Cross-Border Trade and the Spread of Infections

In 2008, total global merchandise trade was valued at more than $15.8 trillion (WTO, 2009). Although the annual rate of growth in global trade dropped from 8 percent in 2006 to 6 percent in 2007 and continued its decline in 2008, the international exchange of goods and services has continued to increase, albeit at a slower rate. The following case studies examine the risks that emerge in a world in which people and products are continually crossing borders.

### Far-Flung Distribution

The 2006 multistate outbreak of *Escherichia coli* O157:H7 across the United States (Grant et al., 2008) linked to spinach grown in California aptly demonstrates how cross-border trade can expand the scope and complexity of outbreaks. Between August 5 and September 5, a total of 84 cases were detected in 20 states. Only one of the 84 cases was in California; the other 83 were spread across the country, from Oregon to Wisconsin to New York to Tennessee. Conse-

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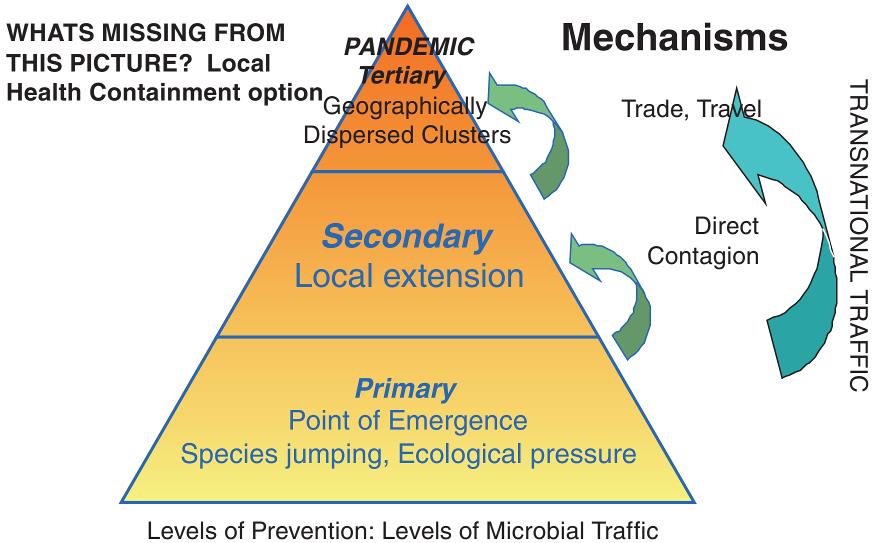


**FIGURE 2-9** Trade and travel are key to global dissemination of disease.

quently, there was no ability at the local level to detect the outbreak or identify its source. It was not until investigators conducted the molecular epidemiology across affected states that the cases could be linked and the source identified.

Trade across borders (state or national) creates a new, very direct dissemination of infection and a new challenge for public health, both at the local and the global levels. As Figure 2-9 illustrates, trade and travel are the mechanisms by which local outbreaks become pandemics. And as the blue arrow indicates, it is the growth of transnational trade and travel that enhances the risk of the transnational spread of disease. The *E. coli* outbreak described above shows that, when agents enter the cross-border trade flow, local public health authorities at the source may not, in fact, be in a position to perceive and address disease clusters.

### The Perfect Storm: H5N1

The influences of the global economy, in particular increased urbanization and intensified agricultural processes, have contributed to the brewing threat of an avian influenza pandemic. These dynamics are particularly evident in areas of Southeast Asia, where poor families are moving, along with their animals, from rural areas to crowded periurban settings in pursuit of economic opportunity. The families maintain their food animals in backyard farms with poor sanitation and water supply—an opportune blend for the emergence of bird flu. Further compounding the risk

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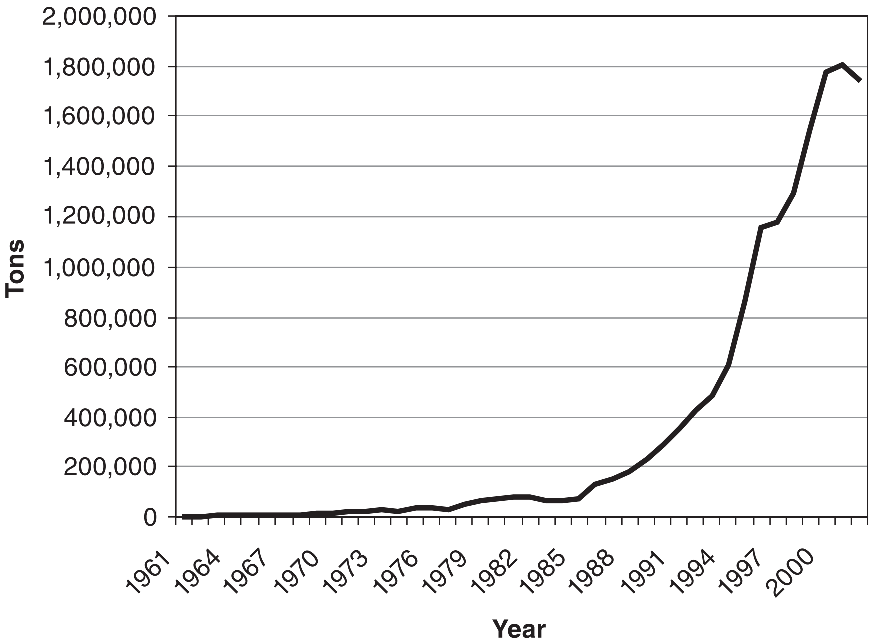


**FIGURE 2-10** Poultry exports from Far East Asian countries from 1961 to 2002.
SOURCE: Based on data in FAOSTAT 2003 and reprinted from Kimball (2006) with permission from Ashgate Publishing.

of spread is the nearby introduction of intensive poultry agriculture operations that raise thousands of birds from hatching through slaughter. Between 1980 and 2000, poultry exports from Far East Asian countries leapt from less than 200,000 tons of exports to nearly 1,800,000 tons (Figure 2-10; Kimball, 2006). These burgeoning poultry operations generate a variety of potential biosecurity risks such as crowded coops with large volumes of waste—risks that they do not always have the resources or incentive to mitigate. Added to the mix are free-ranging ducks that serve as asymptomatic reservoirs for the H5NI virus.

Ultimately, these communities crowded with people and poultry are approaching an ecological tipping point that could someday result in an influenza A (H5N1) pandemic among humans. There are, in fact, two distinct opinions on this issue: (1) large industrial operations provide enhanced biosecurity and backyard poultry should be eliminated to reduce risk, and (2) the large-scale operations are themselves risky. While definitive studies are lacking, a careful review of the Thai experience suggests that the second opinion is more aligned with the evidence (Graham et al., 2008). Already, H5N1 outbreaks have occurred in poultry throughout Asia. As of September 2009, 442 cases of human H5N1 and 262 deaths had been

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documented in 15 countries, including China, Hong Kong, Thailand, Vietnam, Cambodia, and Indonesia (WHO Global Alert and Response, 2009). To date, the H5N1 virus has had limited ability to move from poultry to humans and even less ability to move from person to person. The rapid global spread of the recent H1N1 virus linked to pigs provides sobering evidence of the pandemic potential once an agent that originates in animals develops the capacity to spread among humans.

### Bovine Spongiform Encephalopathy and New-Variant Creutzfeldt-Jakob Disease

The emergence of BSE and new-variant Creutzfeldt-Jakob disease (nvCJD) provides another example of the potential consequences of the pressures that result from global trade. In this case, the chain of events arguably began when the United Kingdom entered the World Trade Organization (WTO) in 1993 (Gibbs and Shaw, 1996). As a condition of joining the WTO, the United Kingdom lifted some 13 percent of the tariffs charged for beef imports, thus opening their beef market to greater global competition. This in turn resulted in a consolidation of the previously fragmented beef industry. As part of that transition, beef producers changed their rendering practice and, to some extent, their animal husbandry practices.[8] Specifically, they changed their rendering process from a so-called batch procedure to a lower-temperature vacuum-extraction process. This process cost less and enabled continuous production, but unfortunately it had a hidden downside as well—it did not deactivate the prion, a new pathogenic agent with a 10-year incubation period. This long incubation period enabled extensive circulation before any problems were detected. During this period, meat and bone meal that had been rendered in Great Britain from cattle infected with BSE were shipped around the world in animal feed.

In the mid-1990s, a new series of cases of vCJD began to appear in the United Kingdom. The frightening disease, which claims victims' lives in 18 months and has no known treatment, was linked through case-control studies to consumption of beef from the United Kingdom. While scientists continue to debate the causal link between prion disease in cattle and prion disease in humans, the global markets reacted swiftly to the possibility. UK beef exports plummeted in 1996 (Figure 2-11) after trading partners began embargoing beef shipments under the WTO's Sanitary and Phytosanitary (SPS) agreement. The SPS agreement allows importers to issue "urgent notifications" that they will suspend import of a particular product when human safety is at risk (WTO, 2000). Thus, in the world of global food trade, where safety concerns can amount to economic devastation, incentives run against reporting potential risks.

[8]Contrary to popular belief, the global pressures did not prompt ranchers to begin feeding bits of sheep to cattle as a protein source. They began that practice during World War II, when the price of soybeans went up.

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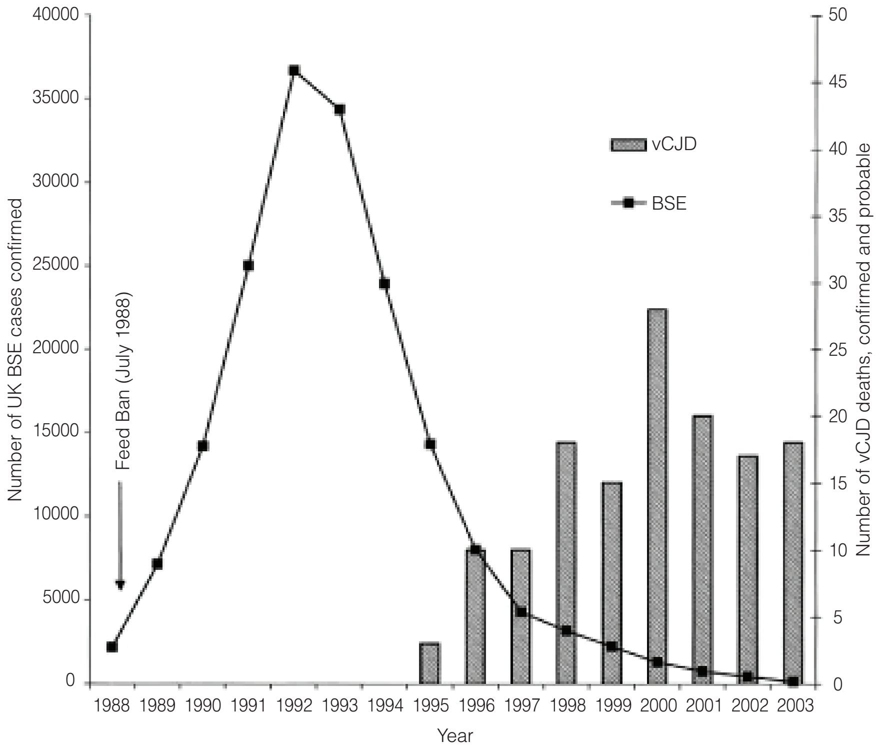


**FIGURE 2-11** Superimposed epidemics. Long incubation period of up to 10 years allowed extensive circulation of meat and bone meal-infected product in the global market prior to identification of risk.
SOURCE: Reprinted from Beisel and Morens (2004).

## Antimicrobials in Farm Animals

Global economic pressures have contributed to other risky practices in animal husbandry, including the use of antibiotics as growth promoters, which fosters the development of antibiotic-resistant pathogens in both animals and humans. It is estimated that, in the United States alone, some 12 to 70 million kg of antibiotics are administered annually in this way (Aarestrup and Pires, 2008). Evidence suggests that the use of antibiotics in animal feed may be even higher in developing economies that carry heavier disease burdens. In some parts of Asia, integrated fish farming facilities feed fish farm-animal waste that is laced with antibiotics to suppress the level of microbes. Humans in turn consume the fish, along with the antibiotics, potentially perpetuating the spread of antibiotic-resistant pathogens

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The European Union has banned the use of antibiotics as growth promoters in food animals (Silbergeld et al., 2008). A similar global ban prohibiting the application of antibiotics for farm animals outside of therapeutic use would be well advised.

The use of antimicrobials as growth hormones and in feed is another illustration that underscores the fact that incentives in global trade often are misaligned with the interests of biosecurity. Add to that the far-reaching and rapid distribution system for food products and the result is a pandemic risk that cannot be ignored.

### Beyond Food: Xenotransplantation

Another growing facet of global trade in services that poses a significant microbial risk is xenotransplantation, or the transplantation of animal parts into humans. Implanting animal organs or valves in humans introduces yet another level of cross-species exposure to pathogens. A variety of global pressures are driving this trade, including increases in diabetes and other chronic conditions detrimental to organ health, a lack of effective therapies for degenerative conditions, and, in countries such as the United States, an upcoming surge of baby boomers entering old age. As a result, the number of people seeking organs far exceeds the number of organs available for transplant and in many countries, people seeking transplants face long waiting lists.

Some players in the global marketplace have responded to the growing demand for organs and alternative therapies by venturing into experimental areas such as xenotransplantation and stem cell therapies that are strictly regulated or even prohibited in other countries. Stem cell procedures and "precursor" stem cell procedures are promoted, often via the Internet, on the global medical marketplace. They include various donor species, such as rabbits and pigs.[9] The majority of these procedures are offered without systematic protocols, primate studies, or regulation.

In the United States, the transplantation of tissues from other mammalian species is highly regulated. For instance, although the pig has been extensively explored as a potentially promising donor source, the United States has prevented the licensure of pig organs (with the exception of heart valves) because pigs carry in their genetic material endogenous retrovirus known as "PERV" (Porcine Endogenous Retrovirus), which potentially could infect its human host post-transplantation. In light of such concerns, the World Health Assembly in 2004 passed a resolution on xenogenic transplantation that urges member states to establish regulation and surveillance mechanisms and to collaborate on global strategies to prevent infections (Resolution 57-18 2004, section II). Although the United States was a key promoter of this resolution, it did not invest in World Health Organization (WHO) programming to support the initiative. Consequently,

[9] For example, see http://www.bcro-stemcells.com.

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xenotransplantation regulatory progress has lagged on a global level. The WHO collaborating center at Geneva University attempts to keep a dataset on xenotransplantation therapies;[10] however, the information is not exhaustive.

## Global Problem: Global Solutions

The foregoing cases have demonstrated how our increasingly global economy, with growing international travel and trade (including trade in services such as transplantation), has ultimately made virtually any emerging microbial risk global in nature. In the examples of foodborne *E. coli* and BSE, we see the globalization of direct infectious risk. In the instance of the overuse of antimicrobials in food animals, we see the globalization of antimicrobial resistance. With medical travel for organ transplants, we see traveling patients become potential vectors for the spread of disease.

While microbial risks have been globalized along with commerce, the corresponding health and protective measures for the most part have not. The second edition of the IHR (2005), which took effect in 2007, provides some important safeguards to help limit the international spread of infectious disease. The IHR require countries to conduct surveillance for and report to the WHO a "public health emergency of international concern," that is, an event "that may cause international disease spread." If WHO determines such a threat exists, as it did with the recent H1N1 outbreak, it may issue recommendations to curb the spread of disease, such as quarantine or travel restrictions for affected or potentially affected individuals. As the experience with H1N1 demonstrated, WHO must carefully balance the threat of disease spread with the potential economic consequences of any travel or trade restrictions in order to minimize disincentives for countries to report potential threats. While WHO Director-General Dr. Margaret Chan raised the "Pandemic Alert" level to 6 (the highest), WHO actively discouraged trade and travel restrictions after determining that they would not be effective in curbing the spread of the influenza virus and could needlessly result in significant economic repercussions. Instead, WHO focused on identifying and treating individuals with infection and urged those individuals with illness or symptoms to avoid travel and contact with others. This did not stop some countries from instituting their own travel restrictions. Several nations banned flights to Mexico, and China quarantined more than 70 travelers from Mexico (Browne, 2009). Despite the moderated response, Mexican authorities estimated $2.2 billion losses to the nation's economy as a result of the outbreak, including more than a 40 percent drop in tourism revenue (Llana, 2009).

The revised IHR represent an important step toward a more coherent global response to microbial threats. However, the full implementation of the core capacities for public health competency will not be in place until 2011, and resources will

[10] See http://www.humanxenotransplant.org.

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be needed to achieve that benchmark. Another promising initiative has been the efforts of the Asia Pacific Economic Cooperation (APEC) to create a community of interest in health across the 21 APEC economies, including a communications platform to enable members to collaborate in the event of public health emergencies. The APEC effort actively seeks to bring in the vibrant private sector through collaborative projects in biopreparedness led by its Health Working Group. The full engagement of the private sector as a stakeholder would bring a key "driver" of global trade into the discussion and implementation of public health protection.

In conclusion, there are some key questions raised by these case studies for which critical information is missing: (1) What exactly is the nature of emergent influenza risk of industrialized poultry and swine practices in poor and medium-income settings and can these be mitigated? and (2) What surveillance of trade product and practice would be useful to inform global public health? Moreover, at a global level, the IHR process requires support to ensure capacity building to enhance global access to surveillance, laboratory, and epidemiological investigation capabilities; and community building to improve cross-border communications and collaboration.

Our discussion of xenotransplantation highlights some of the risks entailed in the growing practice of medical tourism, or the movement of patients across international borders, issues that we explore in greater depth elsewhere (Hodges and Kimball, in preparation).

Finally, as we move into the pandemic phase of H1N1 and the Northern Hemisphere moves into its next influenza season, it is timely to reflect seriously on the risk our ever-globalizing trade, travel, and food production poses to population health and biosecurity.

## GLOBALIZATION OF THE FOOD SUPPLY: TIME FOR CHANGE IN APPROACH

*David W. K. Acheson, M.D., F.R.C.P.*[11]
Food and Drug Administration

The globalization of the food supply is causing changes in regulatory thinking at the FDA and moving us toward a new approach. In this paper, I share with you some of the challenges our agency currently faces, illustrated with examples of recent episodes of food contamination.

Many of these regulatory challenges result from the fact that American consumers want all kinds of food, and they expect it to be available year-round. Their demand drives global food trade, which is in turn influenced by the relative cheapness of growing and producing food in countries other than the United States, and

[11] At the time of this workshop, Dr. Acheson was Associate Commissioner for Foods at FDA; however, at the time of publication he is Managing Director, Food and Import Safety, Leavitt Partners, LLC.

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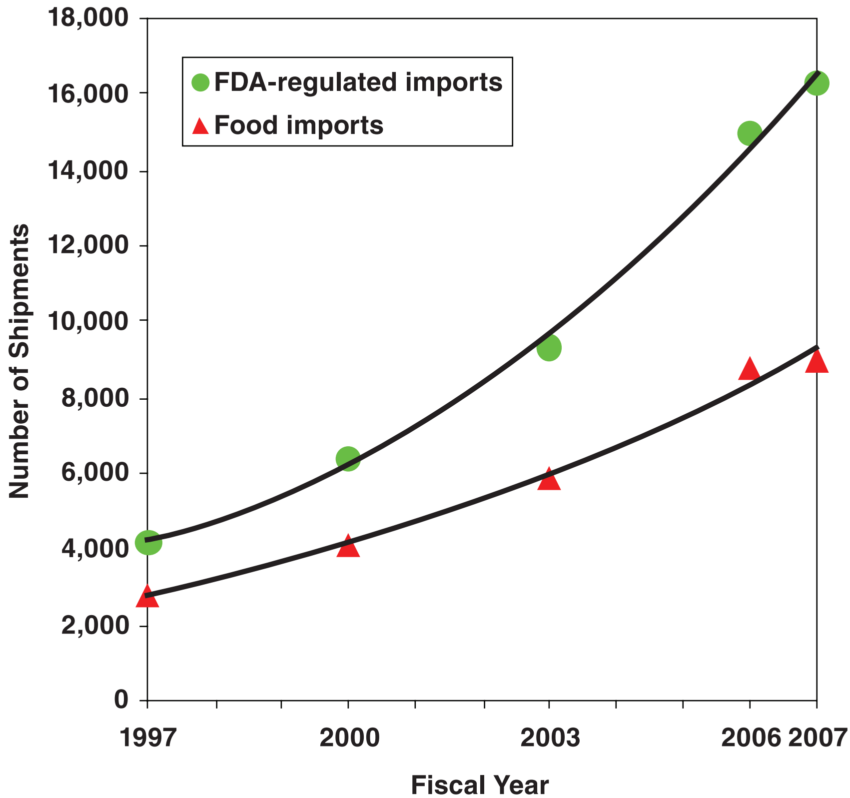


**FIGURE 2-12** Food and other FDA-regulated imports to the United States.
SOURCE: Food and Drug Administration Food Protection Plan.

shipping it to its destination. One challenge is that many of those foreign food-producing countries may lack food safety standards on a par with ours.

Approximately 15 percent of all food consumed in the United States is imported. This includes more than 80 percent of aquacultured seafood, and more than 50 percent of fresh produce; other items, such as dairy, are imported in relatively small amounts. Foods imported to the United States come from more than 200,000 foreign registered facilities (each of which is registered with the FDA) in more than 200 countries and territories. Imported food enters the United States through more than 300 ports.

There has been a steady increase in food importation into the United States over the past 10 years (Figure 2-12). The global economic crisis may have an impact on this trend, but it is difficult to predict whether it will cause food imports to increase or decrease. If imports remain substantially cheaper than domestically-produced foods, demand for imports may grow.

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### Real-World Challenges

The FDA has encountered several issues linked to the globalization of the food supply. The most pervasive is the nondeliberate or accidental contamination of food. For example, in 2003, a massive hepatitis-A outbreak of more than 1,000 cases across multiple states was linked to green onions imported from Mexico. In 2008, an outbreak of *Salmonella* Saintpaul caused by contaminated hot peppers imported from Mexico resulted in 1,450 documented cases, which probably represents a fraction of the actual number of people who got sick.

We have also dealt with the deliberate contamination of food for the purpose of economic gain. This opened a new arena for regulatory consideration, because, unlike bioterrorism, these deliberate acts are not intended to cause harm. One such case occurred in 2007, when it was discovered that the chemical melamine had been added to wheat gluten by Chinese manufacturers (FDA, 2008a). Because melamine is high in nitrogen, it increased the apparent protein content of the wheat gluten (which is gauged by nitrogen content), and therefore its price. The use of this adulterated wheat gluten in pet foods manufactured in the United States resulted in animal deaths due to kidney failure. Unfortunately, lessons were not learned from this experience, and within a year, the FDA was investigating melamine-contaminated dairy products from China, where some infants allegedly died after ingesting formula containing melamine, and more than 50,000 were reportedly hospitalized in China for urinary problems (FDA, 2007; WHO, 2009).

The following descriptions of the investigations of foodborne *Salmonella* Saintpaul in 2008 and melamine in pet food in 2007 illustrate the complexities involved in determining the sources of contaminants once they enter the globalized food system.

### *Salmonella* Saintpaul in Peppers

The 1,450 cases confirmed in the 2008 *Salmonella* Saintpaul outbreak occurred in 43 states and the District of Columbia, and they were linked to multiple food types. The outbreak came to the attention of the FDA via an alert from the Centers for Disease Control and Prevention (CDC) in early May 2008. Within two weeks, tomatoes had emerged as the likely vehicle, so we initiated a traceback to determine the origin of the contamination. This led us to Florida and Mexico, where we began inspecting tomato farms and their supply chains.

When we approached the Mexican government about this issue, they were very cooperative and met with us daily. The FDA visited several farms in the state of Sinaloa, Mexico, but failed to find tomatoes contaminated with *Salmonella*, and as the epidemiological investigation continued, other food sources were implicated. In July, we began tracing back peppers, as illustrated in Figure 2-13.

As Figure 2-13 illustrates, this was an extremely complicated process, and it begs the question as to how such episodes of contamination, which are occurring

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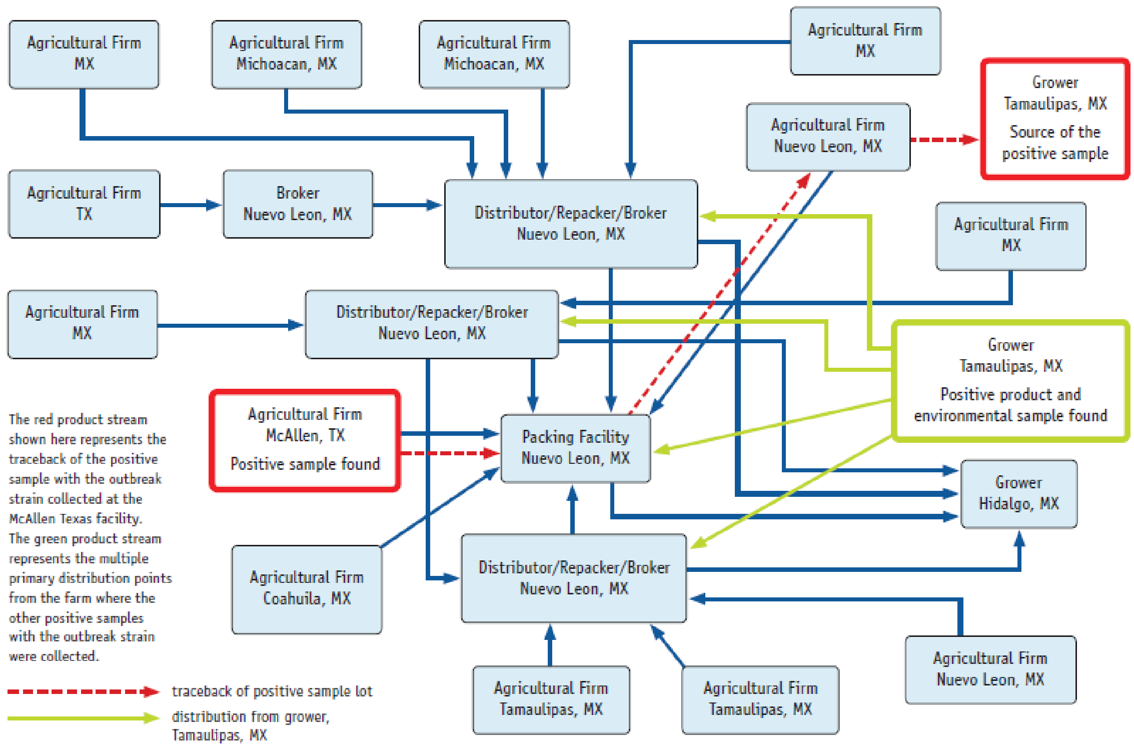


**FIGURE 2-13** *Salmonella* Saintpaul outbreak traceback and distribution. Partial view of the traceback and distribution of peppers from Mexico, July 16-22, 2008.
SOURCE: FDA (2008b).

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with increasing frequency, can best be prevented and addressed. The investigation led us to a distributor in McAllen, Texas, where we found positive pepper samples. They had received their jalapeno peppers from a packing facility in Nueva Leone, Mexico, so we returned to an entirely different part of that country to inspect pepper farms. On July 30, we found the outbreak strain, *Salmonella* Saintpaul, in irrigation water and on remaining peppers on a farm in Tamaulipas, Mexico.

### Melamine in Pet Food

This investigation began with reports of sick pets from consumers, and also from a pet food company whose research animals developed kidney failure following routine taste tests (FDA, 2008a). The only associated change in pet food formulation was the source of the wheat gluten it contained.

Once this was recognized, we soon determined that scraps from affected pet food manufacturers were being used to produce food for livestock, which could in turn introduce the adulterant into foods consumed by humans. Thus, melamine was traveling up the food chain, beginning with food ingredient manufacturers, and onward to feed mills, to poultry farms and hog farms, and from there to chicken and pork in supermarkets. A joint risk assessment was conducted between the FDA and the U.S. Department of Agriculture (USDA) to determine if the levels in poultry and pork were of a concern to public health. The assessment concluded the levels were not a public health concern. We also discovered that not only was this wheat gluten coming into the United States, but a U.S. company was also importing it to Canada. We alerted the Canadian authorities, who found that the gluten was being used there to make fish feed that was being shipped back into the United States.

The complete U.S. distribution chain of the melamine-contaminated wheat gluten is shown in Figure 2-14. It makes the point that contaminants—including pathogens—connected to food may be disseminated through vast and complex systems that profoundly affect international trade and economic relationships, as other workshop participants noted.

### Time for a New Approach

In light of these complexities, the FDA is attempting to change its approach by becoming more proactive in addressing food safety by addressing the whole supply chain. One important route to this goal is to conduct targeted, risk-based inspections, but these may be difficult to identify. Risk-based inspections are dependent on having adequate data, analytical capabilities, and inspectors. Currently such inspections are conducted at ports of entry, where it is decided whether a given product made in a foreign country and shipped to the United States will be inspected or tested for chemical or microbiological contamination, based on the various factors such as the nature of the product, its origin and

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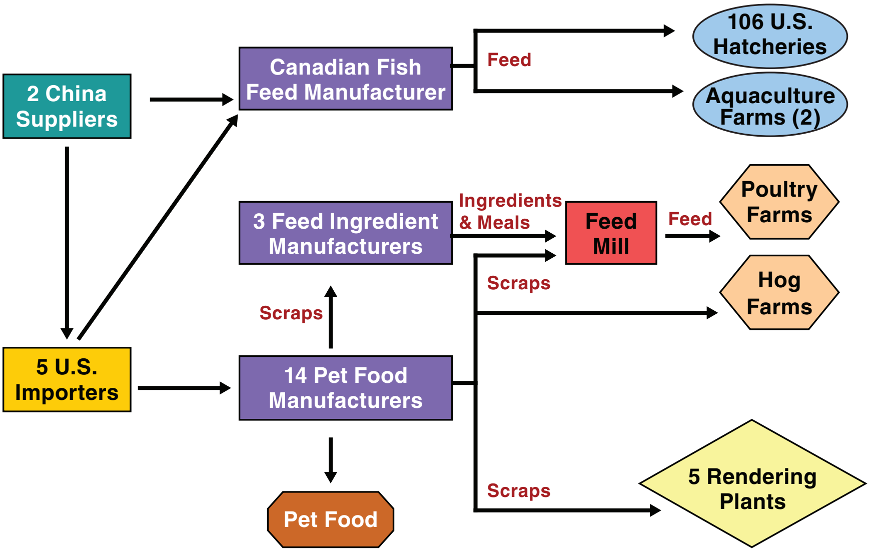


**FIGURE 2-14** Sequence of events—different routes of melamine-contaminated wheat gluten into the United States.
SOURCE: Food and Drug Administration.

destination, and the past inspection history of similar products. This procedure, euphemistically called a "snapshot," examines only one point in the distribution chain: importation. In the future, our goal is to gain greater assurance for the complete supply chain—from grower to manufacturer to shipper to importer to distributor to retailer—of imported food products. This is going to require a multifaceted approach that includes more inspections.

There are significant challenges and scarce resources for pursuing inspections of overseas growers and manufacturers, among them the sheer numbers (approximately 200,000, as previously noted) of registered foreign food facilities. There is no way, despite some peoples' wishes, that we could inspect and sample every import at the port of entry. Rather, we must try to optimize inspection based on risk. We cannot simply test or inspect our way to safe food and having appropriate preventive controls throughout is a key step.

### Risk-Based Inspections

To pursue a risk-based approach to food safety, we need leverage with foreign governments and with industry in order to gather information on the status of foreign growers, manufacturers, and foreign governments. Using these data, we must conduct effective analyses to inform risk-based decisions at the port of

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entry. Finally, rather than determining whether to examine food products on a case-by-case basis, we need to build a decision-making system.

We are currently using a prototype of such a system, which we call PREDICT, to maximize the use of FDA data in making risk-based decisions. PREDICT software allows the FDA to make risk-based decisions for import inspections and has the capacity to receive new datasets as other data streams come online. A pilot project, conducted in the Port of Los Angeles, employed PREDICT to make inspection decisions regarding seafood, for which clear inspection standards had already been established. In this trial, PREDICT prompted inspectors to detect contaminated foods more frequently than did the existing inspection system (known as OASIS). The FDA is currently attempting to expand PREDICT, recognizing that this system is only as good as the data provided to it.

### Increased Foreign Presence

Another way the FDA is supporting a more proactive stance on addressing threats to the globalized food supply is by establishing a greater foreign presence. To that end, we recently opened three offices in China—in Beijing, Shanghai, and Guangzhou—staffed by about a dozen permanent FDA employees. Although their staffs are too small to conduct significant numbers of inspections, these foreign offices will be able to strengthen relationships with the Chinese government that will improve our ability to exchange information and deal with contamination issues as they arise, and potentially before they become problems for the United States. In order to situate FDA personnel throughout the world, we are opening similar outreach offices in New Delhi and Mumbai, India; in central South America; and in Europe.

#### *Increased Inspections*

Currently the FDA performs between 100 and 155 inspections of foreign food manufacturers per year. We plan to perform 1,000 such inspections per year by 2011. While we recognize that we cannot inspect our way to safe food, we think that targeted inspections associated with the most potentially risky products are an important move forward.

### Use of Third-Party Data

The food industry extensively inspects and tests foods that are imported into the United States. Can the FDA make use of this information? Recognizing that this is a potentially contentious issue (see below), our goal is to examine the process surrounding third-party certifications and determine how the FDA can use that information to better protect the public and make maximal use of resources. One aspect of this is to use standards for third parties that provide information

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supplied to the FDA, whether it is derived from state agencies, foreign governments, or private third parties. We then want to be able to use that information to inform the risk-based inspection process. Currently, the PREDICT model at ports of entry operates primarily on U.S. compliance data. Incorporating inspection data and information from overseas and from industry into our analyses should improve our ability to make risk-based decisions.

*Ensuring Confidence*

Any risk-based decision-making system that employs third-party data must be completely transparent, and it must be clear that providing data to the FDA will not enable industry or importers to bypass inspections at the port of entry.

In order to increase confidence in such a system by all stakeholders—which include companies, consumers, regulators, and Congress—the FDA issued a guidance document in January 2009[12] describing attributes that a third-party certification program should have in order for the FDA to have confidence in the quality of the audit conducted by the program. It also provides information on the certification process, including guidance on application, certification, recertification, and withdrawal of certification. In order to determine how such a third-party certification program might operate, the FDA has established a pilot program focused on aquacultured shrimp. We issued a *Federal Register* Notice[13] asking for volunteers among companies that import shrimp into the United States to submit an application to this certification program. By processing these applications, we hope to determine infrastructure needs for handling these kinds of data, find out whether importers can meet our data standards, and establish processes for evaluating third-party certification programs.

This pilot program does not guarantee entry into the U.S. market by participating shrimp importers. We are not using the data they provide to make importation decisions; rather, this pilot study should identify strengths and weaknesses in our developing third-party certification program and help us learn how to make such a program transparent and credible.

## Conclusion

The regulatory challenges involved in providing safe food to the United States will increase as globalization of the food system continues. The complexities of the food supply are enormous, and there is considerable economic benefit in making food distribution as rapid and efficient as possible. It is therefore

[12] *Guidance for Industry Voluntary Third Party Certification Programs for Foods and Feeds*. See http://www.fda.gov/oc/guidance/thirdpartycert.html.

[13] See http://www.regulations.gov/fdmspublic/component/main?main=DocumentDetail&o=090000648066388c; Docket No.: FDA-2008-N-0382.

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critical that we abandon the practice of focusing our efforts on ports of entry and instead embrace a new approach focused on the whole supply chain that attempts to understand foodborne threats in foreign countries, anticipates their potential to spread globally, and uses risk-based inspections to detect them before an outbreak occurs in the United States.

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# 3

# Mobile Animals and Disease

## OVERVIEW

As discussed in the previous chapter, trade in livestock, poultry, and animal products precipitated the emergence of several important zoonotic diseases, including H5N1 influenza and bovine spongiform encephalopathy (BSE). The essays collected in this chapter consider additional mobile animals, such as pets, wildlife, research animals, and insect vectors (with and without their various hosts) as factors in infectious disease emergence. In addition to introducing diseases to new animal and human populations, some of these animals are changing ecosystems in ways that alter the transmission dynamics of infectious diseases.

The first paper, by workshop speaker Nina Marano and colleagues of the Centers for Disease Control and Prevention (CDC), describes regulatory procedures designed to reduce the threat of zoonotic diseases to the United States. The CDC is one of four government agencies that regulate the importation of animals based on their risk for zoonotic disease; the others are the Department of Homeland Security (Customs and Border Protection), the Department of Agriculture (Animal and Plant Health Inspection Service), and the Department of the Interior (Fish and Wildlife Service). Marano et al. review the CDC's animal regulations, including those that were developed in response to such noteworthy events as an Ebola outbreak among research animals in a government primate research facility in Reston, Virginia; the emergence of monkeypox in pet prairie dogs; the detection of zoonotic viruses in bushmeat; and the presence of highly pathogenic avian influenza in imported birds.

Until recently, the CDC's regulatory actions to address disease threats from imported animals have been largely reactive, species-specific, and pathogen-



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specific, the authors state. Now the agency—much like the Food and Drug Administration (FDA) as described by Acheson in the previous chapter—is engaged in developing a "risk based, proactive approach to preventing the importation of animals and vectors that pose a zoonotic disease risk," according to Marano et al. This effort, which they describe in some detail, focuses on the systematic and targeted surveillance of high-risk animals, animal products, and vectors in their countries of origin.

Rapid expansion of trade and transportation during the Industrial Revolution resulted in the global proliferation of mosquito-borne diseases, such as dengue and chikungunya. Thanks to today's globalized economy, these and other vector-borne diseases—once considered well-controlled in industrialized countries—are poised for resurgence, while others, such as West Nile viral fever and chikungunya, have significantly expanded their geographic range. In his contribution to this chapter, workshop speaker Paul Reiter, of Institut Pasteur, examines the role of human activities in the dispersal of several important insect vectors (such as the mosquito species that transmit malaria and yellow fever to humans) and of vector-borne diseases of both humans and animals, including chikungunya, West Nile viral fever, Rift Valley fever, and bluetongue. He also predicts future range expansions for certain vectors and vector-borne diseases; for example, he expects that *Aedes gambiae*, "perhaps [the] most effective malaria vector on earth," will migrate northward out of its native home in sub-Saharan Africa, and also across the Atlantic to South America.

Reiter, who captured the first specimen of the mosquito species *Aedes albopictus* in the United States in 1983, and who subsequently discovered that this Asian native had been distributed globally in shipments of used tires, observes that, while "it is not difficult to survey a species once it has been detected, it is much more difficult to detect new introductions when they occur, particularly when cargoes are imported in locked containers." Therefore, he concludes, "with a few exceptions—e.g., the enforcement of vaccination requirements—we must expect the continued establishment of new exotic species as an inevitable consequence of modern transportation technology."

Might it be possible to prevent the emergence of infectious diseases by anticipating and blocking the movements of pathogens into new ecosystems? This question is posed by speaker Andy Dobson of Princeton University and Sarah Cleaveland of the University of Glasgow in this chapter's final essay. Through a detailed examination of the circumstances that led up to the emergence of Nipah virus in Malaysia, the authors provide a number of insights into how other "novel" pathogens are likely to emerge, and they suggest a series of general questions that must be answered in order to predict and prevent future outbreaks of emerging infectious diseases.

To quantify the risk presented by a novel microbe to a potential host, Dobson and Cleaveland explain, information must be gathered and assessed at each of several stages in the development of an epidemic, from characterizing the back-

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ground of all potential pathogens to analyzing transmission dynamics among novel hosts. "Ultimately the only way we can quantify the risk of novel microbes to humans (and domestic livestock) is to create a huge phylogeny of all pathogens and their hosts," they write. "We then need to examine the pathology of closely related pathogens, in their reservoir hosts and other host species they infect and examine the factors that modify virulence and transmissibility." Such an effort "will require considerable capacity-building in areas that are woefully under-funded," they acknowledge.

## PUBLIC HEALTH IMPACT OF GLOBAL TRADE IN ANIMALS

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### Introduction

Zoonoses are diseases that are transmissible from animals to people. The prevention and management of zoonoses in humans pose unique considerations for surveillance and detection of these diseases and require acknowledgment of the role of animals in disease transmission. Wildlife and animals intended for the pet trade can serve as hosts for a variety of well-known and emerging zoonotic pathogens. The Centers for Disease Control and Prevention's (CDC's) regulations exist to prevent the importation of animals and animal by-products that pose a risk to public health. However, globalization of the food supply, consumer goods, and live animals—combined with human behaviors and preferences for the exotic—are ever-growing risk factors for translocation to the United States of zoonotic diseases from parts of the world where they are endemic (or exist in a reservoir state) (Smith et al., 2009). This paper describes the CDC's regulatory framework for mitigating response to the introduction of zoonotic diseases, which has traditionally been reactive. The challenges of the twenty-first century call for a more proactive approach rooted in a risk-based strategy to prevent the introduction of animals and vectors that pose a risk to public health.

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## CDC's Animal Regulations: Mitigating Public Health Threats

Under Section 361 of the Public Health Service Act[3] (42 USC § 264), the CDC is responsible for regulations to prevent the introduction, transmission, and spread of communicable diseases from foreign countries into the United States. The CDC currently regulates the importation of nonhuman primates, dogs and cats, small turtles, African rodents, civets, and Asian birds to prevent the entry of zoonotic diseases and also regulates the importation of etiologic agents, hosts, and vectors (HHS, 2001).

### *Nonhuman Primates*

Nonhuman primates (NHPs), particularly those recently captured in the wild, may harbor agents in their blood or other body tissues that are infectious to humans. Persons working in temporary and long-term animal holding facilities and individuals involved in transporting animals (e.g., cargo handlers and inspectors) are especially at risk for infection. NHPs are a potential source of pathogens that can cause severe or fatal disease in humans, including filoviruses, hepatitis, herpes B virus, rabies, tuberculosis, and parasitic infections (NRC, 2003). Some cynomolgus, African green, and rhesus monkeys imported into the United States have been previously demonstrated to be infected with Ebola Reston virus (CDC, 1990). An epidemiologic link between hepatitis A infections in NHPs, especially chimpanzees, and their caretakers has been demonstrated (Robertson, 2001). Herpes B virus is a zoonotic agent that naturally infects only macaque monkeys causing mild illness or no illness but can cause fatal encephalomyelitis in humans. Previously reported fatal cases of herpes B virus disease in humans have been caused by animal bites, scratches, or mucous membrane contact with infected materials (Cohen et al., 2002). NHPs, especially macaques, are highly susceptible to tuberculosis and rabies and most are imported from areas of the world with a high prevalence of these diseases in humans and animals (CDC, 1993). NHPs may also be a source of flaviviruses (e.g., yellow fever virus), which may be transmitted to humans by mosquitoes that have previously fed on an infected NHP (Mansfield and King, 1998); transmission of yellow fever to humans in NHP research work has also occurred (Richardson, 1987). Quarantine requirements for imported NHPs are designed to reduce these infectious disease risks. Since October 10, 1975, the CDC, through 42 CFR § 71.53, has prohibited the importation of NHPs except for scientific, educational, or exhibition purposes. Under this regulation, NHP importers are required to register with the CDC and this registra-

[3]The Public Health Service Act is a U.S. federal law enacted in 1946. The full act is captured under Title 42 of the United States Code "The Public Health and Welfare," Chapter 6A, "Public Health Service." Under Section 361 of the Public Health Service Act (42 U.S.C. § 264), the U.S. Secretary of Health and Human Services is authorized to take measures to prevent the entry and spread of communicable diseases from foreign countries into the United States and between states.

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tion must be renewed every two years. NHPs are required to be held in quarantine for a minimum of 31 days following entry into the United States. This regulation also requires registered importers to maintain records on imported NHPs and to immediately report illness suspected of being communicable to humans. Imported NHPs and the offspring of imported NHPs may not be maintained as pets, a hobby, or as an avocation with occasional display to the general public. Additional requirements for importers of NHPs were developed and implemented in response to specific public health threats. On January 19, 1990, the CDC published interim guidelines for handling NHPs during transit and quarantine in response to identification of Ebola virus (Reston strain) in NHPs imported from the Philippines (CDC, 1990). In April 1990, there was confirmation of Ebola virus infection in four NHP caretakers, and serologic findings suggested that cynomolgus, African green, and rhesus monkeys posed a risk for human filovirus infection. As a result of these findings, the CDC placed additional restrictions and permit requirements for importers wishing to import these species.

*Dogs*

The CDC restricts the importation of dogs primarily to prevent the entry of rabies (CDC, 2003a). Rabies is a lyssavirus that causes a fatal encephalitis in mammals. In the United States, widespread mandatory vaccination of dogs has eliminated the canine variant of rabies and dramatically reduced the number of human cases (Velasco-Villa et al., 2008). However, canine rabies virus variants continue to be imported via unvaccinated dogs from areas where rabies is enzootic, such as Asia, Africa, the Middle East, and parts of Latin America. Globally, canine variants are responsible for most of the estimated 55,000 human rabies deaths worldwide each year (HHS, 2001; WHO, 2009). Since May 2004, there have been at least four documented instances of dogs being imported to the United States from rabies enzootic areas that subsequently were diagnosed with rabies, necessitating extensive public health investigations to identify persons at risk of exposure and in need of post-exposure prophylaxis (PEP), as shown in Table 3-1 (CDC, 2008b). "In May 2004, an unvaccinated puppy was flown from Puerto Rico to Massachusetts as part of an animal rescue program. The day after arrival, the puppy exhibited neurologic signs, was euthanized, and was subsequently confirmed to have rabies" (CDC, 2008b), with a variant identified as enzootic to dogs and mongoose from Puerto Rico. Among 11 people evaluated, 6 persons were recommended to receive PEP because of potential exposure (personal communication, Frederic Cantor, Massachusetts Department of Public Health, June 20, 2004; CDC, 2008b).

"In June 2004, an unvaccinated puppy adopted by a U.S. resident in Thailand was confirmed to have rabies by the California Department of Public Health" (CDC, 2008b), and a dog rabies virus variant identified as enzootic to Thailand. Of 40 persons interviewed for potential rabies exposure, 12 received PEP (personal communication, Ben Sun, California Department of Public Health, August 16,

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**TABLE 3-1** Importations of Rabid Dogs to the Continental United States, 2004-2008

| Month/Year | No. of Dogs with Rabies/ No. of Animals in Shipment | Territory or Country of Origin | No. of persons receiving PEP/ No. of persons interviewed |
|---|---|---|---|
| May 2004[a] | 1/6 | Puerto Rico | 6/11 |
| June 2004[b] | 1/1 | Thailand | 12/40 |
| March 2007[c] | 1/2 | India | 8/20 |
| June 2008[d] | 1/24 | Iraq | 13/38 |

Based on data from:
[a]Massachusetts Department of Public Health.
[b]California Department of Public Health.
[c]Alaska Department of Health and Social Services.
[d]New Jersey Department of Health and Senior Services.

2004; CDC, 2008b). "In March 2007, a puppy was adopted by a U.S. veterinarian while volunteering in India. . . . The puppy was flown in cargo to Seattle, Washington then adopted by another veterinarian in Juneau, Alaska, where it was flown seven days after arrival" (CDC, 2008b). The puppy exhibited neurologic signs and was confirmed to have rabies by the Alaska Department of Health and Social Services, with a dog rabies virus variant identified as enzootic to India. Of 20 persons interviewed for potential rabies exposure, eight received PEP (Castrodale et al., 2008). Most recently in June 2008, a shipment of 24 dogs and 2 cats arrived in the United States from Iraq as part of an international animal rescue operation. Subsequently, an 11-month-old dog from this group became ill; rabies was confirmed and the virus was determined to be a rabies virus variant associated with dogs in the Middle East. During the public health investigation, 13 of 28 persons were identified with potential exposure of sufficient magnitude to initiate PEP (personal communication, Faye Sorhage, New Jersey Department of Health and Senior Services, July 1, 2008).

In all four of these cases, the rabies viruses were identified as exotic variants circulating in dogs and terrestrial wildlife in the animal's country or region of origin, and were associated with human fatalities.

Besides the threat of human and domestic animal exposure and the direct public health, veterinary, and economic consequences associated with PEP, particularly during times when supplies of rabies biologics are less than ideal, such events serve to underline the fragility of the canine rabies virus-free status in the United States posed by such introductions. The introduction of canine rabies, and its potential to become enzootic again in domestic animals or wildlife, would increase the demand for prophylaxis and exacerbate fragile supplies of rabies vaccines and immune globulins. Moreover, other lyssaviruses besides rabies virus persist in the Old World. The danger of importation posed by these agents is greatly magnified because current human and veterinary rabies vaccines do not

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cross-protect against lyssaviruses from other phylogroups and no pan-lyssavirus vaccines are on the horizon for serious commercial development.

Since canine variants of rabies remain a very serious health threat in many other countries, preventing the entry of potentially infected dogs into the United States is a critical public health priority. CDC requires dogs entering the United States to be vaccinated for rabies or, if they are not vaccinated, that the importer agree to have the dog vaccinated and confined for 30 days after rabies vaccination to allow for acquisition of vaccine-induced immunity (HHS, 2001). The CDC is currently considering amending its regulations to institute further requirements for entry of dogs and other pet animals to the United States to prevent importation of rabies.

### *Etiologic Agents, Hosts, and Vectors*

Under Section 71.54 of the Public Health Service Act (Foreign Quarantine[4]) the CDC also regulates etiologic agents, hosts, and vectors (2003b). This regulation means that a person may not import into the United States, or distribute after importation, any etiologic agent or any arthropod or other animal host or vector of human disease, or any exotic living arthropod or other animal capable of being a host or vector of human disease unless accompanied by a permit issued by the director. "All live bats require an import permit from the CDC and the U.S. Department of Interior's Fish and Wildlife Services, and may not be imported as pets" (CDC, 2008c; see also HHS and CDC, 2003a). We are particularly concerned about bats as reservoirs for infectious agents, as we recognize that Marburg virus is clearly associated with a species of bat called *Rousettus aegyptiacus*, at least in Uganda, and one or more other species are almost surely associated with Ebola virus (Calisher et al., 2006). In addition, bats are known to be the keystone reservoirs for viruses such as rabies virus, other lyssaviruses related to rabies, and henipaviruses and have most recently been identified as the reservoir for severe acute respiratory syndrome (SARS) coronavirus (Cui et al., 2007). Any living insect or other arthropod that is known or suspected of containing an etiologic agent (human pathogen) requires a CDC import permit, and vector snail species capable of transmitting a human pathogen require a permit as well (CDC, 2008c; HHS, 2001).

CDC limits imports of small turtles; those with a shell length of less than four inches may not be imported for any commercial purpose (CDC, 2008d; HHS and CDC, 2003b). "This rule was implemented in 1975 after it was discovered that small turtles frequently transmitted *Salmonella* to humans, particularly young children" (CDC, 2008d; see also HHS, 2001).

[4]The provisions of 42 CFR Part 71 of the Public Health Service Act (Foreign Quarantine) contain the regulations to prevent the introduction, transmission, and spread of communicable disease from foreign countries into the States or possessions of the United States.

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> Zoonotic pathogens are important not only because of the known illnesses they cause—which can move to new parts of the world—but also because of new human diseases that can arise from animal sources. In 2003, an outbreak of SARS in humans spread worldwide, and the initial transmission to humans was linked to infected civets sold for food in [Chinese wet markets]. The emergence of SARS in humans following exposure to wild animals is an example of how a previously unrecognized zoonotic disease can quickly cause unexpected illness in human populations. (CDC, 2007b)

In 2003, the CDC issued an order to ban the importation of civets because of concerns at the time that these animals were involved in the transmission of SARS coronavirus to humans (CDC, 2004a).

*Birds*

Since 1997, and to the present, the outbreaks of avian influenza H5N1 in birds and humans are a prime example of how globalization of the food supply affects public and animal health. In November 1997, the Hong Kong Special Administrative Region Department of Health[5] detected new cases of a human illness caused by an avian influenza H5N1 virus.

> By late December, the total number of confirmed new cases had climbed to 17, of which 5 were fatal. . . . Except for one doubtful unconfirmed case, all illnesses or laboratory evidence of infection was in patients who had been near live chickens (e.g., in market places) in the days before onset of illness, which suggested direct transmission of virus from chickens to human rather than person-to-person spread. . . . Because these cases occurred at the beginning of the usual influenza season in Hong Kong, public health officials were concerned that human [influenza] strains might cocirculate with avian influenza strains to generate human and avian reassortant viruses with [the] capacity for efficient person-to-person spread.
>
> [In December 1997,] veterinary authorities began to slaughter all 1.6 million chickens present in wholesale facilities or vendors within Hong Kong, and importation of chickens from neighboring areas was stopped. Subsequently, no more human cases caused by avian influenza virus were detected. (Snacken et al., 1999)

Highly pathogenic avian influenza (HPAI) H5N1 in poultry and wild birds reemerged in Asia in 2003 and has become established as a veterinary and human health threat throughout the world, presenting challenges for control due to the widespread geographic areas and large numbers of poultry that are affected.

[5]See http://www.who.int/mediacentre/factsheets/avian_influenza/en/#history (accessed July 13, 2009).

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Because birds imported into the United States from countries with HPAI H5N1 could pose a risk for human infection or spread of virus to U.S. birds, in 2004 the CDC issued emergency orders to ban the importation of birds and bird products from specific countries with HPAI H5N1. These orders mirrored similar regulatory actions taken by the U.S. Department of Agriculture Animal and Plant Health Inspection Service (USDA/APHIS) to prevent the importation of birds with HPAI H5N1 (CDC, 2007a). On January 21, 2008, the CDC published a notice in the *Federal Register* seeking public comment on a proposal to rescind its bird embargoes (CDC, 2004b). In 2004, when HPAI H5N1 was first recognized as a threat, CDC took emergency action to ban the importation of birds and thus prevent the disease from entering the United States.

> Since that time, partnerships with public health and agricultural agencies around the world have increased the capacity for surveillance and communication about emerging outbreaks of HPAI [H5N1]. . . . All the bird embargoes currently in force under USDA regulations will remain in force. (CDC, 2009)
>
> CDC continues to work closely with USDA, the World Health Organization, the World Animal Health Organization, the Food and Agriculture Organization, and individual ministries of health to monitor the situation regarding HPAI [H5N1 abroad] to ensure that the threat to human health is being adequately addressed through animal control measures. If necessary, CDC can take measures to control a human health threat based upon its authority to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the United States. (CDC, 2009)

### *Rodents*

The emergence of human monkeypox in the Western Hemisphere in May and June 2003 is a vivid reminder of why we are, and should continue to be, concerned about the importation of wild animals into the United States. Monkeypox is a zoonotic disease endemic to Central and West Africa. African rodents are considered to be the natural hosts of the virus which, in humans, causes rashes similar to smallpox, fever, chills, and headache (CDC, 2004c; Khodakevich et al., 1988). Human infections during the 2003 outbreak were traced back and were determined to have resulted from contact with pet prairie dogs that contracted monkeypox from diseased African rodents imported for the commercial pet trade (CDC, 2003; Hutson et al., 2007; Reed et al., 2004) (Figure 3-1). The shipment of mammals imported from Ghana contained more than six species and a total of 762 African rodents, some of which were confirmed to be infected with monkeypox. The monkeypox outbreak resulted in 72 human cases, with 37 of those cases being laboratory-confirmed (CDC, 2003). Most patients had direct or close contact with the infected prairie dogs, including 28 children at a day care center and veterinary clinic staff (Reynolds et al., 2007).

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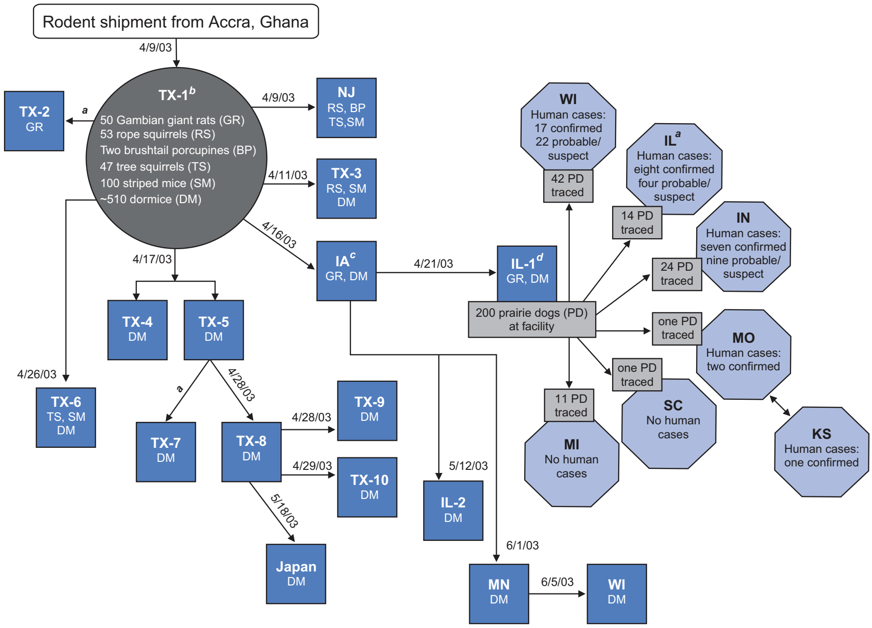


**FIGURE 3-1** Movement of imported African rodents to animal distributors and distribution of prairie dogs from an animal distributor associated with human cases of monkeypox, 11 states, as of July 8, 2003: Illinois (IL), Indiana (IN), Iowa (IA), Kansas (KS), Michigan (MI), Minnesota (MN), Missouri (MO), New Jersey (NJ), South Carolina (SC), Texas (TX), and Wisconsin (WI). Japan is included among sites having received shipments of rodents implicated in this outbreak. Does not include one probable human case from Ohio; investigation is ongoing. Includes two persons who were employees at IL-1.

[a]Date of shipment unknown.

[b]Identified as distributor C in *MMWR* 2003; 52:561-564.

[c]Identified as distributor D in *MMWR* 2003; 52:561-564.

[d]Identified as distributor B in *MMWR* 2003; 52:561-564.

SOURCE: CDC (2003).

On June 11, 2003, the CDC and the Food and Drug Administration (FDA) pursuant to 42 CFR § 70.2 and 21 CFR § 1240.30, respectively, issued a joint order prohibiting, until further notice, the transportation or offering of transportation in interstate commerce, or the sale, offering for sale, or offering for any other type of commercial or public distribution, including release into the environment, of prairie dogs and the six implicated species of African rodents (FDA, 2003; Gerberding and McClellan, 2003). In addition, pursuant to 42 CFR § 71.32(b), the CDC implemented an immediate embargo on the importation of all rodents (order Rodentia) from Africa. This emergency order was superseded on November 4,

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2003, when the two agencies issued an interim final rule creating two complementary regulations restricting both domestic trade and importation, intended to prevent the further introduction, establishment, and spread of the monkeypox virus in the United States.

We are also concerned about rodents that originate outside of Africa, from other parts of the world such as Asia, Europe, and South America. We recently conducted an analysis of the numbers and origins of rodents imported to the United States since our African rodent ban was instituted in 2003. We analyzed data from the U.S. Fish and Wildlife Service's Law Enforcement Management Information System (LEMIS) database, which records the entry of wildlife species to the United States. Since 2003, our ban has effectively limited legal importation of African rodents; the number of different rodent species entering the United States has decreased by 31 percent (Table 3-2). This decrease appears to be due to the restrictions on importation of African-origin rodents.

> However, the commercial pet market has found a new niche in rodents from other parts of the world, as the number of rodents from Asia, Europe, and South America has increased by 223 percent. Rodents harbor hantaviruses, [resulting in] more than 100,000 hospitalized cases of hemorrhagic fevers in Europe and Asia (McKee et al., 1991). Rodents are also associated with rickettsial diseases. (CDC, 2008e)

Scrub typhus and murine typhus cause hundreds of thousands of cases annually; up to 50 percent of some human populations in Asia have antibodies to *R. typhus* (Azad, 1990). Outbreaks of *Salmonella* Typhimurium (CDC, 2005) and lymphocytic choriomeningitis (CDC, 2008a) have been associated with pet rodents in recent years. Since they are easier to care for than a dog or cat, these "pocket pets" are considered good choices for children. Because children interact with their pets in a closer and more intimate manner than they do with other animals, they may be at a heightened risk of infection. Table 3-3 provides a listing of pathogens in rodents that meet the following qualifications: they are zoonotic; nonindigenous; capable of causing significant human illness; and, if vector-borne, the vector is present in the United States (Acha and Szyfres, 2003; Eremeeva and Dasch, 2008; Heymann, 2008; Hugh-Jones et al., 1995). Rodents, once established, have several traits that make them ideal hosts for zoonotic diseases. They reproduce rapidly, and, unlike many other species of larger wild mammals, can be found in our gardens, storage buildings, and homes.

### *Insectivorous Mammals*

Another potential concern for CDC may be insectivorous mammals, as there is some new evidence for hantaviruses being associated with shrews. We do not know whether these shrew-associated hantaviruses are human pathogens, and

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**TABLE 3-2** Numbers of Individual Rodents and Rodent Species Imported into the United States Pre-CDC African Rodent Ban (1999-2003) and Post-Ban (2004-2006)

| | 1999-2003 | 2004-2006 | % Change |
|---|---|---|---|
| Rodents | 53,068 | 171,421 | +223 |
| Species | 77 | 53 | –31 |

SOURCE: Department of Interior, U.S. Fish and Wildlife Service LEMIS.

**TABLE 3-3** Some Important Rodent-Borne Zoonotic Pathogens and Their Hosts[a]

| Pathogen | Host species | Disease |
|---|---|---|
| | **Viruses** | |
| Cowpox virus | *Apodemus, Myodes* | Cowpox |
| Monkeypox virus | Rodents | Monkeypox |
| Omsk hemorrhagic fever virus | Rodents | Omsk hemorrhagic fever |
| Kyasanur forest disease virus | Rodents | Kyasanur forest disease |
| | **Arenaviruses** | |
| Flexal virus | Unidentified rodent | Hemorrhagic fever |
| Guanarito virus | *Zygodontomys brevicauda* | Venezuelan hemorrhagic fever |
| Junín virus | *Calomys musculinus* | Argentine hemorrhagic fever |
| Lassa virus | *Mastomys natalensis* | Lassa fever |
| Sabiá virus | Unidentified rodent | Brazilian hemorrhagic fever |
| Chapare virus | Unidentified rodent | |
| | **Hantaviruses** | |
| Amur virus | *Apodemus peninsulae* | HFRS |
| Dobrava-Belgrade virus | *Apodemus flavicollis* | HFRS |
| Hantaan virus | *Apodemus agrarius* | HFRS |
| Muju virus | *Myodes regulus* | HFRS |
| Puumala virus | *Myodes glareolus* | HFRS |
| Saaremaa virus | *Apodemus agrarius* | HFRS |
| Seoul virus | *Rattus norvegicus* | HFRS |
| Thailand virus | *Bandicota indica* | HFRS |
| Andes virus | *Oligoryzomys longicaudatus* | HPS |
| Araraquara virus | *Necromys lasiurus* | HPS |
| Bermejo virus | *Oligoryzomys flavescens* | HPS |
| Castelo dos Sonhos virus | Unidentified rodent | HPS |
| Central Plata virus | *Oligoryzomys flavescens* | HPS |
| Choclo virus | *Oligoryzomys fulvescens* | HPS |
| Juquitiba virus | *Oligoryzomys nigripes* | HPS |
| Laguna Negra virus | *Calomys laucha* | HPS |
| Lechiguanas virus | *Oligoryzomys flavescens* | HPS |
| Oran virus | *Oligoryzomys chacoensis* | HPS |

*continued*

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**TABLE 3-3** Continued

| Pathogen | Host species | Disease |
|---|---|---|
| | **Rickettsial infections** | |
| *Orientia tsutsugamushi* | *Rattus spp.* | Scrub typhus |
| *Rickettsia conori* | Rodents | Mediterranean spotted fevers |
| *R. sibirica* | | North Asian tick typhus |
| *R. africae* | Rodents | African tick-bite fever |
| | | Queensland tick typhus |
| *R. helvetica* | Rodents | Aneruptive fever |
| *R. marmionii* | Rodents | Australian spotted fever |
| *R. heilongjiangensis* | Rodents | Far Eastern spotted fever |
| *R. sibirica* | Rodents | Lymphangitis associated rickettsiosis |
| *R. parkeri* | Rodents | Maculatum infection |
| *R. japonica* | Rodents | Oriental spotted fever |
| *R. slovaca* | Rodents | Tick-borne lymphadenopathy |
| | **Parasitic diseases** | |
| *Angiostrongylus sp.* | Rodents | Angiostrongyliasis |
| *Gastrodiscoides hominis* | Rodents | Amphistomiasis |
| *Metagonimus yokogawai* | Rodents | Metagonimiasis |
| *Clonorchis sinensis* | Rodents | Clonorchiasis |
| *Schistosoma sp.* | Rodents | Schistosomiasis |
| *Trypanosoma cruzi* | Rodents | Chagas disease |

NOTE: HFRS, hemorrhagic fever with renal syndrome; HPS, hantavirus pulmonary syndrome.
[a]Agents listed are zoonotic and may cause significant disease in humans, may be hosted by rodent (although not necessarily exclusively), and are not known to be endemic to the United States.
SOURCES: Based on data from Acha and Szyfres (1987); Eremeeva and Dasch (2008); Heymann (2008); and Hugh-Jones et al. (1995).

humans rarely have contact with shrews. However, that could change rapidly if someone decided to import shrews as pets (Song et al., 2007).

### *Animal Products*

CDC's regulations also prohibit the importation of products that originate from the animals we regulate. Rodents, bats, NHPs, and other mammals serve as a food source called bushmeat in other parts of the world, especially in parts of West Africa. The Bushmeat Crisis Task Force estimates that approximately 15,000 pounds of meat harvested from African wildlife is illegally imported into the United States each month (Goldman, 2007). Bushmeat may be derived from any species of wildlife, including rodents, bats, antelope, and NHPs. It is an important source of food and it is highly desired among many African expatriates. Bushmeat may enter the United States through large-scale vendors seeking

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a commercial sale or may be carried in piece by piece by immigrants seeking a "taste of home." Many methods have been used to disguise bushmeat: wrapping luggage in plastic to hide the odor, burying bushmeat under legal smoked fish, or mailing bushmeat via FedEx or DHL. Regardless of how it is brought in, unregulated overharvesting of wildlife for food, fur, or fiber has negative implications on conservation efforts and is a potentially dangerous source of disease for humans and animals in the United States.

## Discussion

### *Challenges*

There are many challenges facing public health to effectively control zoonotic diseases related to movement of animals across international borders. At the CDC, the public health response to SARS involved participation by 866 employees including deployments to 10 foreign countries and 19 domestic ports of entry. The number of person-days during the SARS response equaled 46,714 (Posid et al., 2005). In addition, the impacts of a globally emerging zoonotic disease are far reaching and extend well beyond the public health realm. Worldwide, the economic impact of SARS was estimated to be $30-50 billion, largely due to its impact on tourism and thus the global economy, as shown in Figure 3-2 (Newcomb, 2003).

The monkeypox outbreak illustrates the possibility of animals as sources of human infections and the special risk associated with keeping wild animals as pets. During the monkeypox outbreak our investigators could not identify many potentially infected animals because no accurate records were available to trace their movements. The importation of wildlife poses a health risk because shipments often involve a high volume of animals, most of which are wild-caught and not captive-raised. "Many shipments also include different species comingled and/or kept in close proximity in confined spaces—conditions ideal for the transmission of disease. For most species, there is no screening for the presence of infectious diseases prior to shipment, and no holding or testing is required on entry into the United States" (Humane Society, 2009), which creates an opportunity for the widespread exposure of humans to pathogens these animals could be harboring. "High mortality rates among some animals, such as rodents, are common, and current U.S. [statutes and] regulations do not require importers to have [diagnostic necropsies] performed to determine whether the mortality is from a [pathogen] that could have an adverse effect on public health" (Pet Relocation, 2007).

We are further challenged by the fact that currently no single agency has the lead for implementing animal import regulations at ports of entry. Thus, depending on whether the import is classified as a food item or a product, livestock, wildlife, or endangered species, different agencies including the Department of

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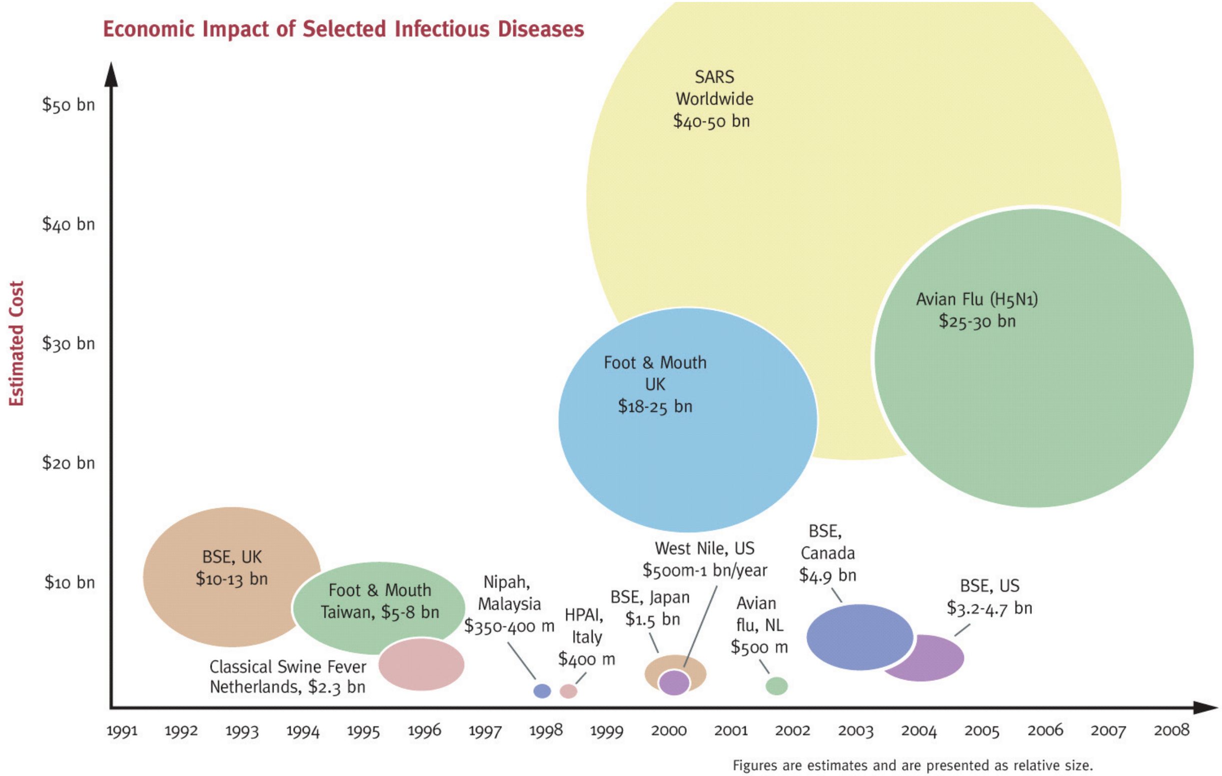


**FIGURE 3-2** Economic impacts of selected infectious diseases.
SOURCE: Reprinted with permission from Bio-era.

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Homeland Security, the FDA, the Department of the Interior, the USDA, and the Department of Health of Human Services are called in to handle the situation. Additionally, federal agencies have variable amounts of resources at points of entry; thus, regulations are not applied consistently and comprehensively everywhere.

The regulatory approach to controlling zoonotic diseases creates opportunities for further mitigation but also leaves gaps in public health protection. In September 2008, the FDA lifted its portion of the ban on interstate movement of prairie dogs because the agency had determined through a risk-assessment process that the virus implicated in the 2003 outbreak no longer persisted in the environment. However, because prairie dogs are vectors for other zoonotic diseases, including tularemia and plague, the ban on interstate movement limited the possibility of human exposure to other diseases via widespread sale and adoption of prairie dogs as pets, and also limited the possibility of prairie dogs being exported to other countries. Until 2003, it was estimated that several thousand prairie dogs were sold within the United States as pets annually, and it was reported that the United States exported approximately15,000 prairie dogs as pets to other countries. As of 2003, Japan was the main importer of U.S. prairie dogs, but it had placed a ban on prairie dog importation in March of that year. Tularemia and plague, in addition to causing an estimated 200 natural human infections in the United States each year, are also listed as CDC Category A bioterrorism agents;[6] thus, exportation of animal vectors of these diseases may be viewed under the International Health Regulations (2005) as a threat to international health and safety.

*Potential Solutions*

### Regulatory approaches

> CDC believes a number of approaches could further limit the transmission of zoonotic diseases. Potential solutions to this problem include screening animals with reliable laboratory tests, [vaccinating or] treating the animals empirically for known diseases, or quarantining the animals upon entry into the United States for the duration of an incubation period or duration of transmissibility. Many of those solutions, however, are currently not feasible [either as part of

[6]The U.S. public health system and primary health care providers must be prepared to address various biological agents, including pathogens that are rarely seen in the United States. Category A agents are high-priority agents—they include organisms that pose a risk to national security because they can (1) be easily disseminated or transmitted from person to person; (2) result in high mortality rates and have the potential for major public health impacts; (3) might cause public panic and social disruption; and (4) require special action for public health preparedness. Category A agents include Anthrax (*Bacillus anthracis*), botulism (*Clostridium botulinum* toxin), plague (*Yersinia pestis*), smallpox (Variola major), tularemia (*Francisella tularensis*), and viral hemorrhagic fevers (filoviruses [e.g., Ebola, Marburg] and arenaviruses [e.g., Lassa, Machupo]).

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> pre-departure or post-arrival protocols,] or practical to employ on the large volume of imported animals. In addition, the control measures cannot prevent new or emerging pathogens or infections for which no laboratory tests or no empiric treatments exist, when practical experiences regarding a species' susceptibility are lacking, when incubation periods are unknown, or when the infections are subclinical. In these instances, import restrictions of a wider range of species than currently regulated could be the only effective means of preventing the introduction of exotic infections into this country.
>
> In May 2006, CDC hosted a public meeting on the subject of infectious disease threats associated with the importation and trade of exotic animals. Stakeholders, [including the National Association of State Public Health Veterinarians, the Wildlife Conservation Society, and the American Veterinary Medical Association] submitted a variety of positions and views to the public meeting. Of the 22 statements received for consideration, 7 indicated a measure of support for increased restrictions on the importation and sale of exotic species, while 15 expressed support for alternatives to regulatory or legal restrictions, or opposition to possible restrictions. (HHS and CDC, 2007a)

On July 31, 2007, the CDC published an Advance Notice of Proposed Rulemaking (ANPRM) to begin the process of revising our animal importation regulations (CDC, 2007b). This ANPRM was intended to solicit public comment and feedback on the issue of animal importation to determine the need for further rulemaking. We received more than 800 comments from our ANPRM posting and we are currently in the process of reviewing these comments to assist in new rulemaking.

The CDC's current approach to controlling zoonotic disease threats has been to issue emergency orders or rules prohibiting importation of implicated animals. These actions are usually reactive—taken after an outbreak occurs rather than to proactively prevent outbreaks from known high-risk animals. This approach appears insufficient to prevent the introduction of many zoonotic diseases, especially given the high volume and speed of globalized trade in animal species and their byproducts. For public health purposes we need a risk-based, proactive approach to preventing the importation of animals and vectors that pose a zoonotic disease risk. The risk-based approach should include systematic and targeted surveillance of high-risk animals and animal products and vectors in the countries of origin. Emphasis should be placed on restricting the importation of animals and vectors of diseases not already present in the United States.

To effectively restrict importation of these vectors we must build the capacity of existing systems to accurately identify and track imported animal species and quantity of shipments. A recent analysis of the U.S. Fish and Wildlife Service LEMIS database indicated that the United States imported more than 1.1 billion live animals from 2000 to 2004. Of these, only 17 percent were species native to the United States. Only 27 percent of shipments were identified taxonomically lower than the family level, making it impossible to assess the diversity of ani-

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mals imported or calculate the risk of nonnative species or pathogen introduction (Jenkins et al., 2007).

In 2008, legislation was introduced to Congress entitled the Non-Native Wildlife Invasion Prevention Act (U.S. Congress, House, 2008). This act required the Secretary of the Interior to formulate regulations establishing a process for assessing the risk of all nonnative wildlife species proposed for importation into the United States, other than those included in a list of approved species established under the act. Factors that must be considered at a minimum included the identity of the organism to the species level, its geographic source, and the likelihood of spread and harm to groups of species or habitats. The bill received considerable feedback from groups supporting it and from those opposed to it. Although the bill did not pass in the most recent legislative session, it is hoped that elements of the bill can be retained and modified to further mitigate the risks posed by the importation of animals to the United States that will protect public health and the environment.

*Educational Approaches*

Regulatory approaches may reduce the supply of animals, but we also need to educate the public to reduce demand. For example, with bushmeat, we need to educate bushmeat importers and consumers about the laws against and potential health risks involved with hunting, transport, and consumption of bushmeat. Though there have been extensive studies of African wildlife covering both conservation and disease outbreaks, little work has been done to understand the social reasons behind the importation of bushmeat into the United States and to effectively target the expatriate population. To understand the desire for bushmeat and be able to create prevention materials, the CDC is partnering with the Bushmeat Crisis Task Force (BCTF) and Zoo Atlanta to conduct focus groups among African expatriates. Preliminary information gathered during focus group sessions held by BCTF in New York City found that African immigrants crave African wildlife because of its perceived wholesomeness and often do not understand why bushmeat is prohibited from entering the United States. When results of these ongoing studies are compiled, the CDC, together with its partners, will develop an educational program regarding the consumption and illegal importation of bushmeat into the United States. The program will have material focusing on conservation and the potential health hazards of consuming bushmeat, as well as the regulations surrounding its importation.

Educational strategies have already been implemented, but need to be expanded, to inform the public about the risks of zoonotic diseases. Recent zoonotic transmissions of infectious diseases from pets, such as tularemia, salmonellosis, and lymphocytic choriomeningitis from pet hamsters, have served as opportunities to educate the public about safe handling of animals. Pet retailers have been and can continue to be valuable partners in this effort. Guidance

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published by the American Academy of Pediatrics, the CDC, and the National Association of State Public Health Veterinarians (CDC, 2007c; National Association of State Public Health Veterinarians, 2007; Pickering et al., 2008) also remind the public of the dangers of contact with *any* wildlife, whether imported or domestic.

## A MOLLUSC ON THE LEG OF A BEETLE: HUMAN ACTIVITIES AND THE GLOBAL DISPERSAL OF VECTORS AND VECTOR-BORNE PATHOGENS

*Paul Reiter, Ph.D.*[7]
Institut Pasteur

Charles Darwin's last published article was a letter to *Nature* in which he described a specimen of *Dytiscus marginalis*—a water beetle common in Britain and much of Europe—that had been captured with a minute mollusc attached to its middle leg (Darwin, 1882). The beetle and its passenger had been sent to him by W. D. Crick,[8] an amateur naturalist who, like Darwin, was intrigued by mechanisms for dispersal.

Darwin was keenly interested because he recognized that dispersal—and its antithesis, isolation—are key to the biogeography and evolution of species. He observed that dispersal takes many forms, but that passive dispersal—dispersal that takes advantage of the activities of other species or of movements of the physical environment such as wind or ocean currents[9]—was of outstanding importance. This review considers the dispersal of vectors and vector-borne pathogens by the activities of humankind.

### Malaria

The principal parasites that cause malaria are strictly human pathogens, so their geographic range is determined by the presence of humans. There is a widespread misconception that the disease is strictly "tropical," yet until the mid-nineteenth century, it was common as far north as central Sweden, Siberia, and the northern United States (Reiter, 2008a). In the past 150 years, the factors that have contributed to the reduction of its range are a reversal of the expansion that occurred with the development of agricultural settlements and the geographic expansion of humankind.

Molecular studies of the diversity of *Plasmodium falciparum* give strong evidence that it originated in Africa and advanced into Eurasia with the spread of

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[8]Grandfather of Francis Crick.
[9]Or of movements of the physical environment.

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the human population, some 100,000 years ago (Carter and Mendis, 2002; Hume et al., 2003). Less attention has been paid to the other three species, but it is clear that transmission could not have occurred in Northern Europe until the retreat of the ice caps at the end of the last ice age. Whatever their origin, this passive dispersal was, of course, contingent on the presence of suitable vectors, which also had a changing geographic distribution.

In the New World, malaria has a much more recent history; it is unlikely that the disease was present before its introduction from Africa during the slave trade. African species of mosquitoes do not exist in the Americas,[10] but several indigenous anophelines are highly effective malaria vectors. Importation was not restricted to parasites from the tropics. Until the late-nineteenth century malaria was a major cause of morbidity and mortality in farming communities in the upper Mississippi Valley (Ackerknecht, 1945), and there is good evidence that it arrived with peasant immigrants from Scandinavia, where *P. vivax* was endemic (Hulden and Heliovaara, 2005).

### *Aedes aegypti* and Yellow Fever

Unlike human malaria, yellow fever is a zoonotic[11] disease. It circulates among African primates in forested areas, transmitted by day-active mosquitoes of the genus *Aedes* (sub-genera *Stegomyia* and *Diceromyia*), which feed exclusively on primates. Humans who enter the forest, or live close to forested areas, are infected by the bites of infected mosquitoes. Outside the forest, inter-human transmission can continue if suitable vectors are present. Chief among these is *Ae. aegypti*, a species that is remarkable because it has adopted the peridomestic environment to great advantage.

In its natural habitat, *Ae. aegypti* breeds in tree-holes, plant axils, rock-holes, and other small items that hold water. In the peridomestic environment it remains strictly primatophilic,[12] but freely lays its eggs in man-made containers. In villages close to enzootic transmission,[13] water storage jars are usually the principal breeding sites; in cultures where water storage is not traditional, human-to-human transmission of yellow fever may not occur. In the modern peridomestic environment, *Ae. aegypti*—and *Ae. albopictus* (Figure 3-3)—a species with similar sylvatic origins—exploits other man-made articles that retain water such as discarded tires, buckets, saucers under flowerpots, and flower vases. Indeed, humans are literally the perfect host: they provide safe shelter, plentiful food, and abundant sites for procreation (Reiter, 2007).

[10]An accidental infestation in Brazil by the highly effective malaria vector, *Anopheles gambiae*, was eliminated by a massive campaign by the Rockefeller Foundation in the 1930s.

[11]A disease that normally circulates in nature or in domestic animals, but can also infect humans.

[12]Feeds on primates in preference to other vertebrates.

[13]Transmission among nonhuman primates.

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**FIGURE 3-3** *Ae. albopictus*, the Asian tiger mosquito. In less than 30 years, this species—native to Asia from northern China, Korea, and Japan to the tropics—has become established, often common, in many countries in North and South America, Europe, Africa, and the Middle East. In 2006-2007, it was responsible for major epidemics of chikungunya virus on islands in the Indian Ocean, and for a small outbreak in Northern Italy. The principal "vector" for the mosquito has been a global trade in used tires.
SOURCE: Institut Pasteur.

From the seventeenth century onward, yellow fever was one of the most feared diseases, not only in Africa, but in much of the New World and in many European cities in the Old World. It was not uncommon for ships to arrive in port with dead or dying persons aboard, hence the yellow flag of quarantine. The principal source of this scourge was the transatlantic slave trade (Figure 3-4). Transmission was often active in the coastal slave-trading settlements and in the hinterland where the slaves were captured. The passage to the Americas from the west coast of Africa by boat under sail took four to six weeks. Given that viremia[14] sufficient to infect mosquitoes does not usually last much more than a week, the virus could not have survived onboard without transmission *en voyage*. The critical factor, therefore, was the presence of the vector; prior to departure, tens of thousands of litres of drinking water were stowed below the lower decks in wooden casks. This water undoubtedly contained enough organic material to support rapid development of large numbers of *Ae. aegypti* larvae, particularly as the voyage progressed, so these casks must have been prolific breeding sites, with several generations of mosquito per voyage. The humid environment below deck was ideal for the adult mosquitoes, and the crew and the slaves were a copious source of blood.

Virus passed ashore in infected mosquitoes and humans. In the days before

[14]The titre of virus in the blood.

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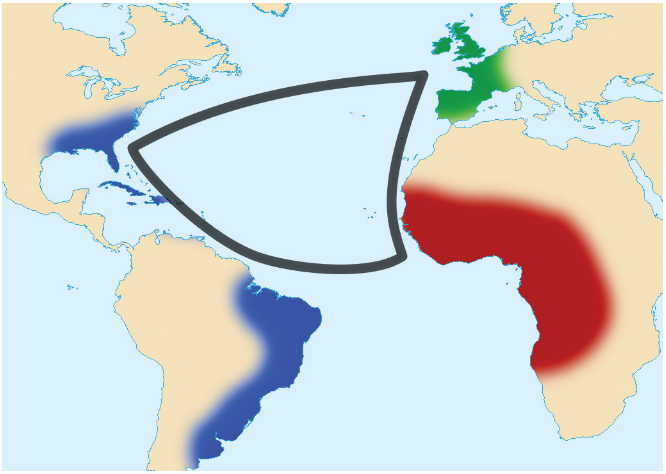

**FIGURE 3-4** The transatlantic triangular trade. From the seventeenth to the nineteenth centuries, ships carried goods and supplies from Europe to Africa, for sale or barter for slaves, who were then transported to the New World, from where sugar, tobacco, and other produce was shipped to Europe. Slave ships carried as many as 900 captives; the large volume of freshwater required for their survival was stowed in barrels, and the water was inevitably infested with larvae of the African mosquito *Aedes aegypti*. Yellow fever, also native to Africa, was transmitted on board between humans by these mosquitoes. Devastating epidemics of yellow fever were a frequent event in the neotropics and subtropics, as well as in temperate regions of North America and Europe as far north as Boston and Dublin. Both the mosquito and the virus are now endemic/enzootic in the Americas.
SOURCE: Wikimedia Commons (2009).

piped water, water storage was obligatory, so the mosquitoes were abundant in seaports and inland. Inevitably, devastating epidemics, sometimes with tens of thousands of cases, were common in coastal cities in the Americas as far north as Boston. In Europe, major outbreaks occurred in many port cities from the Mediterranean to as far north as Brest, Bristol, Cardiff, and Dublin.

The disease continued to be a major cause of mortality in many temperate regions, long after prohibition of the slave trade. In 1870, for example, 120,000 panic-stricken people fled from Barcelona when thousands had contracted the disease after several vessels arrived from Cuba with fever onboard.[15] In the United States, the great yellow fever epidemic of 1878-1879 made its way northward from Louisiana by river traffic on the Mississippi, with high mortality at every port of call. Despite advance warning, the authorities in Memphis, Tennessee, were reluctant to prevent the docking of river traffic. There were an estimated

[15] *New York Times*, October 2, 1870.

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19,500 cases, and the fleeing population carried the virus to the interior parts of the country far removed from the river. In all, there were an estimated 100,000 cases with an associated 10 percent mortality. Memphis (temporarily) lost its city charter and never regained its status as the capital of the southern states. Indeed, in the year that followed, there were calls to raze the city to the ground to prevent future epidemic disasters (Bloom, 1993).

The implication of *Ae. aegypti* as a vector of yellow fever by Carlos Finlay in Havana, Cuba, and experimental confirmation by Walter Reed, led to major sanitation campaigns and an end to major urban transmission in most of the Americas. In the 1920s, however, it became clear that the virus had become established in an enzootic cycle in the forests of Mexico, and Central and South America, transmitted by New World mosquitoes of the genera *Sabethes* and *Haemagogus* (Reiter, 2008b). In this circumstance, there is no prospect of eradication from the hemisphere. Epizootics[16] are repeatedly reported in the South American rainforest, and there are small numbers of human cases every year. Sustained control of urban *Ae. aegypti* has rarely been achieved and never sustained (Reiter and Gubler, 1997), but a safe and effective vaccine is available. Few countries, however, have a well-organized vaccination program, so there is an ever-present danger that a massive urban epidemic will occur if the virus is introduced to the many burgeoning cities where *Ae. aegypti* is common.

Curiously, yellow fever has never been reported from any part of Asia. There is no apparent reason for this: endemic *Ae. aegypti* are certainly capable of transmission, and conditions in Asian cities appear as ideal for yellow fever transmission as they are for several other arboviral[17] diseases, notably dengue and chikungunya. It may have been simply a matter of chance that it was never introduced.

### *Aedes albopictus*

#### *Americas*

In June 1983, a single adult specimen of *Aedes (Stegomyia) albopictus* (Skuse), a mosquito native to Asia, was captured during studies of mosquitoes in Memphis, Tennessee (Reiter and Darsie, 1984). The species had been recorded as far west as Hawaii, but never in the Western Hemisphere. It is a vector of dengue and chikungunya in urban areas, albeit considered less effective than *Ae. aegypti* (Reiter et al., 2006). Speculation on how it was introduced into the continental United States drew attention to a major innovation in the transportation industry—containerization—and it was suggested that this new technology would lead to further introductions of medically important insects.

[16] Epidemics of zoonotic disease among nonhumans.
[17] Arthropod-borne virus (i.e., virus transmitted by insects or ticks).

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In 1985, *Ae. albopictus* was detected in Harris County, Texas, which includes the city of Houston. Surveillance by the local authorities revealed that it was widespread and common throughout the area, and had become a major nuisance species. Discarded used tires—abundant in many areas—were infested with the species, and its distribution within the county indicated that it could have been present for several years prior to detection. Investigations in early 1986 revealed that, since the 1960s, there had been an extensive and rapidly growing national and international trade in used tires. Millions were being imported annually from all over the world to destinations throughout the United States (Reiter, 1987). It appeared likely that the new species had been imported in such tires, perhaps from Japan, the world's largest exporter. Discarded used tires provided abundant breeding habitats for these mosquitoes. The used tire trade was not restricted to Japan and the United States. Virtually every country in the world was importing and/or exporting used tires. Tires are an awkward item to handle, so it was evident that this trade could not have been practical without the advent of containerization.

In the same year, a survey of 12 states—Alabama, Arkansas, Florida, Georgia, Illinois, Indiana, Louisiana, Mississippi, Missouri, Ohio, Tennessee, and Texas—revealed that 48 out of 57 counties surveyed (84 percent) were positive for the species. An alert from the Pan American Health Organization (PAHO) prompted national authorities in Brazil to examine specimens of an *Aedes* species that had been awaiting identification. These also proved to be *Ae. albopictus*. By the end of July 1985, infestations had been detected in 63 municipalities in three Brazilian states. Meanwhile, an exhaustive inspection of 22,000 used tires arriving from Japan revealed that 25 percent contained water (Craven et al., 1988) and five species of mosquitoes were identified, including *Ae. albopictus* and three other exotics.

A study of cold-hardiness and the photoperiod required for onset of winter diapause[18] in *Ae. albopictus* gave further evidence that U.S. infestations had originated in northern Asia, perhaps South Korea or Japan (Hawley et al., 1987). Interestingly, Houston was at the minimum latitude for infestations at that time. South Texas, Florida, and Mexico were unaffected, perhaps because maximum day length was too short to terminate winter diapause.

Thus, by late 1986, it was apparent that the species was widely established in the United States and Brazil. It seemed likely, moreover, that the species had been present in both countries for a number of years prior to detection. It was also apparent that domestic interstate traffic in used tires was a major factor in continued dispersal of the insect within both countries. Despite its widespread presence and abundance, there was considerable pressure on the U.S. government to prevent further introductions—mainly on the grounds that this would limit the genetic variation of the newly established population—and to prevent the

[18]A period of physiologically controlled dormancy in insects (http://www.ipm.ucdavis.edu/PMG/glossary.html, accessed June 23, 2009).

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introduction of exotic viruses. A federal regulation was implemented whereby all used tires arriving in the United States from Japan, Korea, Taiwan, Hong Kong, Thailand, and other Asian countries where *Ae. albopictus* was known to occur should be certified as dry, clean, and free from insects. All noncompliant cargoes were to be fumigated with (highly toxic) methyl bromide, or treated with a pressurized spray of detergent/water solution at 88°C, or by steam cleaning.

Inspections and treatments were highly labor-intensive and unlikely to succeed. The maximum charge for noncompliance that could be levied per container was $1,000, hardly a deterrent when staff from the Division of Quarantine of the CDC could only make cursory inspection of at best 10 percent of all cargoes arriving at a few selected seaports (Figures 3-5A and 3-5B). After several years it was apparent that the effort was merely cosmetic, and the regulations were quietly withdrawn.

The federal experience with *Ae. albopictus* and used tire imports underlines four problems that are probably insurmountable:

- Containers are often packed tightly to the roof, so inspection is highly labor-intensive and fumigation is of doubtful efficacy unless their contents are unloaded.
- In port, containers are handled with speed and efficiency; delays for inspection are neither practical nor acceptable to the shippers.
- Containers are designed to be delivered by truck, rail, or barge—unopened—directly to the customer. This is of paramount importance: in the past, cargoes could be inspected piece-by-piece as they were being unloaded at the dock-side. With containers, this step has been eliminated, so attempts to detect vectors at the port of entry have become largely irrelevant.
- Under international law, imports are generally the responsibility of the importer.

In summary, although it is not difficult to survey a species once it has been detected, it is much more difficult to detect new introductions when they occur, particularly when cargoes are imported in locked containers. It is unrealistic to expect authorities to establish routine surveillance for imported species that have not been detected in the past, particularly when potential infestation sites may be anywhere on a whole continent.

*Europe*

In retrospect, after the initial detection of the species in Memphis, Tennessee, it was learned that *Ae. albopictus* had been present in Albania for at least 10 years and was a major nuisance in many areas (Adhami and Reiter, 1998). At that time, the country was politically isolated, a virtual enclave in the Balkans, with little or

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**FIGURE 3-5** Containerization. Approximately 90 percent of non-bulk cargo worldwide moves by containers stacked on transport ships. More than 20 million such containers make over 200 million voyages per year; some ships can carry more than 14,500 units. The speed, efficiency, and convenience of this form of transport enable cargoes to be delivered directly from the ship to their destination with minimum delay at the dockside. In consequence, it has become totally impractical to make routine inspections, either at the port of arrival or at the point where the container is finally opened.
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no contact with the outside world except China. Since that time, *Ae. albopictus* has been detected at least once in 16 countries and is considered present and expanding its range in Albania, Croatia, France, Greece, Monaco, Montenegro, Italy, San Marino, Slovenia, Spain, and Vatican City.[19] Italy is by far the most widely infested, and in many places, infestation rates are remarkably high; in some parts of Rome, including important tourist sites, biting rates are intolerably high for at least five months of the year. As with those mosquitoes that have become established in the United States, the European strains are adapted to survive northern winters. If winter temperatures define the limits of distribution, there is little reason to believe that infestations will not move northward, perhaps as far north as Scandinavia.[20] There are also reports that the species is established in the Bekaa Valley, on the Lebanon/Syria border (anonymous source to the author). Here again, it is not unlikely that the species will eventually move eastward into central Asia. Finally, *Ae. albopictus* is common in urban areas and in rubber plantations in Cameroon, Gabon, and southeast Nigeria. It has been implicated in an outbreak of chikungunya in Gabon and there are fears that it may become a significant vector of yellow fever.

Italian entomologists have traced at least one of their *Ae. albopictus* infestations to imports of used tires from Atlanta, Georgia[21] (Dalla Pozza et al., 1994). Thus, in the space of a few decades, an alien species has exploited a chain of modern transport that has brought it from Asia to the Americas and thence to Europe.

### Dengue, Chikungunya, and the Passenger Aircraft

Dengue (DEN) is caused by a virus closely related to yellow fever; both are in the Japanese encephalitis subgroup of the family *Flaviviridae*. It is generally accepted that it originated in Asian forests, transmitted between monkeys by primatophilic *Aedes* mosquitoes, although at least one serotype[22] circulates in a sylvatic cycle in West Africa (Diallo et al., 2005). The first major epidemic of what is considered to have been dengue was recorded in Philadelphia in 1780 and was concurrent with documented epidemics in Indonesia, India, Persia, Arabia,

[19] Interestingly, in The Netherlands, there have been several instances of importation of *Ae. albopictus* in shipments of "Lucky Bamboo" from southern China, causing a severe nuisance in glasshouses (Scholte et al., 2008), but the species has not, as yet, become established outdoors. This may be because the south China strain is not adapted to temperate climates.

[20] The average minimum temperatures in January in Beijing, China (–10ºC), and Seoul, South Korea (–6ºC), both within the original range of distribution of *Ae. albopictus*, are on a par with Stockholm, Sweden (–3ºC).

[21] Another exotic species, *Ae. atropalpus*, is suspected to have been imported from Minnesota or Quebec.

[22] Unlike yellow fever, DEN exists in four distinct serotypes; in theory, a person can suffer four infections before becoming immune to the disease.

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Egypt, and Spain (Gubler, 1998). Epidemics were common in North America and in Europe until the mid-twentieth century. Indeed, one of the largest epidemics on record occurred in Greece in 1927-1928 with an estimated 1 million cases and 1,000 deaths (Rosen, 1986).[23] As with yellow fever, the principal peridomestic vector is *Ae. aegypti*, *Ae. albopictus* is generally considered a "secondary" vector because it does not feed exclusively on humans, but significant epidemics have occurred in regions where *Ae. aegypti* is not present (Coulanges et al., 1979).

Dengue is now the most important mosquito-borne viral disease affecting humans. Its global distribution is comparable to that of malaria, and an estimated 2.5 billion people live in areas at risk for epidemic transmission. It is above all an urban disease, and it thrives in the crowded cities of the tropics, where homes are often so close together and *Ae. aegypti* breeding sites so abundant that urbanizations can be regarded as a single unit—a factory for the vector and the virus. Unlike yellow fever, DEN exists in four distinct serotypes so in theory a person can suffer four infections before becoming immune to the disease. Serosurveys[24] reveal that by the age of 15 up to 80 percent of children in cities such as Bangkok and Kuala Lumpur have been infected by at least one serotype. In cities where populations exceed several million, all four serotypes may be in circulation simultaneously, though peaks of transmission may be asynchronous, with timing dominated by local history of transmission[25] (Gubler, 2004).

Chikungunya (CHIK), like yellow fever and DEN, is a primatophilic virus (family *Togaviridae*) that is enzootic in African (and perhaps Asian) forests and transmitted by primatophilic mosquitoes. Although not generally life threatening, symptoms include arthritic joint pain that can persist for months and even years. Both DEN and CHIK present remarkable examples of the worldwide dispersal of arboviruses by a new vector, the passenger aircraft. Thousands of imported cases of DEN are reported every year in Europe and the United States, many in tourists returning from the tropics.

Serotype and sequence data of viruses isolated in widely separated countries confirm frequent intercontinental movement of the viruses. Best documented are successive exports of Asian strains of dengue virus (DENV) to the New World. In the first half of the twentieth century, DENV-2 was the only serotype in circulation. This changed in 1963, when an Asian strain of DENV-3 appeared in Puerto Rico and spread rapidly southward through the Antilles to South America. An Asian strain of DENV-1 appeared in 1977, followed by DENV-4 in 1981, and

[23] *Ae. aegypti* is no longer present in Europe. Its disappearance remains an enigma: it has been attributed to control of anopheline species with DDT in the malaria eradication campaigns after World War II, but, given the difference of the habitats of vector species involved, this explanation is hard to accept.

[24] Systematic surveys to determine the prevalence of persons who have acquired antibodies by infection with the virus.

[25] The prevalence of antibody in a population—the "herd immunity"—will determine the rate of transmission of the virus; viruses can spread more rapidly if the herd immunity is low.

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a new strain of DENV-3 in 1994 (Effler et al., 2005; Gubler, 2005; Imrie et al., 2006; Neff et al., 1967).

A more recent example is the pandemic of chikungunya virus (CHIKV) that was first apparent in 2004 in Mombassa and Lamu (Chretien et al., 2007), on the Kenya coast, and subsequently appeared in a succession of small islands in the western Indian Ocean—the Comoros, Mayotte, Mauritius, Reunion, and the Seychelles—undoubtedly introduced by infected air passengers (Charrel et al., 2007). A massive epidemic followed in India, with estimates of at least 6.9 million cases (Mavalankar et al., 2007), and swept eastward to Southeast Asia, Indonesia, and the Philippines, where high rates of transmission continue at the time of writing (June 2009).

The most graphic event was the appearance of the virus in June 2007 in two contiguous villages in the Emilia-Romagna region of the province of Ravenna, in northwest Italy.[26] The introduction was traced to a single traveler who arrived from India on June 21, developed fever on the afternoon of June 23, and triggered 205 infections in the region between early July and late September (Rezza et al., 2007). The vector, *Ae. albopictus*, was superabundant in the area. As had occurred with yellow fever in the Americas, transmission of CHIKV was by an exotic mosquito matched with an exotic virus.

There is evidence that the strain of CHIKV involved in the pandemic may have a particular affinity for *Ae. albopictus* (Tsetsarkin et al., 2009; Vazeille et al., 2007), although *Ae. aegypti* was certainly involved in transmission as well. The high rate of transmission in India undoubtedly raised the likelihood of introduction into Europe, but such circumstances are likely to recur. Moreover, even if the species has an exceptional susceptibility for recent CHIKV strains, it has also been responsible for epidemics of DEN where *Ae. aegypti* is absent (Coulanges et al., 1979), so we may well see the return of transmission to Europe. Of course, if *Ae. aegypti* were to become reestablished on the continent, repetition of the DEN epidemics of the past would also be possible.

Viruses cannot hop over oceans, but, as with the expansion of malaria in paleolithic times, they travel in people; only the rate of movement has changed (Figure 3-6). In addition to air transport, of course, tens of millions of people travel on land, within cities, within countries, and between countries; a few minutes spent in a crowded railway station, say, in India, will leave no doubt that this is a powerful engine for dispersal. The only requirement is the presence of a competent vector at the destination. The history of yellow fever, DEN, and CHIK confirms that this is perfectly feasible.

[26]Interestingly, the villages are on land reclaimed from the Po River delta, a region once notorious for malaria transmission.

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**FIGURE 3-6** An infected person can travel to virtually any airport destination in the world in less than 48 hours, far shorter than the period of incubation and infectivity of vector-borne infections. The air-passenger industry carries more than 2 billion passengers in more than 23,000 aircraft and 28 million scheduled flights to more than 3,700 airports worldwide. The growth of world air travel has averaged 5 percent per year for the past 30 years, and the current rate of increase is greatest in the emerging economies of the world, particularly India, China, Southeast Asia, and the Middle East (IATA, 2009).
SOURCE: Fotosearch, LLC.

### West Nile Virus

West Nile virus (WNV) is by far the most widely distributed arbovirus in the world. It is classified in the family Flaviviridae, which also includes dengue and yellow fever, but it is transmitted in an avian cycle by mosquitoes—chiefly of the genus *Culex*—that primarily feed on birds. Mammals, including humans and horses, can also be infected, but are considered "dead end" hosts because viremia is generally too low to infect mosquitoes.

In its original range, WNV is enzootic throughout Africa, parts of Europe, Asia, and Australia, but it received little attention until 1999, when a strain circulating in the eastern Mediterranean appeared in the Bronx, New York (Gubler et al., 2000; Hayes et al., 2005). The epizootic that followed was spectacular and unprecedented: within five years, the virus appeared ubiquitous, sometimes common, in nearly all counties of all states east of the Rocky Mountains, as well as parts of western Nevada and southern California. Sizeable outbreaks were also observed

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in six Canadian provinces. It is now widely established from Canada to Venezuela (Petersen and Hayes, 2008) and has also been confirmed in Argentina (Morales et al., 2006). In the United States to date (1999-2008), 28,943 clinical cases and 1,393 deaths have been reported in humans, and more than 27,000 cases in horses, with a case fatality rate of about 33 percent (CDC, 2009). Two-thirds of the U.S. horse population are now vaccinated, but no vaccine is available for humans.

In Eurasia, epizootics are rarely evident except when there are cases of neurologic disease in humans or horses. By contrast, in the United States, fatal infections have been recorded in more than 320 species of birds. The virus is highly infectious by the oral route and is shed in the oral cavity and in the feces (Komar et al., 2003). The American crow appears particularly vulnerable, probably because it is a scavenger. Mortality among raptors is also high, presumably because they feed on infected prey.

The contrast in pathogenicity between virus in the Old and the New World is indicative of a long association between the virus and its avian hosts in its original range. Indeed, even during major epizootics, mortality appears rare in two superabundant urban species, the house sparrow (*Passer domesticus*) and the rock dove (*Colomba livi*); both are exotics imported from the Old World. In this context, there is a clear parallel with yellow fever; in Africa, its original range, infections in wild primates are generally asymptomatic, but in the Americas, the virus is lethal to monkeys. Local inhabitants recognize an epizootic when there is mass mortality among howler monkeys (*Alouatta palliata*): the forest goes silent.

In both cases, the introduction of an exotic zoonotic virus that is not pathogenic in its original range has had a catastrophic impact on the local fauna in its new habitat. This is an important point, because there are many examples of destructive impact after the introduction of exotic pathogens that enter zoonotic transmission. In the case of infections that can also affect humans, a high incidence of infection in the zoonotic cycle will raise the probability of human infections. This is precisely what has happened with WNV in the New World.

The mode of introduction of WNV to New York is unknown, but presumably, just as with DENV and CHIKV, it arrived in an infected vertebrate. Viremia in humans, horses, and other mammals is generally assumed insufficient to infect mosquitoes. It is far more likely that the virus was imported in caged wild birds; in the early 1990s, an estimated five million wild birds of more than 3,000 species were traded annually, with the United States as the world's largest importer (Wildlife Extra, 2008).[27] Caged wild birds are highly susceptible to stress, so direct flights and speed of transit is critical.[28] On arrival, they are held indoors in quarantine but not necessarily isolated from local mosquitoes. The implications for the importation of WNV and other avian pathogens are clear.

[27]The European Community banned the trade in 2007, but there is concern that this will only drive it underground (Cooney and Jepson, 2006).

[28]Details of the procedure are given in http://petrelocation.blogspot.com/2008/03/importing-birds-to-usa.html (accessed February 3, 2010).

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### Veterinary Diseases

Modern transportation has also given unprecedented mobility to livestock. Millions of sheep and cattle are shipped between countries worldwide. Racehorses fly between international racetracks like executives to business meetings. Hundreds of millions of day-old chicks travel between countries as geographically separate as China and Nigeria. With these livestock, inevitably, come pathogens. In the past three years, examples include the following:

- *Trypanosoma evansi* is a blood parasite that causes acute disease in camels and horses, and chronic disease in domestic livestock. In 2006, an outbreak occurred in dromedary camels exported to France from the Canary Islands, France (Desquesnes et al., 2008). Indigenous biting flies (probably *Stomoxyx spp*.) passed the parasite on to local sheep. Transmission by such flies is mechanical, so no species-specificity is involved.
- Rift Valley fever virus is a zoonotic mosquito-borne pathogen that primarily infects livestock. It is readily transmitted to humans by handling infected tissues, and can be fatal. In 2007-2008, an outbreak occurred in the Comoros Islands and the French territory of Mayotte. The mode of entry is not known, but a major epidemic was under way in East Africa, and it is probable that the virus arrived in (illegally) imported infected animals or meat (Sissoko et al., 2009).
- Bluetongue virus (BTV) is an orbivirus, transmitted by *Culicoides* sandflies, that affects ruminants. It has long been a veterinary problem in the United States (up to and occasionally over the Canadian border), Africa, the Middle East, parts of Asia, and Australia. Prior to 1998, however, transmission in Europe had only been documented in Spain, but in the following six years, multiple outbreaks of six strains spread across 12 countries that included Turkey, the Balkans, Italy, and new regions of Spain. This astonishing proliferation into new territory included the islands of Sicily, Sardinia, Corsica, Majorca, and Menorca, and continued in 2006, when six serotypes of the virus suddenly appeared in the Netherlands, Belgium, Germany, and Luxembourg, and more recently in the Czech Republic, Britain, Norway, and Sweden. The mode of introduction remains an enigma, but transport of animals or materials contaminated with infected vectors is clearly implicated.

### Conclusion

In 1988, the federal employees who had laboriously searched for mosquitoes in 79 container loads of Asian used tires (Craven et al., 1988) wrote:

> *Ae. albopictus* has joined the housefly, the flour beetle, the cockroach, the Mediterranean fruit fly, the yellow fever mosquito and many other insects that have

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> vastly extended their range by virtue of their association with mankind. Time will tell whether *Ae. albopictus* also joins the list of exotic vectors that transmit human or animal pathogens.

*Ae. albopictus* has indeed joined the list, and it is inevitable that more vectors and vector-borne pathogens will follow, perhaps with serious consequences. For example:

- *An. gambiae* is perhaps the most effective malaria vector on Earth. Like *Ae. aegypti*, it is closely associated with the peridomestic environment and is strictly primatophilic. At present, it only exists in sub-Saharan Africa, but a new trade route from Lagos to Algiers is nearly complete and three other highways are proposed. A significant malaria problem could arise if the species were to be established in North Africa. The same would apply if it were to be reintroduced to Brazil, or to other regions in Latin America.
- Saint Louis encephalitis virus is a New World pathogen, closely related to WNV, with the same vectors (in the Americas), the same transmission cycles, and similar pathology. If exported to Eurasia or Africa, it could enter a local transmission cycle, transmitted by local vectors, with similar, perhaps catastrophic, impact on wildlife, human, and veterinary health.
- Japanese encephalitis virus is an avian pathogen transmitted by ornithophilic mosquitoes that can cause severe illness and death in humans. In Asia, pigs serve as amplifying hosts because they develop high viremia and infect large numbers of mosquitoes; human disease is prevalent where people live in close proximity to pigs. If exported to Mexico or Central America, competent vectors such as *Cx. quinquefasciatus* could perpetuate transmission in the widespread communities where pigs are also abundant in the peridomestic environment.

In conclusion, with a few exceptions—such as the enforcement of vaccination requirements—we can expect the continued establishment of exotic species and pathogens as an inevitable consequence of modern transportation technology.

### Final Remark

It is regrettable that in recent years, outbreaks of yellow fever, dengue, chikungunya, WNV, bluetongue, and other vector-borne pathogens, as well as the appearance of *Ae. albopictus* and *Ae. aegypti* in new regions, have all been attributed to anthropogenic climate change or "global warming." Statements to this effect are not limited to lay persons. For example, after the chikungunya outbreak in Italy, a United Nations official stated: "We cannot be *certain* [sic] that this outbreak was *caused* by global warming, but at least we now know that the

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Asian tiger (mosquito) can survive in northern Italy." The statement, taken up by the world press on the eve of an international climate change conference, ignored the fact that the villages were on the site of what was once a malarious swamp, and that, for *Ae. albopictus*, the Mediterranean winter is surely preferable to the bitter cold of Beijing and Seoul. Another example is bluetongue: there is no doubt that the climate of Europe has been warming over the past 200 years, but summer temperatures in Norway and Sweden have yet to reach those of North Africa and southern Spain, and winter temperatures in The Netherlands and surrounding countries cannot be compared to those in Montana, Wyoming, or the Balkans.

In the opinion of the author, the issue is an important one. Global warming has become the defining moral and political issue of our age. Draconian measures are being implemented that will have enormous impact on the economies and well-being of people all over the world. Vector-borne diseases continue to feature high in the list of perceived dangers, despite attempts to rationalize the debate by specialists in the field (Gubler et al., 2001; Hay et al., 2002; Reiter et al., 2004; Shanks et al., 2002; Sumilo et al., 2007). This review is no place to debate the science or the politics of the issue, but it is surely important to maintain perspective on a phenomenon that is better explained by the attachment of a mollusk to the leg of a beetle.

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## PREDICTING AND PREVENTING EMERGENT DISEASE OUTBREAKS

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In 1998, a mysterious new disease syndrome appeared in pigs in Malaysia; it was then diagnosed in pig handlers. The pathology in humans implied an encephalitis-like virus that could cause significant mortality. Initial work by

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local animal health expert Paul Chua and scientists from Australia's Commonwealth Scientific and Industrial Research Organization (CSIRO) suggested the disease was similar to Hendra virus, a pathogen that had recently emerged in Australia (Lam and Chua, 2002). As outbreaks began to occur at different locations throughout Malaysia, the authorities decided to eradicate all pigs from the Malaysian peninsula; this resulted in the slaughter of over a million pigs and the complete collapse of the entire Malaysian pork industry. The causative agent was identified as Nipah virus, a Paramyxoviridae quite closely related to Hendra virus and one that also uses pteropid fruit bats as its reservoir host (Philbey et al., 1998). A detailed examination of the circumstances that led up to the emergence of Nipah virus in Malaysia provides a number of important insights into how other "novel" pathogens are likely to emerge. It also suggests a number of broader questions that need to be addressed if we are to capitalize on a resurgence of interest in predicting and preventing emergent disease outbreaks.

The past 25 years have seen a steady stream of "new diseases" emerge and enter either the human population or populations of domestic livestock. A recent study suggests that we are seeing approximately two new viral pathogens emerge each year (Woolhouse and Gaunt, 2007; Woolhouse et al., 2008). A significant number of emerging pathogens are strains of bacteria that have evolved resistance to the drugs that have been used to keep their ancestors at bay over the past 50 years. Others are older pathogens that have resurged due to the reduced levels of immune-competence in patients suffering from HIV. A small number were not previously known to science—HIV would be the classic example here—but the past decade has also seen the emergence of several viral diseases including SARS, Nipah, and Hendra viruses, and chikungunya, causing significant epidemics in their new host-environment contexts (Weiss, 2001). There are still other pathogens that we thought were new when outbreaks first occurred, but these ultimately proved to be pathogens we had forgotten about (e.g., Hanta virus), particularly if their scientific records predated the contemporary web-based collations of knowledge about microbes (Daszak et al., 2000; Garrett, 1994; Morse, 1995; Murphy, 1994).

Understanding how to predict and prevent future outbreaks could be a hugely beneficial exercise. What would we need to do to achieve this goal? And what are the major constraints to achieving success in this endeavor?

### Predicting and Preventing Future Outbreaks: Probability and Cost

If we are interested in attempting to quantify the risk of new pathogens "emerging" and infecting humans, or populations of livestock and the plants that are central to our food supply, then we need to subdivide the process of emergence into a number of discrete steps (Lloyd-Smith et al., 2009). We then need to quantify the probability that each step will proceed to the next one while

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simultaneously estimating the cost of preventing this from happening. As with any risk analysis, our key goal is to examine the interaction between probability and cost that creates the risk associated with an event we may wish to prevent (Burgman, 2005). For example, the emergence of Nipah virus in Malaysia breaks into a number of key steps that are likely to occur in slightly modified form in other "emergent pathogens" (Figure 3-7). Let us briefly consider the probability and cost associated with each of these stages.

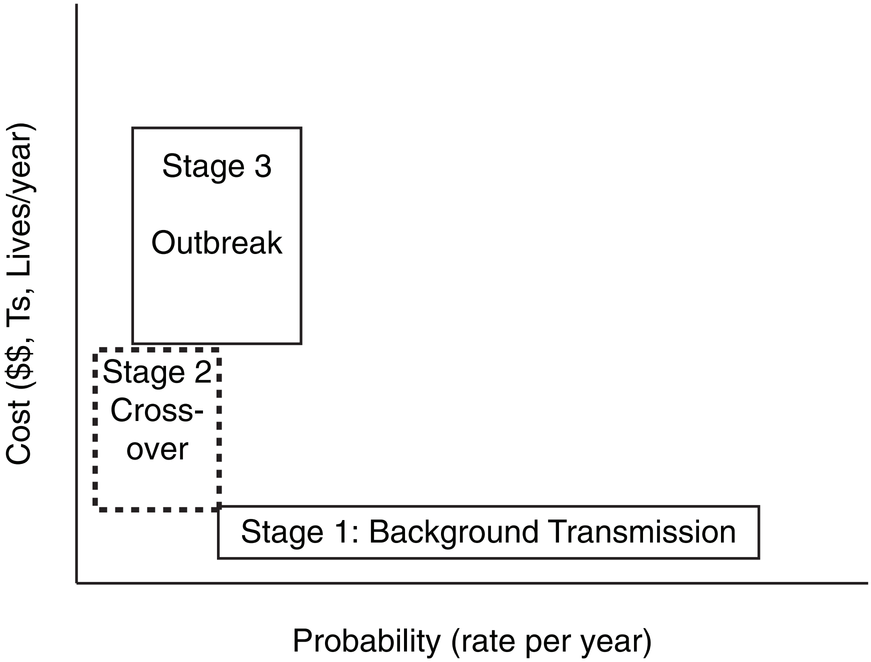


**FIGURE 3-7** Relative risk of pathogen emergence. Stages in the emergence of a new pathogen at which we need to quantify the trade-off between probabilities of occurrence and cost of intervention that define "risk" of emergence. Stage 1 is transmission in the reservoir, which we assume is ongoing and occurs at least every year (during the mating season), if not every day. Stage 2 occurs when a novel host species acquires an infection.[a] Stage 3 occurs when successful chains of transmission are established in the human (or domestic livestock) population and individuals become seriously ill and may die.[b]

[a]Our biggest worry is that this is a human host, but costs are associated with novel infections in domestic livestock and even exotic species that may have value for tourism or as pollinators or predators of pests. Most of these crossover events will not lead to any further transmission and many will go undetected.

[b]Most emerging pathogens are only detected at this stage, when the cost of intervention and economic and human suffering impact can be highly significant.

SOURCE: Dobson (in review).

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*Stage One: Background Transmission*

The background stage carries the highest probability of occurrence, and the lowest risk of threat; paradoxically, it is likely the most expensive to study, with the smallest probability of detecting new "pathogens." Every day pathogens that are potentially devastating to humans are transmitted harmlessly between individuals of their natural hosts, which we parochially term "reservoir host" species. This goes on in the forests of central Africa, South America, and the few remaining forests of Indonesia; it also continues in the savannas of East Africa, and within the communities of small mammals that inhabit the world's tundra and mountain ranges. In most cases, the pathogens are unknown to science and have only a negligible impact on the fitness of their reservoir hosts; they have coexisted with them for millennia. A subset of the pathogens are potentially capable of crossing the species barrier from their reservoir host and either entering humans or passing into domestic livestock populations. However, we have very limited facilities for differentiating between the small proportion of these as-yet-undiscovered pathogen species that can be transmitted within humans (or livestock) and even fewer ways of quantifying their potential pathological impact.

At first glance our only way to quantify the threat posed by any of the large number of potentially novel pathogens detected in epidemiological "fishing expeditions" into the habitats listed above would be to extrapolate their properties from their similarity to pathogens that have already crossed the species barrier into humans. I personally find the Nipah and Hendra viruses very scary, because they are fairly closely related to measles, which is arguably the most successful and devastating of human pathogens. But should we be more worried about pathogens that are totally dissimilar to ones that have already crossed the species barrier? HIV is completely different from most other human pathogens, yet it is steadily creating one of the most devastating epidemics in human history.

Ultimately, the only way we can quantify the risk of novel microbes to humans (and domestic livestock) is to create a huge phylogeny of all pathogens and their hosts. We then need to examine the pathology of closely related pathogens, in their reservoir hosts and other host species they infect, and examine the factors that modify virulence and transmissibility. This is a nontrivial exercise. It is one to which genomics will only supply limited insights in the absence of controlled etiological data and exhaustive field surveys. Furthermore, it is a task whose scale is beyond any current level of funding. At present, we have only a rudimentary estimate of the number of species that share the planet with us (May, 1988, 1990) and an even less clear picture of how many pathogens and parasites utilize these species as hosts (Dobson et al., 2008). But as soon as we restrict our search for emergent pathogens to host species that are either close to humans in their evolutionary origins or live in close physical proximity to humans, we then risk missing the rare and unexpected event(s) that create a new epidemic. This is the ultimate "catch 22" of the fish and microchip quests to discover emergent

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pathogens in habitats where we only have a limited understanding of what we are actually looking for.

*Stage Two: Crossover Transmission*

The second stage in "successful" disease emergence occurs when a pathogen is transmitted between its reservoir host and a novel host species. This is both a rare event and one whose outcome is often missed. In most cases, the novel host's immune system will overcome the pathogen's arrival, or more commonly the pathogen will be unable to survive in the novel host species. The host may only suffer mild discomfort and we are only likely to detect the event if the host is human or if a domestic species monitored during routine slaughter is checked before entering the human food chain. Don Burke has called these events "viral chatter"[31]—they occur all the time, but only a tiny subset gives rise to cases where the virus (not forgetting bacteria, protozoa, fungi, prions, and the parasitic helminthes) is able to infect the host and reproduce in a way that leads to transmission to other members of the novel host species. In many cases, these initial "stuttering chains" of transmission will be broken by rapid intervention or, more often, because the new host is not a particularly good environment for the pathogen (for example, the index case may be an immunologically compromised host, whereas subsequent hosts with healthy immune systems can withstand infection).

Analysis of the risks involved at this stage need to focus on the circumstances that caused increased contact between the reservoir host and the novel host species. Changes in the environment are particularly important here. In the case of Nipah virus in Malaysia, for example, deforestation had removed the natural habitat of fruit bats. Their populations were increasingly concentrated in the remaining areas of habitat with fruit trees. Unfortunately, fruit trees were often left around pig farms as they provided shade for the pigpens and an additional source of revenue for pig farmers. Because of the weight constraints of flight, bats only partially eat fruit by sucking out the juices and then regurgitating the seeds and fruit pith below the fruit tree where they have been feeding (Dobson, 2005). The regurgitated fruit can then be eaten by pigs at a time when it is covered by saliva that may be contaminated by Nipah virus. Similar spatial mechanisms are likely to occur as the reservoir hosts of other pathogens become increasingly contained in the fragmented patches of natural habitat that remain when humans have converted the rest of the landscape into agricultural land, shopping malls, and golf courses. If the patches of land contain too few resources to support wildlife, the reservoir hosts may well develop ways of exploiting food resources that are more closely associated with humans, thus increasing the risk of disease transmission to humans.

[31] See http://magazine.jhsph.edu/2005/Fall/features/page_4.cfm.

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Analogous effects occur during the build-up of mice populations in small forest fragments in the eastern United States; these help amplify the spread of Lyme disease (Ostfeld and LoGiudice, 2003). Considerably lower abundances of small mammals occur in large continuous forests where their abundance is reduced by predatory species that cannot survive on the more limited food resources in smaller forest fragments. Similarly, increased populations of domestic livestock will lead to increased contact between these species and remaining populations of wildlife. A potential disease transmission event can occur just as easily when a cow or sheep breaks through a fence and enters a wood or grassland nature reserve, as when an infected sparrow finds its way into a chicken barn.

Most of the novel disease events that occur in livestock will also go undetected and rapidly fade out. The tiny subset that does initiate an epidemic outbreak can usually be stopped by culling all infected hosts along with those in which they have been in contact. However, this requires significant vigilance on the part of animal health inspection services and also assumes that farmers will not try to sell or move their livestock before movement restriction orders are put in place. Unfortunately, this assumes all farmers are honest; in Malaysia (during the Nipah outbreak) and in the United Kingdom during the 2001 foot-and-mouth outbreak (Ferguson et al., 2001; Keeling et al., 2001), farmers illegally moved infected livestock into previously uncontaminated areas and initiated new outbreaks that considerably increased the spatial scale of the outbreak and the number of livestock that ultimately had to be destroyed. The economic theory of "crime and punishment" provides important insights here (Becker, 1968; Sutinen and Anderson, 1985); ultimately, detecting the pathogen at the earliest stage of the epidemic and detecting illegal movement of potentially infected livestock will be much more effective in minimizing the size of the epidemic outbreak than will retrospectively imposed large fines or long prison sentences on the small subset of farmers eventually found guilty of illegally moving livestock.

### *Stage Three: Outbreak*

Detecting infected individuals is crucial if the initial stuttering chains begin to give rise to a sustained epidemic. Two factors are crucial here: (1) the rate of transmission between infectious and susceptible hosts and (2) the ratio of the duration of time before symptoms appear to the duration of time before the hosts can transmit the disease (Fraser et al., 2004). If symptoms appear before transmission is efficient, then control of the outbreak can be achieved by isolation of infected individuals and their primary contacts, particularly when combined with relatively low transmission rates. This is primarily why it was relatively straightforward to contain the SARS outbreak (Anderson et al., 2004). In contrast, when symptoms do not appear until long after transmission has been established, the pathogen can spread and infect a significant number of hosts; HIV is the classic example.

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Once an outbreak has been established and is spreading, the direct and indirect costs will start to increase faster than the exponential spread of the pathogen between hosts. Stories in the media have dynamics that are similar to epidemics; their transmission rates are much more efficient and their impact is often out of scale from the actual risk involved. The economic cost of the SARS epidemic in Southeast Asia was huge given the small number of people who actually became sick or died (McLean et al., 2005). The economic cost of the foot-and-mouth epidemic in the United Kingdom far exceeded the cost of all the cattle slaughtered due to the large indirect impact on tourism and movement restrictions in rural areas.

Searching for novel pathogens and understanding their potential threat and risk of crossing over will require considerable capacity-building in areas that are woefully underfunded. The world has less than 100 people trained to understand the ecology and population dynamics of infectious diseases; this is roughly comparable to the number of knee specialists in New Jersey. Ultimately, this lack of intellectual capacity at the population level within the National Institutes of Health (NIH) has led to the current underestimate of the scale and impact of the H1N1 influenza epidemic in the United States. Equally disconcerting is that the annual meeting of the Wildlife Disease Association attracts less than 400 people and more than 80 percent of them are interested graduate students who are training as veterinarians. The scariest and most intriguing thing about their annual meetings is that each seems to provide an example of a novel pathogen that no one has heard about before and that requires a paradigm shift in the thinking and of people working in the discipline. This year it was white-nose syndrome in bats; last year Tasmanian Devil facial tumors; the year before that, highly pathogenic avian influenza. It is hard to think of another scientific society where a major paradigm shift occurs on an annual basis.

## Summary

The past 25 years have seen major advances in our understanding of the mathematical population dynamic processes that underlie the movement of pathogens within and between host species (Anderson and May, 1991; Grenfell and Dobson, 1995). Over the past 25 years, this whole intellectual enterprise has moved beyond its origins as an area of applied mathematics to one that provides central quantitative insights into public health response to infectious disease outbreaks (Smith et al., 2005). This quantitative ecological-based understanding is central to our understanding of emerging disease dynamics. Any discussion of these problems in the absence of a quantititative mathematical framework are arguably best left in the cocktail reception.

The spatial and temporal scales at which epidemic outbreaks occur requires the use of this mathematical machinery; attempting to understand disease dynamics in its absence is equivalent to attempting pathology without a microscope.

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Unfortunately, levels of funding and training within the United States are considerably below adequate. It is thus likely to be an area where the United States will be increasingly dependent upon talent trained overseas. This is ironic because of the considerable pool of people in the United States trained in physics and mathematics who could make a huge contribution to this area, particularly when coupled into the U.S. domination of the world's microcomputers, which will increasingly be needed to understand the dynamics of pathogens in populations and communities with complex spatial and temporal connections to each other.

Detecting and preventing new pathogens from entering populations of humans and domestic livestock is an important initiative that can potentially tell a lot about the diversity of pathogens that currently inhabit the planet. Even an initial survey of what is out there suggests that there are hundreds of thousands of potentially pathogenic microorganisms already sharing the planet with us. While this is disconcerting, it makes me totally unconcerned about novel ones that might arrive from other planets—the pathetically thin arguments for these "alien pathogens" strike me as little more than a further plea from the National Aeronautics and Space Administration (NASA) for some form of relevance to studies of life on Earth. But, if we are worried about the emergence of new pathogens, early detection will always be significantly less costly than later prevention. If nothing else, there are no indirect costs associated with early detection, and everything to be gained.

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# 4

# Global Public Health Governance and the Revised International Health Regulations

## OVERVIEW

As globalization renders national and geographic boundaries increasingly permeable to pathogens, infectious disease control necessitates international cooperation and coordination. This became abundantly clear when severe acute respiratory syndrome (SARS) emerged in 2003, and it provided a powerful rationale for global public health governance, according to presenter David Heymann of the World Health Organization (WHO). In his contribution to this chapter, Heymann describes the process by which the International Health Regulations (IHR) were revised in the wake of the SARS epidemic and discusses two important challenges that have compromised implementation of IHR 2005: the suspension of polio vaccinations in northern Nigeria and the refusal of Indonesia to share samples of H5N1 influenza viruses collected in that country with the WHO (also discussed in a subsequent essay by Fidler; see below).

"The global public health community has come a long way since the time of the 1918 influenza pandemic," Heymann observes, as evidenced by the first full application of the IHR 2005 in response to influenza A (H1N1) in 2009. The procedures used by the WHO to declare this event a "public health emergency of international concern" (PHEIC), as stipulated by IHR 2005, are discussed in additional papers in this chapter by Chu et al. and Fidler. Despite this progress, until the issues surrounding the H5N1 virus sharing are resolved, the IHR 2005 "remain a valuable but potential framework within which to address infectious diseases across international borders," Heymann asserts.

Another challenge to IHR 2005 implementation involves its requirement for significant public health capacity-building, particularly with regard to infectious



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disease surveillance. In their contribution to this chapter, speaker May Chu and WHO colleagues Heymann and Guénaël Rodier discuss the obligation of signatories to the IHR 2005 to develop the capacity to detect, assess, and report a possible PHEIC, and they describe steps being taken by the WHO to support progress toward this ambitious and crucial goal by member nations. Chu et al. note that countries may take a variety of routes to build surveillance capacity, including collaboration and networking with other member nations and nongovernmental organizations (NGOs) not limited to the WHO. They also consider the crucial role of information networks, such as the Global Outbreak Alert and Response Network (GOARN), coordinated by the WHO, in broadcasting timely disease alerts to the worldwide health community.

The chapter's third paper presents a view of the IHR 2005 from the perspective of the developing world. Workshop speaker Oyewale Tomori, of Redeemer's University in Nigeria, notes that the successful implementation of the IHR 2005 depends on addressing the concerns of policy makers from resource-constrained countries. While some of these concerns are country- and region-specific, he states that "a large proportion of policy-makers in resource-constrained countries perceive that the emphasis of the IHR 2005 on the international spread of disease evinces little concern regarding the burden of infectious diseases on the nations in which they occur."

Tomori examines significant obstacles to implementing IHR 2005 in Africa, which include multiple barriers to the establishment of surveillance systems; lack of political will and commitment to global public health; barriers to sharing public health information among countries; and constraints imposed by donor agencies on funded projects. He also describes steps that could be taken to correct misperceptions of the IHR 2005 in Africa (and elsewhere) and to enable implementation of these regulations in resource-constrained countries.

In his workshop presentation, David Fidler of Indiana University stated that the IHR 2005 represents a "radical departure from all previous uses of international law for public health purposes." After examining the basis for this statement in his contribution to this chapter, Fidler explores a series of challenges that must be overcome if the IHR 2005 are to live up to their promise. His focus is Indonesia's refusal to share H5N1 viral samples with the WHO's H5N1 influenza surveillance team and the significance of this controversy to the implementation of IHR 2005 and to global public health governance in general.

In 2006, Indonesia claimed "viral sovereignty" over samples of H5N1 collected within its borders and announced that it would not share them until the WHO and developed countries established an equitable means of sharing the benefits (e.g., vaccine) that could derive from such viruses. Proposals to use IHR 2005 as a means to force Indonesia to share the samples for global surveillance purposes have failed; Fidler notes that this incident highlights the important, yet ambiguous, position of health as a foreign policy issue and its broad implications for global public health governance.

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The lack of effective international efforts to address many of the factors that encourage the emergence and spread of infectious diseases (e.g., migration, environmental change, antimicrobial resistance, and armed conflict) increases the potential significance of the IHR 2005 to the future of global health, Fidler argues. He notes that the emergence of influenza A (H1N1) has brought the IHR 2005 renewed political attention and appreciation of its value, and it has demonstrated the WHO's ability to implement the regulations in a crisis. However, the IHR 2005 must weather far more severe crises than this epidemic to date, Fidler concludes, as well as a host of global trends that threaten to derail advances toward global public health governance.

## PUBLIC HEALTH, GLOBAL GOVERNANCE, AND THE REVISED INTERNATIONAL HEALTH REGULATIONS

*David Heymann, M.D.*[1]
World Health Organization

### Communicating Disease Risk: Then and Now

The 2003 outbreak of SARS was an event of singular importance in demonstrating the need for global public health governance. It began when a physician, who had treated patients with an unknown respiratory disease in the Guangdong Province of China, traveled to Hong Kong on February 21, 2003. From his visit to Hong Kong, the disease that was eventually named SARS began to spread around the world. When the WHO was alerted about the outbreak of an unknown respiratory disease in Hong Kong on March 12, there was only one way to provide 194 ministers of health throughout the world with the information about this threat simultaneously: a press release. It soon became clear that the message had been received: on March 14, the health ministries of Canada and Singapore reported to WHO that persons in their countries who had recently traveled to Hong Kong had a similar disease.

Early Saturday morning, March 15, in Geneva, the WHO duty officer received a call from the Singapore health ministry. A medical doctor who had treated the patients in Singapore had traveled to the United States for a medical conference and was on a return flight to Frankfurt, Germany. WHO was asked to help this medical doctor get medical care in Frankfurt and this was accomplished. At the same time it became evident that the disease was spreading internationally, and, once again, the most effective method of communicating this recent development simultaneously was by press release—one that gave the disease a name, provided a case definition,

[1]At the time of the workshop, Dr. Heymann was Assistant Director-General for Communicable Diseases and Representative of the Director-General for Polio Eradication at the World Health Organization; however, at the time of publication he is Chairman of the Health Protection Agency.

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and brought it to the attention of international travelers and health workers alike. Clearly this was a less than desirable way to communicate critical information to ministers of health around the world. The fear was that the message would not spread as rapidly as necessary, particularly because it was a weekend.

Five years later, in late October 2008, the revised IHR were in effect. At that time the ministry of health of Sudan reported an outbreak of Rift Valley fever. WHO, along with partners from the Office International des Epizooties[2] (OIE) and the Food and Agriculture Organization of the United Nations[3] (FAO), was requested by the government of Sudan to support the ministries of health and agriculture in investigation and containment activities. The risk assessment after the outbreak investigation raised great concern because livestock from Sudan, traded across the Red Sea into Yemen and Saudi Arabia, could have been carrying the Rift Valley fever virus. As these animals were being sacrificed during religious ceremonies, the risk of transmission of Rift Valley fever to humans was high.

Unlike in 2003, at the time of the SARS outbreak, WHO was able to transmit information about the infectious disease threat directly and simultaneously to all 194 ministries of health because of the presence of an IHR[4] focal point in each country who is on call 24 hours a day. Health ministers quickly received the information they needed for risk assessment, and they were able to report back to WHO or ask for further clarification electronically and in real time.

Today, the IHR connect national focal points in countries with contact points at WHO regional offices and a universal event management system. The WHO regional offices enter epidemiological and other information necessary for risk analysis and management into this event management system that stores the information and makes it available as needed for risk analysis and management. Feedback to countries through a national IHR focal point completes the reporting link and, if countries require support in outbreak response, a request is transmitted back to the WHO.

[2]The OIE is the intergovernmental organization responsible for improving animal health worldwide. The Office International des Epizooties was created through an international agreement signed on January 25, 1924. In May 2003, the office became the World Organisation for Animal Health but kept its historical acronym OIE. For more information, see http://www.oie.int/eng/OIE/en_about.htm?e1d1 (accessed March 30, 2009).

[3]Achieving food security for all is at the heart of FAO's efforts—to make sure people have regular access to enough high-quality food to lead active, healthy lives. FAO's mandate is to raise levels of nutrition, improve agricultural productivity, better the lives of rural populations, and contribute to the growth of the world economy. For more information, see http://www.fao.org/about/mission-gov/en/ (accessed March 30, 2009).

[4]The International Health Regulations (2005) represent a legally binding agreement that significantly contributes to international public health security by providing a new framework for the coordination of the management of events that may constitute a public health emergency of international concerns, and will improve the capacity of all countries to detect, assess, notify, and respond to public health threats. For more information, see http://www.who.int/csr/ihr/prepare/en/index.html (accessed March 30, 2009).

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### Revising the IHR

The original IHR, established in 1969, were preceded by a long history of public health measures designed to control the spread of infectious diseases across borders (see Gushulak and MacPherson in Chapter 1). These efforts focused on four diseases: plague, cholera, yellow fever, and smallpox. In the case of the IHR (and the accompanying sanitation guidelines for seaports and airports), they attempted to strike a balance between ensuring maximum public health security against the international spread of these four infectious diseases with minimum interference in global commerce and trade.

The original IHR were predicated on the notion that with appropriate measures at border posts it was possible to stop diseases from crossing international borders. Countries in which one of the four reportable diseases (three, after the eradication of smallpox) was occurring were required to notify WHO, and other countries were permitted to take specified measures at airports and seaports to prevent the entry of disease or disease vectors coming from these countries. As an example, when a country reported a yellow fever outbreak to WHO, a report of the infected area was published in the WHO *Weekly Epidemiological Record*. During the period between reporting and certifying that the outbreak was contained, countries could require yellow fever vaccination certificates from passengers arriving from the affected country.

Recognizing that the world contains multiple and diverse infectious threats beyond these reportable diseases, and that advances in communications could be employed to detect and support the control of diseases that threatened to spread internationally, a decision was made in the mid-1990s to revise IHR. The revision process had two primary goals: to make use of modern communication technologies to understand where diseases were occurring and had the potential to spread, and to change the international norm for reporting infectious disease outbreaks so that countries were not only expected to report outbreaks, but also respected for doing so.

Before 1996, WHO acted only when reports of infectious disease were received from affected countries. As the vision for the revision of the IHR became clear, the WHO began to work more proactively, both in detecting diseases that threatened to cross international borders and in more actively supporting countries in outbreak response should they so request. This vision led to the creation of the Global Public Health Information Network (GPHIN)[5] by Health Canada, and the GOARN by the WHO and its technical partners. GPHIN, a web-crawling application,[6] searches open sites on the World Wide Web for key words associated with infectious diseases, in multiple languages. It does a preliminary analysis of the

[5]See http://www.who.int/csr/alertresponse/epidemicintelligence/en/.

[6]A web crawler is a computer program that browses the World Wide Web in a methodical, automated manner. For more information, see http://en.wikipedia.org/wiki/Web_crawler (accessed March 30, 2009).

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information collected and provides this information every 24 hours to the WHO, where it is verified as rapidly as possible through the WHO system. In 2000, WHO formalized GOARN and it is now able to mount coordinated international response to an infectious disease outbreak by linking its technical partners (institutions, organizations, and networks) with countries that request support.[7] Figure 4-1 shows some of the current technical partners of GOARN throughout the world.

GPHIN, and many other global surveillance partners of WHO, were in place when SARS first appeared. While still nameless, SARS was first identified in Asia by GPHIN and several other partners in global surveillance. WHO feared that these reports of an atypical pneumonia with high mortality signaled the beginning of an influenza pandemic because H5N1 was known, since 1997, to be present in that region of China. Within a period of a weeks after the first recognized case, GOARN mobilized more than 115 experts from 26 institutions and 17 countries to support infected countries in outbreak investigation, patient management, and outbreak containment. These experts, and others, exchanged epidemiological, laboratory, and clinical information about the outbreak in real time. WHO used this information to make recommendations on patient management and eventually issued travel recommendations in an attempt to curb, and eventually stop, the international spread of this newly recognized virus.

The SARS outbreak was a turning point in international collaboration on infectious disease control, and many ministers of health became convinced that they must change the way they work together to fit this model. At the World Health Assembly (WHA) in May 2003, a resolution was passed by WHO member states that confirmed that WHO could receive and use infectious disease information from sources other than countries for risk assessment with the affected country in a confidential manner, and it also mandated reporting of a wider range of infectious diseases with potential for international spread rather than just yellow fever, cholera, and plague. This resolution helped increase the pace of the revision of the IHR and, in 2005, the revision process was completed with full endorsement by the WHA. The revised IHR enable more proactive surveillance for an event that could be considered a PHEIC, whether it be infectious, chemical, radiological, or food-related. With a core capacity strengthening requirement for countries in epidemiology and public health laboratory, the revised IHR will strengthen the ability of countries to detect and contain outbreaks at their source so that they do not have the opportunity to spread internationally. Figure 4-2 compares the major distinctions between the 1969 IHR and the 2005 revision.

Specifically, the revised IHR mandate:

- Strengthened national core capacity for surveillance and control, including at border posts;

[7]See http://www.who.int/csr/outbreaknetwork/en/.

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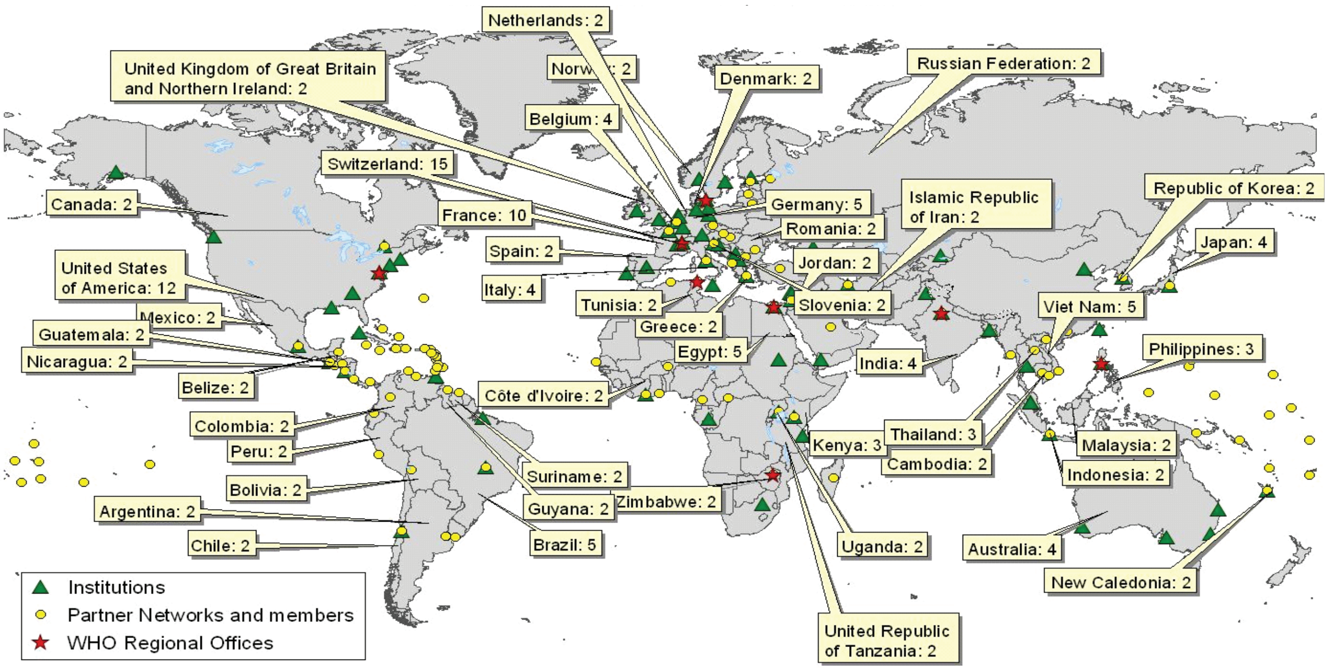


**FIGURE 4-1** Global Outbreak and Alert Network (GOARN): Institutions and members of partner networks.
SOURCE: Reprinted with permission from WHO/GOARN.

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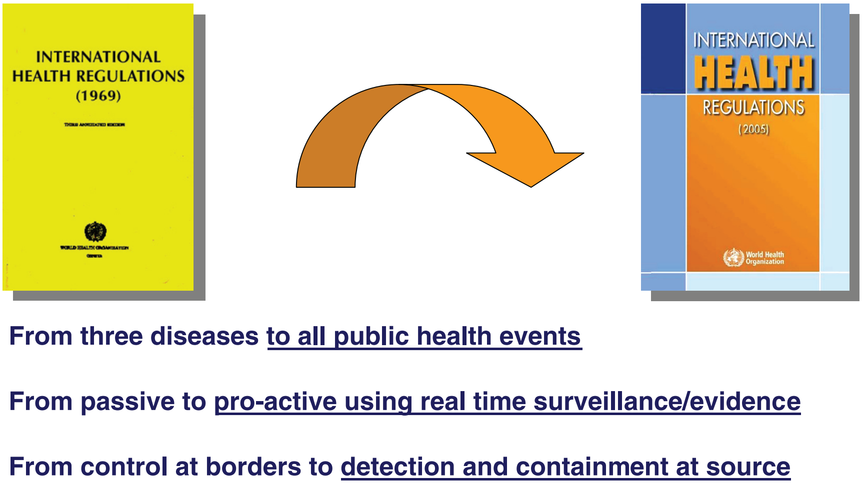


**FIGURE 4-2** Major distinctions between the IHR 1969 and the revised IHR 2005.
SOURCE: Heymann (2008).

- Reporting of possible PHEICs (see Figure 4-3), and of four specific diseases even if only one case is identified: SARS, smallpox, avian influenza, and polio;
- Collective, proactive global collaboration for risk assessment and risk management; and
- Monitoring of implementation by the WHA.

## Global Governance and the Revised IHR

### *Polio Eradication*

In 1988, polio was present in more than 125 countries, where it caused paralysis in approximately 1,000 children each day; and access to polio vaccine was inequitable between countries. Polio vaccine rapidly became available after 1988 in sufficient quantities for all countries and, by 2003, polio remained in only six countries: India, Pakistan, Afghanistan, Egypt, Niger, and Nigeria. Fewer than 1,000 children became paralyzed in the course of that entire year, and there was equitable access to vaccine. But during the latter part of 2003, rumors began circulating that polio vaccines were causing sterility in young girls.

These rumors led to a suspension of polio vaccination in 2003 in northern Nigeria. The result was that the polio virus began to migrate with people from northern Nigeria as they crossed Islamic pilgrimage routes and Muslim trade routes throughout Africa. Polio virus from Nigeria traveled as far as Saudi

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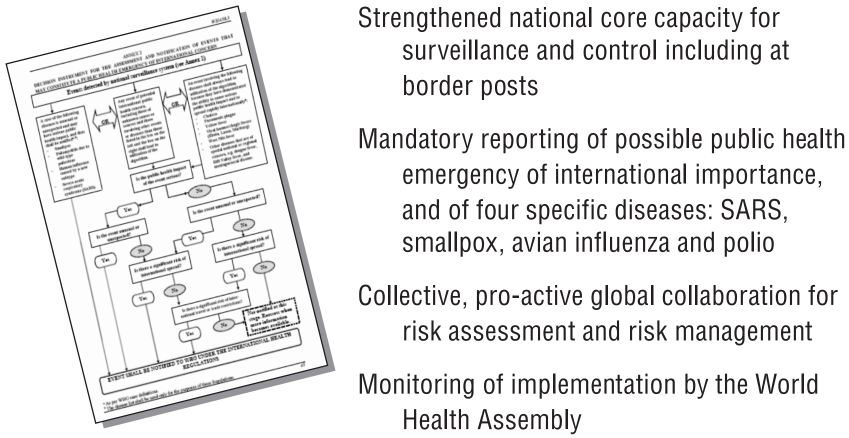


**FIGURE 4-3** Requirements of the IHR 2005.
SOURCE: Heymann (2008).

Arabia, Yemen, and Indonesia, and polio returned to countries that had previously become polio free. In the first year after vaccinations ceased in northern Nigeria, it cost the Global Partnership on Polio Eradication an estimated $500 million to stop polio in reinfected African countries, as illustrated in Figure 4-4.

Initial efforts to deal with this situation involved demonstrating that polio vaccines contained no impurities or hormones that could cause sterility in young girls. Vaccines were sent by the Nigerian government to WHO Collaborating Centers on polio in South Africa and India, and testing was overseen by experts from Nigeria. At the same time, an offer was made by the United Nations Children's Fund (UNICEF) of polio vaccine manufactured in an Islamic country.

WHO representatives, along with Ministry of Health officials, engaged in personal discussions with the governors of the northern Nigerian states who had ordered that polio vaccination be stopped. The governors convened groups of pediatricians to help them determine whether the risk was greater from vaccine or from polio, at a time when approximately 82 percent of all polio in the world was occurring in northern Nigeria. These concerns were also taken to the Organization of Islamic Conferences (OIC), whose members understood the importance of this issue in their own countries. The OIC heads of state discussed the importance of polio eradication in a plenary session at their summit in 2003 in Malaysia, and then passed a resolution to support polio eradication that has been reviewed each year since then at annual OIC minister of health meetings.

Neither proof of vaccine safety nor political and religious advocacy were, however, enough to convince northern Nigeria to resume polio vaccination. The issue was then taken to the broader Islamic community that produced a series of religious

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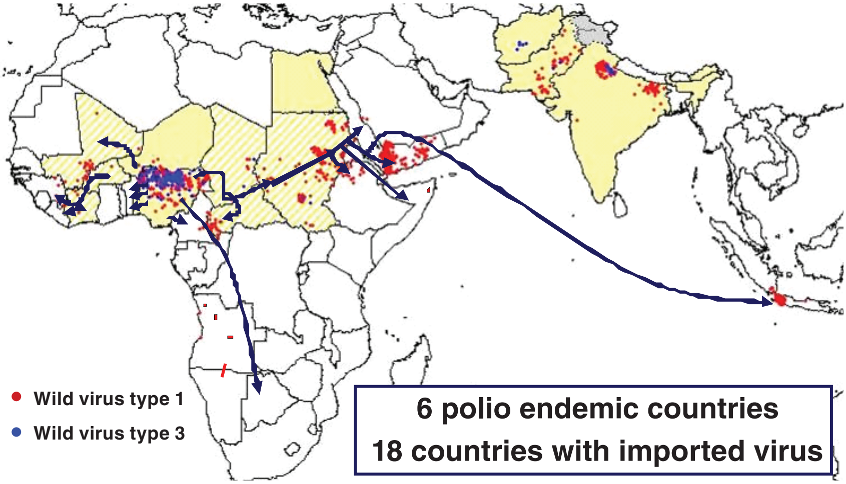


**FIGURE 4-4** The international spread of polio from Nigeria, 2003-2005.
SOURCE: Reprinted from WHO (2005) with permission from the World Health Organization.

fatwas (declarations) and academic statements regarding the safety and importance of polio vaccination. One religious leader in particular, the late Imam Cheik Cisse of Senegal, was very active in northern Nigeria, traveling there to advocate for the importance of polio vaccination, vaccinating children himself as an example.

As an additional measure, WHO convened an *ad hoc* expert advisory group on polio epidemiology and public health to determine if there were any evidence-based measures that could be recommended to stop the international spread of polio. This group concluded that evidence in the scientific literature supported the fact that polio-immune adults could carry the virus in their intestines for periods up to a month, that the polio virus therefore had the potential to be carried wherever persons from polio-infected areas traveled, and that a booster dose of oral polio vaccine could decrease the period the virus was carried. A recommendation was made that a booster dose of oral polio vaccine be provided for persons traveling from countries with polio. Saudi Arabia, where there had been imported polio from Nigeria, followed these recommendations and began requiring booster vaccination of Islamic pilgrims before they left their country if it was polio-infected, and also upon the arrival of the pilgrims in Saudi Arabia. These recommendations continue to stand and are being considered as standing recommendations under the IHR, where polio is one of those four diseases named that even one case requires reporting.

Finally, resolutions were passed in the WHA regarding measures to be taken when polio spread internationally, and the most recent, in 2008, was widely reported

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in the Nigerian press, leading in part to further engagement of Nigerian President Umaru Yar'Adua, who stated publicly that "[w]e will do everything humanly possible to ensure that polio is finally and totally eradicated from Nigeria."

Nevertheless, the polio virus continues to circulate in northern Nigeria. As of April 2009, 184 Nigerian children have been paralyzed from polio this year (WHO, 2009a). The polio virus also continues to spread to neighboring countries, and every aspect of global governance, including work within the framework of the IHR, continues to be used to stop its international spread. While polio vaccination has resumed in northern Nigeria, efforts have not yet been effective enough in reaching children to provide the level of herd immunity necessary to interrupt transmission.

Once countries succeed in interrupting the transmission of polio worldwide, other risks to polio eradication will remain. The Sabin vaccine virus is able to revert to a wild form either through genetic recombination or reassortment. After eradication has been certified, a WHO group of advisers has concluded that it will therefore be necessary to stop the use of oral polio vaccine to minimize this risk, and countries continuing to vaccinate would have inactivated polio vaccine as an alternative. It remains to be seen whether the IHR will be used by member states in any way at the time of oral polio vaccine cessation to ensure that all countries stop its use simultaneously so that no country places others at risk. It likewise remains to be seen if the IHR will be used to address another post-eradication risk, destruction, or consolidation under high security of those polio viruses that remain stored in research and diagnostic laboratories.

Thus, while the IHR provide a useful framework that enables international coordination for the prevention and control of infectious diseases, their use is not automatic. It depends rather on the collective will of WHO member states to use them as a framework to resolve public health issues, on a case-by-case basis.

### Influenza Pandemic Preparedness

WHO facilitates the work of a network of 127 national influenza centers throughout the world that regularly provide seasonal influenza viruses to one of four WHO Collaborating Centers on influenza where genetic characterization is conducted (Figure 4-5). Results of sequencing are then used for a comparative risk analysis, and an annual recommendation is made for the composition of seasonal influenza vaccine.

Once the recommendation is made as to which virus strains should comprise the next seasonal vaccine, it takes up to six months to prepare the vaccine for use. The global capacity for seasonal influenza vaccine production varies between 350 million and 500 million doses, far less than would be required to produce an influenza vaccine for a pandemic.

The same network of laboratories also tracks potential pandemic influenza viruses. Figure 4-6 shows the geographic locations of human zoonotic infections

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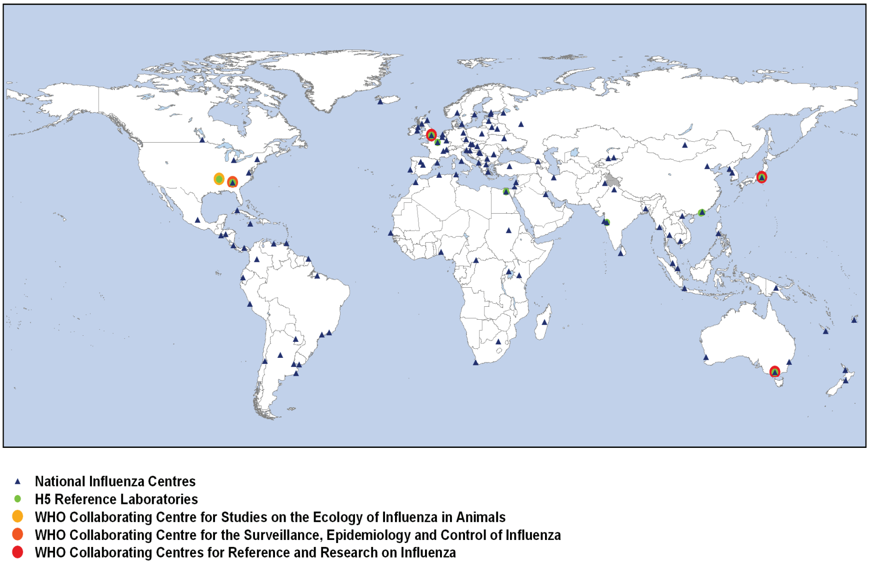


**FIGURE 4-5** WHO Global Influenza Surveillance Network (GISN), July 2008.
SOURCE: Heymann (2008).

with novel avian influenza (H5N1) viruses, in countries where H5N1 influenza is occurring in poultry.

Figure 4-7 presents an analysis of genetic information from the H5N1 virus collected by the Global Influenza Surveillance Network and clearly demonstrates the instability of the virus. It remains to be seen whether the H5N1 virus will undergo an adaptive mutation, such as was thought to have occurred to produce the 1918 (H1N1 influenza A) pandemic virus, or whether genetic reassortment among influenza viruses will produce a pandemic strain as occurred in other twentieth-century influenza pandemics. If either scenario should unfold, WHO will spearhead the global pandemic response as it has done for H1N1 influenza beginning in April 2009.

Figure 4-8 illustrates the current pandemic alert phase of the H5N1 virus. If phase 3 for H5N1, its current level of alert, proceeds to phase 4 with localized human-to-human transmission, and if this change in phase is detected at an early stage, WHO and its partners will work with the county or countries involved to attempt to rapidly ring fence such an outbreak with vaccine and antiviral drugs in hopes of slowing virus spread, or stopping its spread altogether. The capacity for such a rapid response is currently being established in countries and in regions where pandemic influenza is considered most likely to originate, and the emergence H1N1 of 2009 has given countries the opportunity to test their rapid

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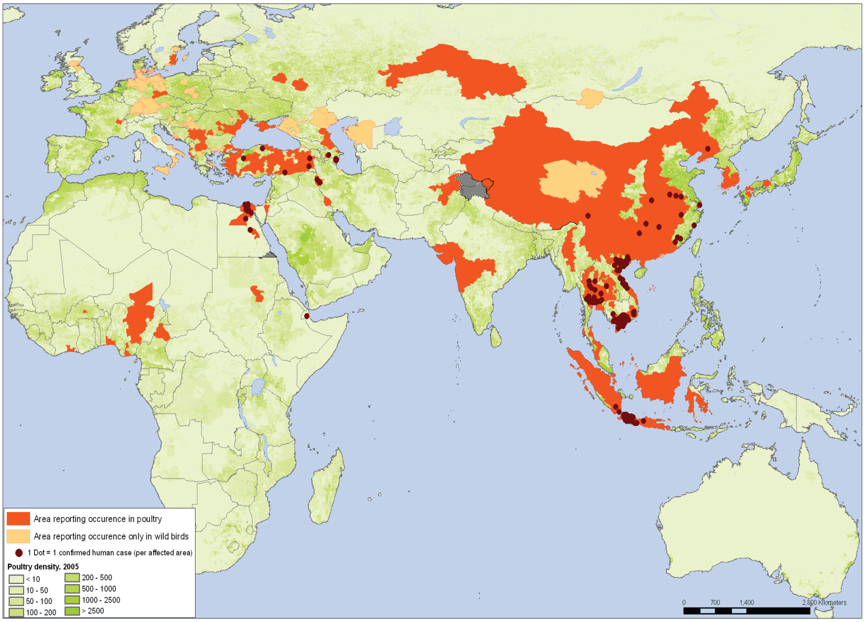


**FIGURE 4-6** Confirmed human and poultry infections since 2003.
SOURCE: Data based on OIE and national governments reporting. Map produced by Public Health Mapping and GIS, Communicable Diseases, WHO. Reprinted with permission from the World Health Organization.

response capacity as the pandemic alert was raised to phase 5 and finally 6 during the first half of 2009. The pandemic scale in Figure 4-8 has been modified to further characterize phase 6 by community level outbreaks in at least one other country and in a different WHO region from that country or those countries where phase 5 has initially been declared.

On June 11, 2009, the WHO raised the pandemic alert level of the influenza A (H1N1) from 5 to 6. Phase 6, the pandemic phase, is characterized by community level outbreaks in at least one other country in a different WHO region in addition to the criteria defined in Phase 5. Designation of this phase indicates that a global pandemic is under way (WHO, 2009b).

In anticipation of a decision to implement a containment strategy, WHO maintains stockpiles of antiviral drugs, as do the U.S. government and the Asia-Pacific Economic Cooperation (APEC), for use by any country in the event of a change in the alert phase. As soon as an H5N1 vaccine is licensed, WHO will also stockpile vaccine. The virus composition for H5N1 vaccine is recommended by the same risk assessment process as that used for seasonal vaccine composition, through the Global Influenza Surveillance Network.

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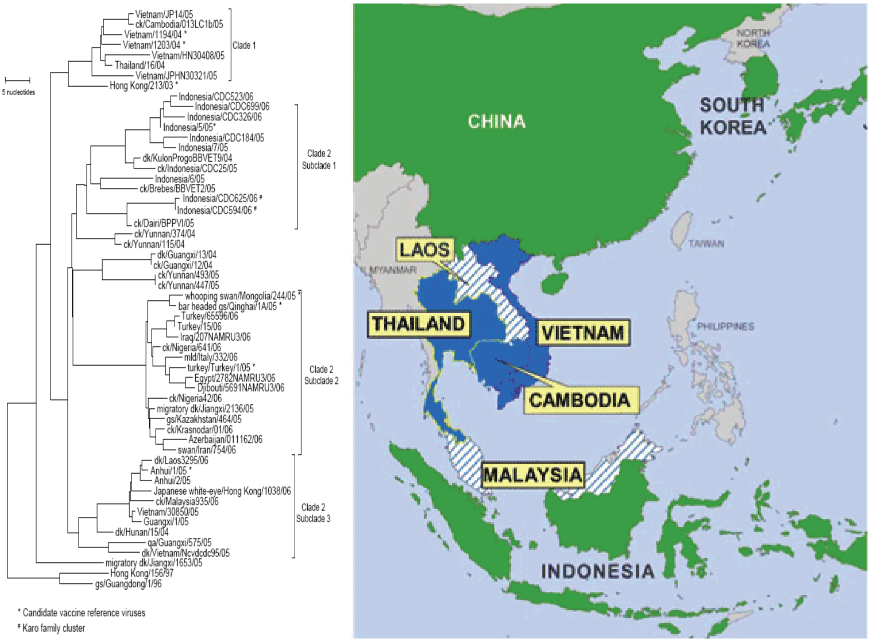


**FIGURE 4-7** Genetic diversity: H5N1 virus groups (clades) infecting humans since 2003.
SOURCE: Heymann (2008).

| | | |
|---|---|---|
| Inter-pandemic period | Phase 1 | No new influenza virus detected in humans. If a new influenza virus presents in animals, the risk of human infection is considered to be low. |
| | Phase 2 | No human infections, but a circulating animal influenza virus poses a risk to humans. |
| Pandemic alert period | Phase 3 | Human infection(s) with a new virus, but no (or very infrequent) human-to-human spread. |
| | Phase 4 | Small cluster(s) with limited human-to-human transmission but spread is highly localized. |
| | Phase 5 | Larger cluster(s) but human-to-human spread still localized |
| Pandemic period | Phase 6 | Increased and sustained transmission in general population. |

**FIGURE 4-8** The current pandemic alert phase of the H5N1 virus.
SOURCE: Heymann (2008).

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In 2007, the Indonesian minister of health raised an important issue concerning preparations for pandemic influenza. She observed that while Indonesia and other developing countries had freely shared influenza viruses obtained within their borders through the Global Influenza Surveillance Network, these countries would be less likely to have vaccine in the event of a pandemic because of issues related to cost and production capacity.

In order to better understand the issues, WHO conducted a meeting of experts, hosted by the government of Indonesia, to understand how countries might more equitably share in the benefits associated with virus sharing. This expert group identified the following issues that needed resolution to ensure more equitable sharing of benefits:

- Greater participation by developing countries in the Global Influenza Surveillance Network, through the strengthening and certification of additional national influenza centers and WHO Collaborating Centers in developing countries;
- Greater transparency by WHO in the handling of influenza viruses; and
- Greater access to pandemic vaccines for all countries, with an increase in developing country vaccine production capacity.

To date, some countries have chosen not to continue to send H5N1 influenza viruses for risk analysis to the WHO Global Influenza Surveillance Network, making risk analysis less complete than previously when all H5N1 viruses were freely shared. As is the case for polio, avian influenza is one of the four named diseases that require reporting under the IHR. Rather than invoke the IHR to address this issue, however, WHO member states have preferred to address the issue of H5N1 virus sharing and sharing of the benefits through a resolution at the WHA in 2007. This resolution has called for a series of intergovernmental meetings currently under way to discuss, debate, and develop a new framework for the sharing of influenza viruses and sharing in the benefits. In addition, WHO is undertaking a number of extra measures, including (1) establishment of a more transparent virus traceability mechanism that permits countries to determine how the viruses they provide to the WHO Global Influenza Surveillance Network are being shared; (2) implementation of a global pandemic influenza vaccine plan that includes vaccine manufacturing technology transfer to developing country vaccine industry; (3) increasing the number of developing country laboratories participating in the Global Influenza Surveillance Network; (4) assessing various financial mechanisms that could be used to purchase pandemic vaccines; and (5) establishing an H5N1 vaccine stockpile for use in rapid response to a phase 4 or phase 5 alert, and provision of vaccine to countries early in a pandemic should it be caused by H5N1.

The global public health community has come a long way since the time of the 1918 influenza pandemic. By revising the IHR in 2005, there is now a frame-

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work within which all countries can collaborate in risk assessment and management in order to limit the impact of the next influenza pandemic. They have now been tested for influenza H1N1 in April 2009 when an emergency committee was convened to assess the risk from H1N1, but so far the IHR have not been selected as the mechanism under which to work in resolving the very important issues related to sharing the H5N1 virus and sharing of the benefits. It remains to be seen when and how the intergovernmental process currently under way will resolve the issues of H5N1 virus sharing and sharing of the benefits through the process established under the WHO Resolution.

### Conclusion

There are many different mechanisms of global governance. They include conventions such as the framework tobacco convention established several years ago through WHO; regulations, such as the IHR; resolutions which express collective political will, such as that for H5N1 virus sharing and sharing of the benefits; norms and standards to which countries are expected to adhere; and finally, some forms of advocacy. Countries together interpret which of these mechanisms to invoke, and global governance is therefore determined collectively as a situation unfolds. In the case of the IHR, they remain a valuable but potential framework within which to address infectious diseases across international borders.

## CAPACITY-BUILDING UNDER THE INTERNATIONAL HEALTH REGULATIONS TO ADDRESS PUBLIC HEALTH EMERGENCIES OF INTERNATIONAL CONCERN

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### Overview of the Historical and Revision of the International Health Regulations: the New Paradigm

When the WHO was chartered in 1949, one of its earliest tasks was to create "The International Sanitary Regulations" (1951), which sought to harmonize and replace 13 or more international agreements concerning quarantine and sanitary

[8]International Health Regulations, Health Security and Environment.

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measures (Hardiman, 2003). In subsequent years, these regulations were added to, revised, and then renamed the International Health Regulations (IHR) in 1969. By 1995, the governing body of WHO, the World Health Assembly (WHA), made up delegates of all the member states, adopted the resolution to modernize the 1969 IHR to take into consideration the evolving stage of global public health threats. Their vision was for the revised IHR to be able to accommodate a world that would be alert and be able to detect and respond to international infectious disease threats and public health events within 24 hours of its first report using the most up-to-date means of global communication and collaboration. The revision would aim to facilitate a change in the norms surrounding reporting, making it expected and respected to report infectious disease outbreaks—particularly public health events (both infectious and noninfectious) that may impact international trade and travel.

The revision was needed to bring the IHR into the modern age and take into account the changes in global climatic and social environments. In the IHR 1969, reporting of disease occurrence was limited to a few diseases (plague, yellow fever, cholera, and smallpox). After eradication, smallpox was removed leaving the three diseases as the only ones reportable to WHO by the affected member state. This rigid approach meant that emerging or reemerging diseases—public health threats that can be rapidly transmitted and transported across the world, such as SARS and pandemic influenza—would not have been notifiable. The IHR (1969) not only limited how such occurrences could be officially reported, they also did not link to potential responses thus leaving a gap in assessing what the risks might be if there was international spread. There was reluctance to report by the affected country because of concerns over halting trade and keeping travelers away; at the same time, other countries did not have equal and open access to the available information The absence of incentives to report and the absence of risk communication and reasonable control measures often led to over-reaction by the global community, heightened the sense of vulnerability, and even exaggerated fear and engendered mistrust. Thus, the key to reestablishing trust and confidence was to demonstrate to all member states that a set of revised procedures would be in the best interest of all countries, whether the member state is experiencing a public health event or seeking to protect themselves from becoming affected (Fidler and Gostin, 2006). Furthermore, capacity strengthening and transparency to share information should be the responsibility of a country to contain the risk and not spread it further to other member states territories. Countries cannot do it alone; therefore, a collaborative environment must be created so that countries can share their experiences and receive benefits for being alert and responsive.

The 58th WHA unanimously adopted resolution WHA58.2, the revised IHR, in 2005. A total of 194 signatory state parties (193 member states plus the Holy See) have committed to this responsibility. Article 2 of the IHR (2005) states that the primary purpose of the IHR (2005) is to "prevent, protect against, control, and provide a public health response to the international spread of disease commen-

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surate with public health risks, and which avoid unnecessary interference with international traffic and trade" (WHO, 2005). The articles reflect a paradigm shift: (1) from reporting three diseases to reporting all public health events that may likely spread internationally and affect travel and trade, (2) from passive reporting and pre-set measures to proactive surveillance and tailed response, using real-time evidence for risk assessment and risk management, and (3) from control at borders to detection and containment at the source of the event. Information from public health events still requires the country to officially report to WHO, although its sources may be gathered from multiple streams of information. WHA58.2 would come into force on June 15, 2007, with a period until 2012 for preparing, review, and planning for each signatory member state (State Party) to meet the requirements of the IHR (2005).

## IHR: States Parties Must Invest in Capacity-Building

The revised IHR (2005) set a new paradigm and opportunity for WHO member states to share health-related risk information affecting travel and trade in a more transparent and organized manner.

Compliance with IHR (2005) requires each State Party to develop, strengthen, and maintain, as soon as possible but no later than 5 years from the entry into force of the regulations (Figure 4-9), the core capacity to detect, assess, notify, and report events. Each of the 194 state parties assumed the responsibility to develop the capacity to respond promptly and effectively to PHEICs as set out in the articles and Annex 1A. Each State Party is asked to utilize existing national structures and resources to meet their core capacity requirements in a national tiered system and the system is operational around the clock. A National Focal

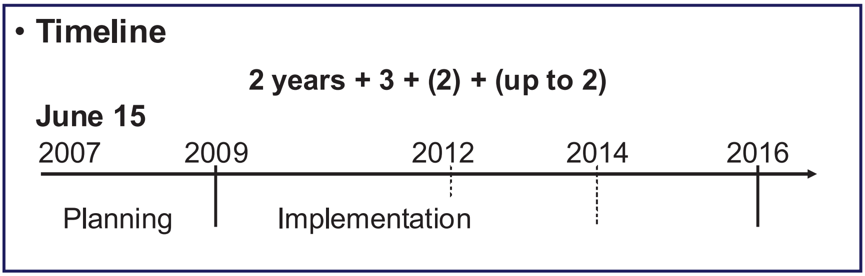


**FIGURE 4-9** Timeline for implementation of the IHR to strengthen national capacity (194 States Parties[a]).

[a]WHO has 193 State Parties. The additional State Party is the Holy See who is not a WHO member state but has joined IHR on a voluntary basis.

SOURCE: Chu (2008).

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Point (NFP) is named by the State Party to serve as the communication conduit with WHO.

In terms of capacities, states parties are required to develop and strengthen core public health capacities for surveillance and response throughout their territories (as well as capacities at some points of entry). As part of these requirements, the IHR (2005) mandate that domestically all "essential information" be communicated from the local to intermediate levels concerning reportable events, including available "laboratory results." At the national level, all states parties must have the domestic capacities to provide support through specialized staff, laboratory analysis of samples (domestically or through collaborating centers), and logistical assistance (e.g., equipment, supplies, and transport), as well as have links for dissemination of information. Countries must also facilitate the transport, entry, exit, processing, and disposal of biological substances and diagnostic specimens, reagents, and other diagnostic materials for verification and public health response purposes.

Annex 2 is a decision instrument tool for the assessment and notification of events that may constitute a PHEIC (Figure 4-10). This decision instrument replaces the list of the three reportable diseases and is designed to aid countries in identifying an event that may spread internationally. There are three situations to be considered: (1) a single occurrence that requires reporting (i.e., a single case of SARS, smallpox, pandemic influenza, and all diseases of high transmissibility with potential to become serious public health threat); (2) any known disease whose source is found in its natural endemic foci but, if spread or appearing outside of its natural environment, could lead to a PHEIC, such as, for example, the plague from New Mexico focus, in the United States, appearing out of context in New York City would require investigation and risk assessment; and (3) any public health event of serious impact in a community with potential to spread beyond its source (i.e., food product contamination) for which answers to the four key questions posed in Annex 2 will determine if the event may constitute a PHEIC, and consequently, be notified to WHO under the IHR (2005). For instance a public health event with potential of international spread should be reported if replies to at least two of the questions are "yes." Upon notification of the event, WHO has the mandate to collect and analyze information regarding the events and to determine its potential to cause disruption in travel and trade, irrespective of the origin or source, and may share such information with countries and intergovernmental organizations following verification with the affected State Party.

There is provision in the IHR (2005), particulary under Article 44, for State Parties to develop collaborations with each other for detection, assessment, facilitation of technical cooperation, and logistical support; share mobilization of financial resources; and to formulate legal instruments for implementation of the IHR (2005). WHO is asked to collaborate with state parties, upon request, to develop, strengthen, and maintain these capacities. Furthermore, collaboration may be implemented through multiple channels, using networks, the

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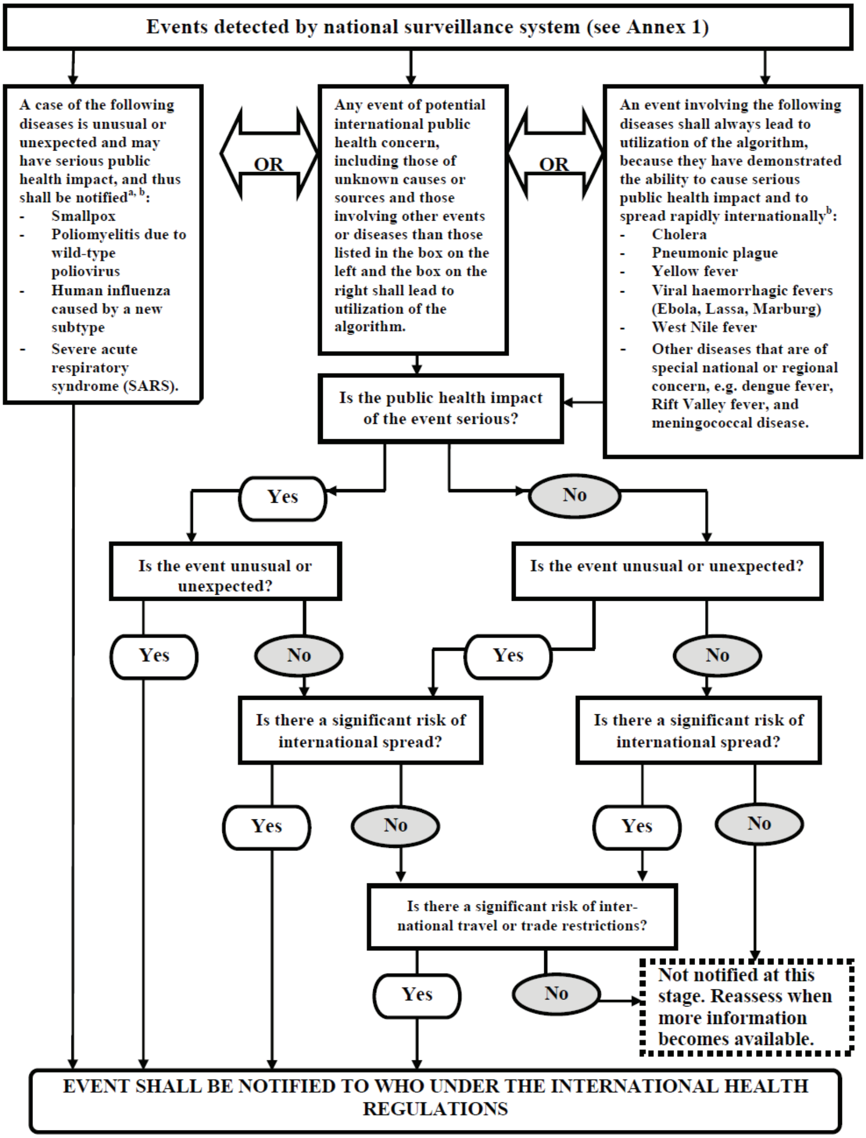


**FIGURE 4-10** Decision instrument for the assessment and notification of events that may constitute a public health emergency of international concern.

[a]As per WHO case definitions.

[b]The disease list shall be used only for the purposes of these Regulations.

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WHO regional offices, and bilateral partnerships, and through intergovernmental organizations and international bodies.

Each State Party shall assess events occurring within its territory by using the decision instrument in Annex 2. Each State Party shall notify WHO, by the most efficient means of communication available, by way of the National IHR Focal Point, and within 24 hours of assessment of public health information, of all events that may constitute a PHEIC within its territory in accordance with the decision instrument, as well as any health measure implemented in response to those events.

Following a notification, a State Party shall continue to communicate to WHO timely, accurate, and sufficiently detailed public health information available to it on the notified event, including, where possible, case definitions, laboratory results, source and type of risk, number of cases and deaths, conditions affecting the spread of the disease and the health measures employed, and report, when necessary, the difficulties faced and support needed in responding to the PHEIC (WHO, 2005).

WHO may request from the affected or reporting country, in response to a specific potential public health risk, relevant data concerning sources of infection or contamination (including vectors and reservoirs) at its point of entry that could result in international disease spread.

### The Challenges: Normative Versus Reality

The responsibilities assumed by the state parties require resources, commitment, and spirit of collaboration. Countries should not be expected to deliver this on their own, nor should they do so without some harmonization of approaches and access to tools to allow them to communicate rapidly and efficiently.

At the core of creating a transparent and informative work space, the WHO has built upon its Event Management System (EMS), which consolidates through its WHO portal daily inputs from a variety of information sources: formal and informal; individual, governmental, intergovernmental and regional; and collected from specifically designed tools that enhance early warning signals of events of high concern. It is the role of the EMS to serve as a clearinghouse, to screen, assess, verify, and report to member states as to the risks and to determine collaboratively the management of the risks. It is through this clearinghouse that the IHR NFP may use the Events Information Site (EIS) to inform, access, and share information with the WHO and to inform their own competent authorities of actions and events. The EIS establishes protected access for IHR-related information, connecting the WHO and the NFP in a privileged but transparent manner that is operational 24 hours every day. New events are posted and shared as soon as they are notified, with risk-assessment comments. Some may argue this approach limits the sharing of information, bypassing previously more spontaneous *ad hoc* reporting and wider access by those interested in sharing outbreak news; others

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feel more at ease with the pass-coded site because more descriptive details are shared freely. Information is shared through the Disease Outbreak News,[9] the Weekly Epidemiological Record,[10] and with partners through GOARN.[11]

Response to and management of public health events is a more established process through the collective experience and synthesis of "lessons learned" from outbreak response. The Alert and Response Operations (ARO), GOARN, and other outbreak response efforts of a number of dedicated teams in WHO has led to the development of a payload concept of operations to support functions. The concept envisions a pre-set, prepared system into which one drops the specific event (be it of chemical, radionuclear, food safety, or epidemic origin), this coordinated approach allows for better communication and field operations support that is constantly under information analysis, verification, and risk assessment while tapping into the expertise of partners through GOARN, regional and national experts, and specific collaborative networks (Kimball et al., 2008; Koplan et al., 2005).

The challenges to building capacity are inherent in the divergence of the systems among the state parties. Essentially, there are 194 flavors because every State Party has built its own system. However, they have the same goals; therefore, each "pathway" will have to be constructed to (1) utilize and build on existing infrastructure, strengthening them as needed, and enjoin partnerships where one country can assist another; (2) build trust and confidence in the data received and provided, thus committing to a quality assurance framework that complies with international standards; (3) incorporate the vertically invested programs for disease control and surveillance, making state parties aware of the IHR requirements and discussing with them the potential leveraging of resources; and (4) support countries to carry out cross-sectoral assessments, planning and implementing their capacity-building process by provision of consultations, tools, and shared costs. Questions unique to each country relate to whether the countries support a centralized (public health clinics to district, to central) or federated systems (multiple supra-national, or regional centers)? Whether there is regulation in place for sample collection and their transport? What would be the minimal level of quality assurance? What types of data should be collected for reporting public health events? Who will be responsible to ensure a functional system and how would it be paid for?

### WHO's Experience in Implementing the Revised IHR

Since the entry into force of the IHR (2005) on June 15, 2007, the WHO regional offices (AFRO, AMRO, EMRO, EURO, SEARO, and WPRO) have

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[9] See http://www.who.int/csr/don/en/.
[10] See http://www.who.int/wer/en/.
[11] See http://www.who.int/csr/outbreaknetwork/en/.

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worked tirelessly to assess their member states' national and regional capacities and to assist them in making their IHR plans for building core capacities. The next steps are to implement the plans using a coordinated and cross-sectoral approach. There is no one solution that fits all the models, and countries differ in their steps to reach the goals; countries also have to request assistance from WHO partners and work through networks to build their capacities.

As of the end of 2008, the IHR NFP roster has been completed. Each country designated an institution to serve as the NFP and named up to three persons who would rotate the responsibility to provide all-time, all-on support. Each State Party has been requested to nominate an expert who may be called upon to serve on the Emergency Committee should a PHEIC be declared, and such expert advisory group needs to be assembled to give advice to the WHO Director-General.

A number of partners and countries have offered to provide resources and expertise to support the implementation of IHR for other state parties. Several key projects in countries are under way to help implement a country's plan through demonstration projects, collaborative network support, national institutes support, global security initiatives, and regional alliances. Some projects are focused on ensuring that countries review and define their legislative support, others are focused on training, and others are focused on awareness workshops, investment in infrastructure, and setting of international norms and standards. Specific disease programs such as polio eradication, influenza, and HIV have also given countries resources and capabilities and have allowed for surge capacity planning. These investments have been critical elements in getting the cross-sectoral buy-in to prepare for the IHR.

As an example, countries have been involved in their own pandemic planning for several years, which has been especially heightened since the emergence of the A (H5N1) avian influenza virus. Though this targeted a specific disease, the preparedness process is very much appreciated by the national planners as they develop plans for IHR implementation. Some countries have had to experience avian influenza outbreaks in real time while others have prepared through drills and exercises. Nevertheless, the overall awareness and confidence in moving forward on IHR implementation has greatly benefited from the experience.

### *A Recent Update*

An update to the Institute of Medicine workshop in December 2008 that fully illustrates the implementation of the IHR (2005) is the emergence of the pandemic A (H1N1) 2009 virus (WHO, 2009). Following the written IHR, an Emergency Committee was convened to review the evidence according to Annex 2 and, based on available evidence, the WHO declared a PHEIC on April 25, 2009. The virus was first detected in the United States in early April and first reported, in retrospect, in Mexico. Specimens were shared with its neighboring alliance countries (Canada and the United States; CDC, 2009), both of whom confirmed

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the emergence of the new virus and made reports through their NFP to the EIS, providing details and updates on a regular basis from that point. Since then, more than 179 countries have reported the appearance of the cases within their borders, and, after collecting information and laboratory-confirmed evidence of the virus, all have reported and maintain updates to the WHO through the EIS. This information is updated in the Disease Outbreak News, which is openly shared with the public on the WHO webpage.[12] The orderliness and openness of the process established under the IHR (2005) reflects how countries have utilized pandemic influenza planning and other developments to successfully and confidently report their findings.

## Conclusions: Using the Full Power of the IHR

The IHR (2005) provides an unprecedented opportunity for its states parties to move toward a "larger freedom," to build parity among countries to share information, and to enjoin in true partnership that has implications for ensuring better global health and security in the twenty-first century (Fidler and Gostin, 2006; Rodier et al., 2007).

This truly is a paradigm shift, to a more transparent and cooperative operations, to respecting that the world needs to share in the information, to move away from the fear that reporting of events leads to plummeting reputation, and to be a true partner in ensuring global health security, not merely in words but in action and trust.

There is certainly the risk of losing momentum and interest if assistance does not come in a timely manner and is not appropriately administered. Here is the chance to follow the conventional approach in guidance, assessment, training, and setting norms and standards; it is also the entry point to using the new tools of the twenty-first century.

No longer can information be sequestered and suppressed to a larger extent; the Internet has opened up access to a multitude of information sources, from web searches and resource bundling, to surveillance tools that cross the physical and cultural divides. Internet surveillance tools offer capabilities for countries that can now connect and receive information (Wilson and Brownstein, 2009). During the SARS outbreak in 2003, it was the World Wide Web, electronic media, personal communications, and NGOs that provided information on key sources of the disease outbreak, far more information than that from the normative formal sources, which provided only 39 percent of the reports (Heymann, 2006). The way the public receives and looks for information has also moved from the normal news and reporting sources.

There is a benefit to linking with local, regional, and supraregional networks such as the Association of Southeast Asian Nations, the GOARN, the Asia-Pacific

[12]See http://www.who.int/en/.

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Economic Cooperation (Kimball et al., 2008), the global health security initiatives, and the International Association of Public Health Institutes (Koplan et al, 2006), because they are key partners in the capacity-building, information sharing and sustainment for IHR core capacity preparedness and implementation. The WHO can only do so much at the global and country levels; these associations bring awareness, recognition, and real partnership to participating countries. The global public health community must find ways to incentivize application and encourage compliance, for clearly the IHR (2005) form a unique political and legal framework for all countries and partners in helping and informing each other. In the twenty-first century, success means using all means possible and committing to the long haul of building and sustaining, over and over and over again.

## IMPLEMENTING THE REVISED INTERNATIONAL HEALTH REGULATIONS IN RESOURCE-CONSTRAINED COUNTRIES: INTENTIONAL AND UNINTENTIONAL REALITIES

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The revised International Health Regulations (hereinafter, the IHR), adopted by the WHA on May 23, 2005 (WHO, 2008b), represent a refreshing and bold departure from their largely impotent predecessors. However, the successful implementation of the IHR depends on addressing the concerns of policy makers from resource-constrained countries.

Trade was once the focus of the IHR, which prior to 2005 sought to limit the spread of a few diseases considered to be of importance to international trade and travel. The revised IHR emphasize public health risks, irrespective of origin or source, due to naturally occurring infectious or noncommunicable diseases and the suspected intentional or accidental release of biological, chemical, or radiological substances. The intent of the IHR is clear and unambiguous: "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, and which avoid unnecessary interference with international traffic and trade" (emphasis added).

Two recent events in Africa illustrate the status of implementation of the revised IHR. The first occurred early in 2007, when the Nigerian government voluntarily confirmed the first human case of avian influenza (*Guardian*, 2007); that government had, in February 2006, officially reported the first outbreak of H5N1 influenza in poultry (Vasagar, 2006). The second event occurred early in 2008, when the government of Zimbabwe, after initially denying a cholera epi-

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demic, later publicly, but reluctantly, confirmed that an outbreak was ongoing in that country (BBC, 2008b; Wang, 2008). While these events might be interpreted as evidence of progress in disease reporting since the introduction of the IHR, it can also be argued that these actions by the Nigerian and Zimbabwean governments resulted from political considerations rather than out of concern for the international spread of diseases.

### Reception of the IHR (2005) by Resource-Constrained Countries

Interest in international tourist traffic and trade naturally determines a given country's interest in implementing the revisions to the IHR. For resource-constrained countries, which attract few tourists and export minimum commodities, it is perhaps understandable that the IHR are accorded minimal priority. Rather, a large proportion of policy makers in resource-constrained countries perceive that the emphasis of the IHR on the international spread of disease evinces little concern regarding the burden of infectious diseases on the nations in which they occur. This perception is fueled by a long-standing history of selective application and implementation of global health policies in order to support the interests of countries in the developed world. For example,

- Disproportionate international reactions to disease outbreaks and other medical emergencies in developed countries—for example, the recent detection of imported cases of traveler-associated Lassa or yellow fever in Europe (WHO, 2006b)—as compared with those taking place in developing countries (the current cholera epidemic in Zimbabwe (WHO, 2008a) and the deaths of children from suspected paracetamol poisoning in Nigeria (BBC, 2008a);
- Preservation of the smallpox virus by the United States and Russia (WHO, 2009);
- Studies that note savings by developing countries as a key reason to support global disease eradication initiatives; and
- Insectide spraying in the cabins of planes leaving resource-constrained countries, whereas similar action is not taken on inbound planes.

In the same light, policy makers in resource-constrained countries perceive that undue and disproportionate emphasis is placed on providing resources to respond to disease outbreaks that might spread internationally, as compared with resources marshalled within national boundaries to prevent outbreaks in the first place. It is therefore not surprising that such policy makers provide only passive support for the implementation of global initiatives such as the IHR.

A Nigerian proverb states that "it is the fear of the stigma that makes men swallow poison." Accordingly, some governments would rather watch an infectious disease rage among their citizens than report its existence and risk interna-

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tional ridicule and global isolation. This principle is expressed when, as in the recent case of cholera in Zimbabwe discussed earlier in this paper, a government denies the existence of an outbreak, minimizes its severity when faced with incontrovertible evidence of its existence, or lays the blame for an outbreak on another government or agent.

### Obstacles to Implementation in Africa

Article 5.1 of the revised IHR states:

> Each State Party shall develop, strengthen and maintain, as soon as possible but no later than five years from the entry into force of these Regulations for that State Party, the capacity to detect, assess, notify and report events in accordance with these Regulations, as specified in Annex 1. (WHO, 2006a)

Given the current rate of progress in the (African) state parties, and, in many cases, within resource-constrained countries in general, the target is not likely to be achieved within the specified time frame, nor sustained thereafter, if the following issues are not resolved. They include:

- Ineffective and unreliable national disease surveillance systems,
- Inadequate political will and committment to disease control and prevention,
- Poor regional networking for disease reporting and response, and
- Donor partner priorities that may be at variance with national priorities.

### Surveillance Systems

In many African countries, major obstacles to an effective disease surveillance and control system include insufficient funding, inadequate staffing, inappropriate or insufficient training of existing personnel, and lack of appreciation of the cost-effectiveness of a reliable disease surveillance system in health care delivery. Public health laboratories that conduct infectious disease surveillance in Africa tend to be poorly staffed and often lack basic equipment and supplies; few are able to communicate or receive epidemiological information or transport laboratory specimens in a timely way.

In many African countries, the infectious disease surveillance system functions vertically, having been established to monitor specific vaccine-preventable diseases such as poliomyelitis, cerebrospinal meningitis, cholera, or yellow fever. This *ad hoc* system of disease-specific surveillance programs has resulted in a lack of integration of disease surveillance and control, a disdain for developing and building local capacity, and a penchant for acquiring imported technologies. Indeed, it can be said that disease-specific surveillance programs have prevented the establishment of reliable and comprehensive national disease surveillance systems.

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Vertical surveillance programs may employ disease-specific data collection tools, reporting formats, and surveillance guidelines for donor-targeted diseases, but these capacities are rarely used to monitor or control endemic diseases. At an operational level, it is the same person or team who performs *all* surveillance activities, leading to a duplication of efforts with increased workload for staff and inefficient utilization of available resources, or to the neglect of the endemic diseases, as the staff or team focus on donor targeted diseases (these are diseases of priority importance in a donor country, which are often of low priority in the recipient country). For example, the United States may wish to provide greater support for studies on anthrax, monkeypox, and so forth—diseases with higher bioterrorism potential—than on measles, yellow fever, and cerebrospinal meningitis, diseases that still ravage and decimate populations in resource-constrained countries. Moreover, many vertical interventions for disease surveillance and control have not been sustained due to lack of appropriately trained local staff. Since most epidemics in Africa originate at the health district level, locally based, comprehensive disease surveillance—and the sense of ownership that goes along with it—would be optimal.

## Political Will and Commitment

A general lack of political will and commitment to public health is evidenced by the inadequate consideration of and financial support for health issues by most African governments at all levels. The leadership of resource-constrained countries must appreciate that global health depends upon a commitment by each country to protect its citizens from disease. Such a commitment is practiced in those developed countries in which citizens' welfare is a bedrock political issue.

## Networking

The impact of diseases, such as yellow fever and cholera, which are endemic in certain regions of the world could be minimized if the countries in the region work together through networking and sharing of data and expertise. However, for reasons of territorial integrity and an absence of formal collaborative agreements, health officials may be reluctant to share information on priority communicable diseases with their counterparts in other countries.

### *Regulatory Constraints*

Donor agencies impose inflexible regulatory constraints that hamper maximum utilization of human and financial resources for integrating disease surveillance systems. In some resource-contrained countries, funds allocated for activites under a donor-funded tuberculosis project may not be applied for activities under, for example, an HIV/AIDS project, even if the outcome of such an

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activitiy will have mutual benefit for both projects. At the individual level, there is a dearth of highly qualified professionals in many resource-constrained countries; therefore, the few available professionals must serve in other capacities, sometimes not directly related to their fields of expertise. The activities of such an individual employed under a donor-funded project are strictly limited to the confines of the donor project. For example, a virologist (who may be the only one in the country) employed under a donor-funded project dealing with measles may not be allowed to place his expertise at the service of his government during an epidemic of yellow fever.

### Enabling Implementation of the IHR 2005 in Resource-Constrained Countries

If the revised IHR are to be successfully implemented in resource-limited countries, there will be a need to correct the misperception that the emphasis of the revised IHR is on the international spread of disease, while the issue of the burden of infectious diseases on the resource-constrained nations is of secondary priority.

The following efforts will help achieve that goal.

### Emphasize Disease Prevention at the National Level

Equal emphasis must be placed upon the national and international spread of diseases. Growing up in Africa, I learned that keeping our individual compounds clean ensured the cleanliness of our entire village; so it must be with our "global village." Thus, the purpose and scope of the revisons to the IHR should be restated as follows:

- Prevent both the *national* and international spread of disease,
- Protect against both the *national* and international spread of disease,
- Control both the *national* and international spread of disease, and
- Provide a public health response to both the *national* and international spread of disease (emphasis added).

### Build National Capacity for Disease Prevention

The practice of "dangling the carrot" of international resources for responding to a disease outbreak (e.g., vaccines, funding, and foreign expertise) as an incentive for reporting such an outbreak may undermine the determination of resource-constrained countries to develop, strengthen, and maintain national core surveillance and response capabilites. Moreover, it is far more efficient to contain disease outbreaks than to respond to full-blown epidemics. Therefore, greater consideration should be given to encouraging countries to develop capacity to

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report, detect, and investigate suspected infectious disease outbreaks and thus prevent sporadic cases (especially of known diseases) from escalating to epidemics, and more resources (training, supplies, funds, and foreign expertise) should be provided for establishing and maintaining disease surveillance systems at the national level.

### Sustainable Surveillance: National Capacity-Building

The polio eradication initiative in Africa has enabled the establishment of a reliable acute flaccid paralysis (AFP) surveillance system, backed by an African region-wide laboratory network. The 16-member polio laboratory network, accessible to the 46 countries in the Africa WHO region, has provided timely and accurate results to national polio control programs. The success of the polio laboratory network has led to the establishment of other disease-specific laboratory networks and surveillance systems. Five additional laboratory networks (measles, yellow fever, and rubella; HIV/AIDS; pediatric bacterial meningitis; rotavirus; human papillomavirus) currently operate in the Africa region with minimal collaboration. These networks provide a foundation upon which comprehensive disease surveillance capacity could be built to enable successful implementation of the IHR.

Surveillance systems will be improved only if their importance to disease control is recognized and appreciated. Reliable disease surveillance can help to improve the prediction, early detection, and control of epidemics; inform the rational allocation of resources; and guide the monitoring and evaluation of health interventions. Building and maintaining robust, national, integrated disease surveillance and response (IDSR) systems for emerging zoonoses and other communicable diseases can considerably reduce morbidity, mortality, and disability associated with these diseases. Achieving this result will require:

- Management and application of surveillance data;
- Communication systems to effectively transmit surveillance data and epidemiological information;
- National, subregional, and regional laboratory networks and their capacity for involvement in IDSR activities;
- Epidemic early warning and rapid response systems, including the preparation and implementation of national emergency preparedness and response plans;
- Training of health workers to participate in IDSR, including the integration of IDSR in training curricula and materials; and
- Research (including operational research) to improve IDSR in resource-limited countries.

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### Conclusion

Article 5.3 of the revised IHR states that the WHO shall assist state parties, upon request, to develop, strengthen, and maintain the capacities to detect, assess, notify, and report disease events of international concern. Many countries need far more guidance than WHO has yet provided, including a clear understanding of their own needs. A greater effort must be made to enable each participating country to own and control its surveillance system within the global network, thereby supporting the successful and timely implementation of the IHR.

## VIRAL SOVEREIGNTY, GLOBAL GOVERNANCE, AND THE IHR 2005: THE H5N1 VIRUS SHARING CONTROVERSY AND ITS IMPLICATIONS FOR GLOBAL HEALTH GOVERNANCE

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### Introduction

This workshop emphasizes the importance of the revised International Health Regulations 2005, hereinafter IHR 2005 (WHO, 2008), as a governance instrument for the challenges globalization presents to countries and international organizations with respect to the movement of pathogens and their hosts. As Dr. David Heymann, then of the WHO, made clear in his presentation, the IHR 2005 represent a significant advance in global health governance, particularly with respect to threat posed by communicable pathogens (Heymann, 2008). My mandate for this workshop was to address the implications for the H5N1 virus sharing controversy for the IHR 2005 specifically and for global health governance generally.

In fulfilling this mandate, I explore why the H5N1 virus sharing controversy raises hard questions about the IHR 2005 and its future. This exploration involves:

- Reviewing the IHR 2005's importance as an innovative global governance regime;
- Examining how the H5N1 virus sharing controversy represents a significant problem for the IHR 2005 and the future of global health governance;
- Considering what the virus sharing controversy reveals about the nature of public health as a foreign policy issue;

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- Analyzing how expected global trends in international politics might affect the issues raised for the IHR 2005 by the virus sharing controversy;
- Considering the implications of the influenza A (H1N1) outbreak in April-May 2009 for the virus sharing controversy and the IHR 2005; and
- Reflecting on the intent of the IHR 2005, the realities facing this global governance regime, and the prospects for more effective implementation in the years ahead.

### The IHR 2005: A Radical New Instrument of Global Health Governance

The story of the emergence, negotiation, and implementation of the IHR 2005 is, on many levels, a fascinating case study of the evolution of a radical "new way of working" with respect to global health governance. The IHR 2005 have their roots in the nineteenth-century origins of diplomacy on international health (i.e., the international sanitary conferences and conventions), began their life as a WHO governance mechanism in the form of the International Sanitary Regulations promulgated in 1951, and broke decisively from the International Health Regulations adopted in 1969 (IHR 1969; Fidler, 2005).

In the interests of brevity, I highlight five of the most significant changes WHO member states negotiated in adopting the IHR 2005 and moving this regime away from the antiquated and stagnated set of rules the IHR 1969 had become by the mid-1990s, when the IHR revision process began. Although incomplete as a description of the IHR 2005, these five changes suffice to communicate how radically different the IHR 2005 are from any regime in the history of the use of international law for public health purposes.

First, the epidemiological and political scopes of the IHR 2005 have been expanded significantly. From the epidemiological perspective, the IHR 2005's scope has increased in three ways:

- Unlike the IHR 1969, which applied to a short list of specified infectious diseases (cholera, plague, and yellow fever), the IHR 2005 apply to a list of specific communicable disease threats and any communicable disease event that may represent a public health emergency of international concern (IHR 2005, Annex 2). Thus, WHO member states must report to WHO any disease event that may constitute a public health emergency of international concern (IHR 2005, Article 6).
- The IHR 1969 only applied to communicable diseases, but the IHR 2005 apply to disease events that involve communicable pathogens, chemical substances, or radiological agents (IHR 2005, Article 7).
- The IHR 2005 apply to the intentional use of biological, chemical, or radiological agents, and thus are designed to facilitate responses to terrorist or state uses of weapons of mass destruction. The IHR 1969 had no such application.

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Politically, the IHR 2005's scope also expanded. The best illustration of the politically expanded scope appears in the IHR 2005's application to biological, chemical, and radiological agents—an application that makes the IHR 2005 important in traditional national security terms. In addition, WHO and many WHO member states promoted the IHR 2005 as an instrument that could help countries strengthen "global health security," a concept that gave "security" a broader meaning and elevated the importance of health in achieving human, national, and global security. Neither the early international sanitary conventions nor the IHR 1969 had ever been associated with concepts of security in the manner the IHR 2005 have been.

Second, the IHR 2005 impose obligations on WHO member states to develop and maintain minimum core capabilities in the areas of surveillance and response (IHR 2005, Articles 5, 13; Annex 1). The most the IHR 1969 required in connection with public health capabilities involved facilities at points of entry and exit (for example, airports, seaports). The minimum core capacities contained in the IHR 2005 as *binding obligations* are unprecedented in the history of this area of international law on public health.

Third, the IHR 2005 empower WHO to collect and use information from nongovernmental sources (IHR 2005, Article 9). Under the IHR 1969, WHO could only officially use information it received from governments, and this limitation proved one of the greatest weaknesses of the IHR 1969 because governments routinely failed to provide WHO with information about outbreaks of diseases subject to the regulations. The IHR 2005 allow WHO to receive information from nongovernmental sources and seek verification of such information from governments (IHR 2005, Article 10). This change in the kinds of information WHO can officially use radically changes the dynamic of the flow of information to WHO about disease events and provides WHO with leverage it could not previously utilize.

Fourth, the IHR 2005 authorize the WHO Director-General to declare a public health emergency of international concern (IHR 2005, Article 12). As noted earlier, WHO member states must report to WHO any disease events that may constitute a public health emergency of international concern, but the IHR 2005 give the WHO Director-General—not WHO member states—the power to declare the actual existence of such an emergency. In addition, this power permits the WHO Director-General to declare such an emergency over the opposition of WHO member states directly affected by the disease event in question.

Fifth, the IHR 2005 incorporate human rights concepts and require WHO member states to apply their public health powers in conformity with the principles of international human rights law.[15] The IHR 1969 contained no such effort to bring human rights concepts to bear on cooperation on infectious disease control.

[15] See Fidler (2005).

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The mere existence of radical changes in the IHR 2005 does not guarantee that the IHR 2005 will radically change global health. As explored more below, serious concerns exist about whether the implementation of the IHR 2005 will actually live up to the promise the radical changes portend. Despite this caveat, evidence does exist that suggests the potential of the IHR 2005 as a global governance regime.

First, the successful global response to the 2003 SARS outbreak was based, in essence, on a rollout by WHO of the concepts and strategies that would eventually be adopted in the IHR 2005. Second, in the brief time the IHR 2005 have been in force (i.e., since June 2007), WHO is convinced of their improved utility over the IHR 1969, particularly in terms of gathering information about disease events, seeking verification from governments, and working more closely with countries to respond to actual and potential disease threats.

## The H5N1 Virus Sharing Controversy and the Revised IHR

### *Indonesia's Exercise of Viral Sovereignty*

Those who supported the adoption of the IHR 2005 knew that, sooner or later, this new regime would face serious tests in the context of disease outbreaks. The first real test of the IHR 2005 emerged, however, in a context most experts did not predict—the refusal of a WHO member state to share samples of the H5N1 avian influenza virus with WHO. In 2006, Indonesia refused to share H5N1 samples with WHO, which alarmed global health experts because this refusal jeopardized WHO's ability to conduct surveillance of the H5N1 virus.

Rather than share these influenza viruses with WHO for global surveillance purposes, Indonesia claimed "viral sovereignty" over the H5N1 viruses isolated in its territory. Indonesia insisted that it would not share H5N1 samples over which it had sovereignty until WHO and developed countries created a more equitable mechanism for sharing the benefits (e.g., vaccines) that result from the exploitation of influenza viruses.

Indonesia argued that it took these actions because it, and other developing countries, was not gaining benefits in terms of response capabilities from sharing of virus samples for purposes of global surveillance. Indonesia criticized WHO's practice of distributing influenza viruses it received for surveillance to pharmaceutical companies, which would make patented vaccines from such samples—vaccines that were often not affordably accessible for developing countries.

According to Indonesia and its supporters, the system of sharing virus samples had produced forms of exploitation and inequity that the exercise of "viral sovereignty" sought to highlight and stop. Indonesia expressly linked future virus sharing for global surveillance with a more equitable system of sharing the benefits that research and development on such virus samples could produce.

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### *Viral Sovereignty and the Revised IHR*

As many recognized when the dispute arose, the H5N1 virus sharing controversy represented an early opportunity to apply the IHR 2005 in connection with a very important global health challenge. However, attempts by WHO to apply the IHR 2005 to Indonesia's actions failed badly. Briefly, the WHO Director-General argued that Indonesia's failure to share H5N1 virus samples constituted a violation of the IHR 2005's requirement to share information with WHO on novel subtypes of human influenza viruses. This position emerged from an interpretation of the IHR 2005's requirements on information sharing that emphasized the IHR 2005's requirement to notify WHO of any case of novel human influenza subtypes and the position that highly pathogenic influenza viruses are public health emergencies of international concern.

Whatever its merits as a legal interpretation of the IHR 2005,[16] this attempted application of the IHR 2005 gained no traction in the context of the H5N1 virus sharing controversy. Indonesia's position has been that the relevant international legal instrument is not the IHR 2005 but is the Convention on Biological Diversity, which recognizes a country's sovereignty over biological resources found in its territory. In addition, as a matter of treaty interpretation, it is not clear that the IHR 2005 require the sharing of biological samples of any kind with respect to the obligation to share information with WHO on disease events that may constitute public health emergencies of international concern. Politically, the attempt to force Indonesia to share H5N1 virus samples for global surveillance purposes fell flat because the IHR 2005 do not address Indonesia's main complaint—the sharing of virus samples leads to inequitable access to the benefits derived from such samples.

The irrelevance of the IHR 2005 to this dispute became clear when WHO member states decided to enter into intergovernmental negotiations to craft a new regime that would deal simultaneously with the sharing of influenza viruses and the sharing of benefits derived from such viruses. Although the possibility of reapplying the IHR 2005 to the failure to share virus samples if the WHO-sponsored intergovernmental negotiations fail to bear fruit exists, the plausibility of this idea is, at this point, questionable. In sum, the first attempt to apply the IHR 2005 in the context of a serious global health crisis ended with the IHR 2005 being marginalized legally and politically.

### *Deeper Implications for Global Health Governance*

The H5N1 virus sharing controversy has deeper implications for global health governance than an unsuccessful application of the IHR 2005. This con-

[16]For a more comprehensive analysis of the international legal arguments of both sides to the virus sharing controversy, see Fidler (2008a).

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**TABLE 4-1** Governance Issues Compared

| Issue | SARS | IHR 2005 | Virus Sharing |
|---|---|---|---|
| Surveillance | Globalized | Global governance | Bargaining chip |
| Response | Effective | Core obligations | Accusations of inequity |
| Sovereignty | Weakened | Reduced as obstacle | Viral sovereignty |
| Role of WHO | Leader | Empowered | Attacked, criticized |
| Role of NGOs | Important for surveillance | Built into regime on surveillance | Supporting viral sovereignty |
| Interests | Global community | Global health security | Diverging national interests |
| Politics | Collaborative | Consensus | Fragmented, divisive |

troversy disrupts a larger governance trajectory seen in the handling of the SARS outbreak and the IHR 2005's adoption. Table 4-1 lists important governance issues and how these issues played out during the SARS crisis, the creation of the IHR 2005, and the H5N1 virus sharing controversy. Under each issue, the H5N1 virus sharing controversy breaks patterns seen in SARS and the development of the IHR 2005.

For example, one of the striking features of the handling of SARS and the content of the IHR is the manner in which countries recognized that surveillance has become globalized and, thus, less susceptible to the prerogative of sovereign states. The same effect is captured in Table 4-1 in the treatment of sovereignty as an issue. However, in the H5N1 virus sharing controversy, Indonesia and its supporters reassert claims of sovereignty (i.e., viral sovereignty) and make global surveillance's need for avian influenza samples a bargaining chip in negotiations over benefit sharing.

Table 4-1 also captures how WHO's role in the virus sharing controversy has differed from the role it played in SARS and the authority it has under the IHR 2005. During SARS, WHO was recognized as the global leader of the response to the outbreak, and WHO's actions during the outbreak helped restore some of WHO's credibility as an effective organization for world health. The IHR 2005 enshrined that leadership role by empowering WHO to use nongovernmental sources of information and to declare the existence of public health emergencies of international concern. In the virus sharing controversy, WHO has been attacked and criticized for operating an inequitable and exploitative global influenza surveillance system, which placed WHO on the defensive in trying to facilitate international negotiations on this issue.

The management of SARS and the adoption of the IHR 2005 revealed countries with shared interests and engaging in effective collective political action. The virus sharing controversy has, however, seen national interests diverge sharply, which has produced a fragmented, divisive political context. The trajectory toward more effective global health governance observable in the handling of

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SARS and the crafting of the IHR 2005 has not continued with respect to one of the most serious global communicable disease threats the world currently faces.

### *The Virus Sharing Controversy: Health as a Foreign Policy Issue*[17]

The dissonance between the cooperation seen in the SARS outbreak and the IHR 2005 and the hard politics under way in the virus sharing controversy draws attention to the nature of health as a foreign policy issue. Health has risen in importance as a foreign policy and diplomatic concern over the past 10-15 years, but the relationship between health and foreign policy still remains ambiguous and contested. The virus sharing controversy is a good case study in this context because it helps highlight characteristics of health within the realm of foreign policy.[18]

### *Agenda Expansion*

One feature of health as a foreign policy issue is the tendency for health-related agendas to expand. Expanding agendas tend to make international politics and diplomacy more difficult because countries have more issues to negotiate and more potentially divergent interests to reconcile. The "agenda expansion" effect can be seen, for example, in the HIV/AIDS context, where health advocates seek to increase treatment programs, improve prevention efforts, and address the underlying social determinants (e.g., poverty, gender inequalities, education) that feed the spread of HIV. Health-driven agenda expansion can fight against the preference of foreign policy makers to prioritize ruthlessly and pursue parsimonious agendas.

The virus sharing controversy features agenda expansion. The issues on the negotiating table include the need for virus samples to conduct global surveillance, the demand for equitable access to influenza vaccines, the operating principle of viral sovereignty as informed by regimes on protecting biodiversity, the need for technology transfer in connection with vaccine production, and the role of intellectual property rights. Many of the issues on this agenda have, in the past, proved difficult for countries trying to negotiate cooperative solutions, especially more equitable access to health technologies, the protection of biodiversity, technology transfer regimes, and the impact of intellectual property rights on access to drugs and vaccines.

[17]This part of the paper utilizes analysis and concepts found in Fidler (2008b).

[18]The characteristics of health as a foreign policy issue described in this section are not unique to health because they appear in other foreign policy contexts as well. Nevertheless, identifying these characteristics within the health and foreign policy relationship helps advance an analytical understanding of this relationship.

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*Issue Linkage*

The tendency for health agendas in the foreign policy arena to expand connects to another feature of health as a foreign policy issue—the phenomenon of issue linkage. With issue linkage, countries link negotiation progress on one issue with progress on a different issue. Issue linkage has occurred in the context of trade negotiations involving health-related elements. For example, developing countries linked progress on clarifying public health flexibilities in the TRIPS Agreement with progress on other trade issues at the World Trade Organization (WTO) Doha Ministerial Meeting in 2001. Similarly, the United States conditions bilateral trade agreements on other countries agreeing to higher levels of protection for intellectual property rights than are found in the TRIPS Agreement.

In the virus sharing controversy, Indonesia and its supporters have tightly linked progress on sharing of H5N1 virus samples for global surveillance purposes with concrete results on improving the sharing of the benefits derived from such samples, especially access to influenza vaccines. Although virus and benefit sharing could be handled separately as a negotiating matter,[19] Indonesia understands the political leverage it gets from keeping the surveillance and response sides of the sharing problem bound together.

*Forum Shifting*

Another feature of the health-foreign policy relationship that appears in the virus sharing controversy is the tactic of "forum shifting." States and nonstate actors often try to shift the negotiating forum of diplomatic disputes into forums more conducive or receptive to their particular interests. Forum shifting has been prominent in the diplomatic maneuvering over intellectual property rights and access to essential medicines. Developing countries and supportive NGOs attempted to shift the diplomacy on this question out of the TRIPS Agreement at the WTO into UN human rights processes and the WHO. Developed countries, such as the United States and the members of the European Union, reshifted the issue into the context of negotiations on bilateral and regional trade agreements.

In the virus sharing controversy, Indonesia and its supporters attempted to shift the dominant governance regime from the IHR 2005 to the Convention on Biological Diversity (CBD). The CBD was more accommodating for Indonesia's assertion of viral sovereignty than the IHR 2005, which contains principles and provisions that reflect a weaker image of sovereignty than that found in the CBD. By and large, Indonesia appears to have been successful in shifting the debate into the CBD model, which simply reinforces the earlier observation that the IHR 2005 has become marginalized in how this dispute will be resolved.

[19]For example, Indonesia could share virus samples with WHO for global surveillance purposes, while negotiations about what WHO and other actors can and cannot do with those samples with respect to vaccine development take place.

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*Health's Elasticity as a Foreign Policy Issue*

The virus sharing controversy also reveals how health exhibits "elasticity" as a foreign policy concern. Health issues tend to rise and fall fairly significantly as foreign policy priorities. When a disease crisis emerges, foreign policy makers are keen to address the health threat. When the crisis seems to stabilize, or simply stops being front-page news, the health issue in question receives less foreign policy attention. This elastic quality contrasts with the fairly inelastic foreign policy attention that other issues receive, particularly national security, military power and preparedness, and intelligence gathering.

The elasticity is particularly difficult for health advocates because this trait means that health is more important politically when it is most imperiled. The mantra of public health is, however, to prevent health harms and protect populations from unusual levels of morbidity and mortality.

The virus sharing controversy highlights the elasticity of health in foreign policy. When the controversy first broke, it raised grave concerns about a global crisis concerning global surveillance for avian influenza and pandemic influenza. As the controversy has dragged on without resolution, it has faded in political notoriety and importance, even though the threat from avian influenza has not significantly abated. In addition, a parade of other global crises involving energy prices, food prices and shortages, climate change, and economic and financial earthquakes has pushed global health (and the virus sharing controversy) farther into the foreign policy background.

### Virus Sharing, IHR 2005, and Trends in Global Politics

The continuation of the virus sharing controversy represents a current policy predicament, but it may also foreshadow difficulties for global health governance in the future. Recently, I taught a seminar in which the students had to analyze the threat of the proliferation of weapons of mass destruction in light of global trends the National Intelligence Council (NIC) identified as likely to have emerged by 2025 (NIC, 2008). Specifically, five global trends identified by the NIC resonated with features of the virus sharing controversy:

1. *Impact of new players:* The NIC report highlighted that international politics will be increasingly affected by "new players," such as China and India, but the NIC also identified Indonesia as one potential new player. The virus sharing controversy was ignited, and has been sustained, by Indonesia, and the Indonesian claim of viral sovereignty has thrown a spanner in the works of the global health governance contemplated by the approach taken in SARS and the strategy found in the IHR 2005.
2. *Globalizing economy:* The NIC emphasized the impact of an increasingly globalized economy on international relations in the years leading

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to 2025. The fears of the ravages pandemic influenza could wreak on the world are closely linked to the globalizing economy's acceleration of the means of pathogenic spread, especially the movement of humans around the planet in very short periods of time. The direction the globalizing economy is moving is undermining other aspects of sovereignty while Indonesia and its supporters champion the notion of viral sovereignty.

3. *Demographics of discord:* The NIC report addressed how changing demographic patterns could lead to increasing resentment and discord in developing countries, which could adversely affect world politics, economics, and health. The virus sharing controversy reflects growing frustration in parts of the developing world that improvements in global health governance, such as the IHR 2005, actually do little to help them deal with their public health problems, which will be exacerbated by the anticipated population growth in the years ahead. Thus, the "demographics of discord" could erode incentives for developing countries to cooperate with developed countries in global health governance.
4. *Growing potential for conflict:* The NIC's analysis of global trends leading to 2025 indicated that the world would experience a growing likelihood of different kinds of conflicts in international relations. Underneath this growing potential for conflict is a widening divergence of national interests—a divergence sometimes encouraged or spurred by nonstate actors—that leads to less cooperation and more conflict among states. The virus sharing controversy reflects a growing divergence of interests between developed and developing states and represents a diplomatic conflict that has, to date, produced no clear path to resurrecting sustainable collective action.
5. *Multipolarity without multilateralism:* A final relevant trend from the NIC report is what it called "multipolarity without multilateralism." The NIC argued that the development of multipolarity in the international system would make constructing and implementing multilateral solutions to problems more difficult. In the context of global health governance, the virus sharing controversy suggests that this trend may well develop because the controversy reveals a growing cast of important actors (multipolarity) emerging simultaneously with the marginalization of multilateral governance regimes (e.g., the IHR 2005) and the harsh criticism of leading multilateral institutions (e.g., WHO). The frustration countries have in not being able to reach a new multilateral strategy for the virus sharing-benefit sharing problem may create incentives for governments to try to cut bilateral or regional deals, which would further erode multilateral approaches to global health threats.

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## Political Problems Pile Up, Policy Questions Multiply

### *Political Problems*

The manner in which the virus sharing controversy has evolved to date has revealed many political problems and policy questions that, so far, have not been adequately addressed. Politically, this controversy has put the existing inequity of benefit sharing starkly into focus, but effectively addressing inequities of all sorts has historically proven one of the most difficult foreign policy and diplomatic challenges. In addition, the controversy has illuminated the existing and growing gaps between the disease surveillance and response capabilities of developed and developing countries.

In terms of the IHR 2005, the dispute has exposed that, for all their radical elements, the new regulations are very weak with respect to providing developing countries with assistance in improving their surveillance and response capabilities. The lack of any clearly identifiable strategy, supported by funding, to help developing countries meet their minimum core surveillance and response obligations under the IHR 2005 has also been made more glaring by the virus sharing controversy.

These political problems point to a harsh message for global health policy—surveillance as the "center of gravity" for global health governance cannot hold without more robust efforts to address the "benefits" imbalance emphasized by the virus sharing controversy. Put another way, the continuation of the status quo will continue to erode the legitimacy of the IHR 2005 as a mechanism of global health governance.

### *Policy Questions*

This controversy is also spawning many different policy questions that require answers. Most prominently, how the virus sharing-benefit sharing dispute will be resolved remains uncertain. Some press reports claimed that the intergovernmental negotiations in December 2008 made progress, but scrutiny of the key passages of the agreed document reveals no clear "meeting of the minds" on the fundamental problems at the heart of the dispute.

For example, the document's preamble noted that the WHO member states recognize that they "have a commitment to share on an equal footing H5N1 and other influenza viruses of human pandemic potential and the benefits considering these as equally important parts of the collective action for global health." How exactly this recognition advances the diplomatic negotiations is not clear. The need for this single statement to include the concept of equality twice suggests continuing tension among WHO member states about which is more important for global health—virus sharing for surveillance, or benefit sharing for response capabilities.

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The virus sharing controversy raises other important policy questions, including the following:

- How will the equity and legitimacy questions raised by the controversy affect the implementation of the IHR 2005?
  - What assistance will be forthcoming for developing countries to help them implement their surveillance and response obligations under the IHR 2005?
  - Without adequate assistance, will developing countries view the IHR 2005 increasingly through the lens of "viral sovereignty"?
- How will policy and governance responses to these challenges fare:
  - With an expanding global health agenda, especially the challenge of integrating human and animal health systems?
  - With increasing competition from other global political, economic, and environmental crises?
  - In the context of anticipated global trends over the next 10-15 years (e.g., demographics of discord, mulitpolarity without multilateralism)?

## IHR 2005: Intent Versus Reality

Rising concerns about the IHR 2005's future focus attention on the growing gap between the intent of these regulations and the reality of their implementation. This section analyzes this gap by contrasting critical aspects of the intent behind the IHR 2005 with the lack of effective strategies to implement the regulations globally.

### *The IHR 2005 as Health in Foreign Policy*

Those crafting the IHR 2005 intended this new regime to have the kind of foreign policy significance for countries that global health policies rarely achieve. This intent becomes clear when we see how the IHR 2005 were designed to service each of the four basic functions of foreign policy (Figure 4-11):

1. Protecting national security (e.g., through military power and alliances);
2. Achieving national economic well-being (e.g., through increasing exports of goods, services, and investment capital);
3. Supporting development of strategically important countries and regions (e.g., through foreign and development assistance); and
4. Fostering human dignity (e.g., through humanitarian assistance and human rights policies).

Identifying these four functions of foreign policy does not mean that any country's foreign policy necessarily follows each function or that pursuit of the

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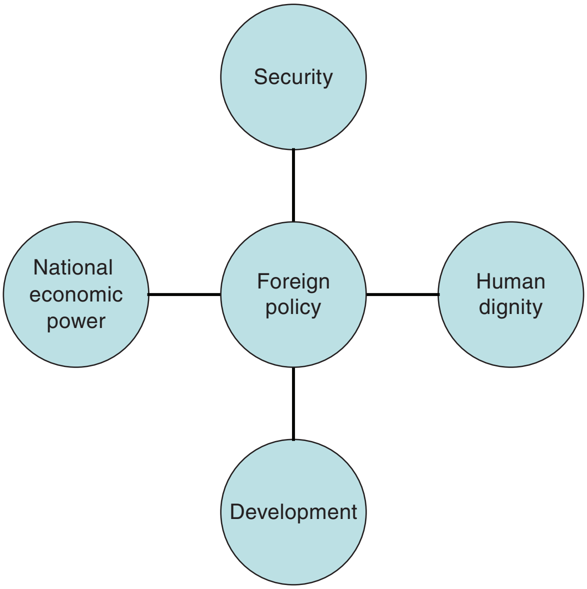


**FIGURE 4-11** Foreign policy functions.

functions is consistent. The four functions provide an analytical framework to assess how foreign policy reflects different issues, such as global health.

The IHR 2005 were designed to connect to each function of foreign policy (Figure 4-12). The WHO conceptualized the IHR 2005 as a strategy for strengthening national and global health security against both naturally occurring infectious diseases and the use of biological, chemical, and radiological agents. Thus, the IHR 2005 hooked into the foreign policy priority of national security.

The express purpose of the IHR 2005 speaks to the foreign policy interest in maintaining economic power and well-being by stating that the regulations seek to address international disease threats in ways that do not unnecessarily interfere with international trade and travel. In addition, the manner in which the IHR 2005 accomplishes this purpose mirrors almost exactly how the trade-health balance is managed in WTO agreements.

The IHR 2005's emphasis on the need for each country to develop and maintain core surveillance and response capacities connects directly to strategies that emphasize the importance of public health to development policies. Over the past decades, efforts to place public health at the heart of development thinking have elevated the importance of public health capabilities to overall development aims. The IHR 2005 integrates these ideas and gives them concrete form.

Finally, the IHR 2005's incorporation and application of human rights principles reflect the foreign policy function of fostering human dignity. Unlike the

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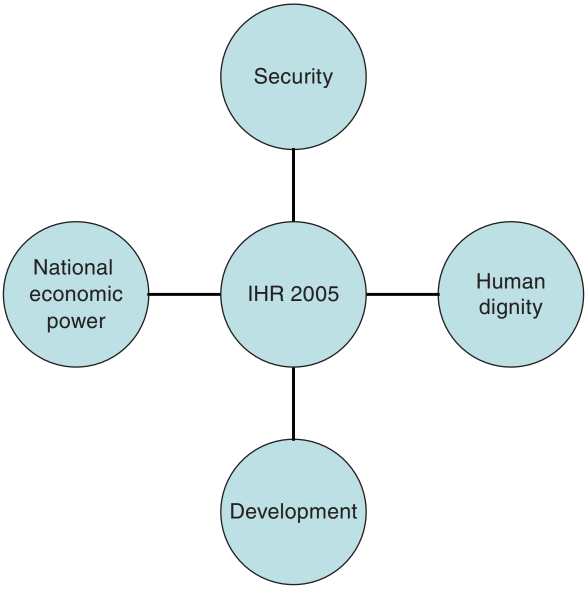


**FIGURE 4-12** The IHR 2005 and the functions of foreign policy.

IHR 1969, the IHR 2005 reflects the human rights revolution in international law and global governance, and embeds the importance of maintaining human dignity in the midst of responding to disease threats, including public health emergencies of international concern.

*The IHR 2005 and "Great Debates" in Global Health*

Another way to sense the intent behind the IHR 2005 is to consider how this radically new global health governance regime relates to some of the "great debates" taking place in global health policy circles, including:

- *Naturally occurring infectious diseases versus bioterrorism:* The IHR 2005 recognize both threats as real and contain provisions that move countries toward building public health capabilities to handle both types of threats.
- *Vertical versus horizontal programs:* With their emphasis on the need to develop and sustain core public health capabilities, the IHR 2005 support the need to craft more policies and initiatives that move toward building horizontal, systemic capabilities.
- *Multilateral versus bilateral efforts:* The IHR 2005 clearly support multilateralism over bilateralism because the regulations represent one of the

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most innovative multilateral governance regimes ever to be created in the context of global health.

- *Levels of governance debates:* In the debate about what level of governance—local, national, or global—deserves policy priority, the IHR 2005's design and substance emphasizes the need to improve public health capabilities at each level of governance, reflecting the epidemiological interdependence that governments and international organizations face in this realm.

How the IHR 2005 factors into these "great debates" in global health helps illustrate why this new global health governance regime has such importance for global health and for foreign policy in this area. The intent behind the IHR 2005 was not to create a regime that was merely technical, narrow, and apolitical. The intent was to produce and implement a regime that could raise the foreign policy importance of global health and be a transformative contribution to global health governance.

### *The IHR 2005 and Other Governance Regimes*

This workshop has considered many "drivers" of disease emergence and spread, including trade, travel, migration, environmental change, antimicrobial resistance, and armed conflict. For many of these drivers of microbial emergence and spread, existing international governance regimes are weak and ineffective, particularly with respect to migration, environmental change, antimicrobial resistance, and armed conflict. The weakness of other governance mechanisms in this realm only reinforces the importance of the IHR 2005 as the global regime designed to strengthen the ability of the countries and the international community to prepare for, protect against, and respond to emerging and reemerging disease threats. This enhanced political significance for the IHR 2005 helps underscore the critical role the IHR 2005 have in the future of global health.

### *IHR 2005 Implementation Realities*

Many presentations at this workshop have raised concerns about problems with the actual implementation of the IHR 2005. These implementation problems include the impact of the H5N1 virus sharing controversy and more general worries about the lack of any robust and funded strategy to assist developing countries to implement the IHR 2005 by the 2012 compliance deadline. I have also raised the concern that other global problems and crises, such as the global energy, food, climate change, and economic crises, have overshadowed the policy challenge of IHR 2005 implementation. In my work on the IHR 2005, I also sense a pervasive lack of understanding and urgency about the importance and the potential of the IHR 2005, which undermines prospects for effective implementation.

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A disappointing example of this lack of understanding and urgency appeared the day before this workshop began, when the IOM released the recommendations for the Obama Administration on U.S. foreign policy and global health from the high-profile Committee on the U.S. Commitment to Global Health (2008) (committee). This committee called "on the next President *to highlight health as a pillar of U.S. foreign policy*" (emphasis in original) and presented the new President with its "ideas for the U.S. government's role in global health under the leadership of a new administration" (IOM, 2008, pp. 1, 5).

This report never even mentions the IHR 2005, let alone includes any recommendations concerning how the Obama Administration should handle IHRs 2005 implementation challenges. How such a high-powered, extensively briefed committee could produce peer-reviewed foreign policy recommendations on global health that fail to mention, even once, the IHR 2005 as relevant to U.S. foreign policy on global health is astonishing and, unfortunately, disappointing evidence of an apparent failure among the committee members and perhaps even the peer reviewers to appreciate the importance of the IHR 2005 to global health and U.S. foreign policy interests in this realm.

Interestingly, and equally astonishing, the committee's report fails to address, let alone make recommendations concerning, two potential threats that contributed significantly to global health becoming more important in U.S. foreign policy over the past 10-15 years—the threats of pandemic influenza and bioterrorism.[20] The UN and the WHO have both emphasized the importance of addressing bioterrorism and pandemic influenza as part of global health activities. The IHR 2005 encompass both of these threats as part of how the regulations, by design, connect to foreign policy interests that countries, including the United States, have in global health. The United States has expended a great deal of foreign policy and diplomatic effort on addressing pandemic influenza and bioterrorism, and, in the event either of these threats emerges, the President of the United States and his national security and foreign policy teams would have to confront such developments. Yet, the committee never directly mentions either threat or provides any recommendations for the Obama Administration to improve how the United States addresses these global health challenges.

## The Influenza A (H1N1) Outbreak of 2009

Although it occurred after the workshop in December 2008, the outbreak of influenza A (H1N1) in April and May 2009 is very important to consider briefly in terms of the issues addressed at the workshop. Although, as of this writing, the

[20]The report contains one mention of "[e]merging pandemic threats like bird flu" (IOM, 2008, p. 15) but no mention of pandemic influenza or all of the diplomatic and foreign policy activity that the threat of pandemic influenza has generated in the last few years.

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outbreak had not fully run its course, five points should be made with respect to the outbreak's relevance to the issues raised in this paper.

*The Importance of the IHR 2005*

The influenza A (H1N1) outbreak triggered the first full-scale application of the IHR 2005 to a communicable disease threat, and, as such, was historic for a number of reasons:

- The novel H1N1 influenza virus was the first new pathogen to emerge since the IHR 2005 entered into force in 2007, and the IHR 2005's direct application to the virus and its emergence underscored the value of the broader scope of the regulations.
- WHO took actions authorized under the IHR 2005 for the first time, including:
  - — convening the Emergency Committee established in the IHR 2005 (Article 48) to advise the WHO Director-General on whether the H1N1 virus and outbreak constituted a public health emergency of international concern;
  - — the Emergency Committee's recommendation that the H1N1 outbreak did constitute a public health emergency of international concern;
  - — the WHO Director-General's declaration under the IHR 2005 (Article 12) that a public health emergency of international concern existed; and
  - — the WHO Director-General's issuance, with the advice of the Emergency Committee, of temporary recommendations under the IHR 2005 (Article 15) to guide state parties in responding to the H1N1 problem.
- Trade measures (e.g., import bans on pork products from affected countries) and measures taken against travelers from affected countries (e.g., quarantine measures China applied against Mexican nationals arriving in China from Mexico) were scrutinized for their compliance with rules in the IHR 2005. Under these rules, WHO
  - — issued statements that trade restrictions on pork products were not necessary from a public health perspective; and
  - — requested that China provide a justification for certain measures it was applying to Mexican nationals (see IHR 2005, Article 43(3)).

*The IHR 2005 and the WHO Pandemic Influenza Alert System*

Another interesting feature of the H1N1 outbreak was that the WHO Director-General used the Emergency Committee authorized under the IHR 2005 to advise her on whether to determine that the outbreak triggered higher pandemic alert

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phases in the WHO's pandemic influenza alert system, which she did twice in the last week of April 2009, ultimately raising the alert level from phase 3 to phase 5. Criticism of the decisions to elevate the pandemic alert phases mounted when the H1N1 virus did not exhibit severity in its effects in the vast majority of human cases. The lack of any criterion for the severity of an influenza virus's impact in the pandemic alert system brought calls for changes in the system, and WHO announced it would undertake a review of the system in light of its use in the H1N1 outbreak.

From the IHR 2005 perspective, the use of the Emergency Committee established under the IHR 2005 raises questions about the use of this Committee to advise on the pandemic influenza alert system. The IHR 2005 contain no references to the pandemic alert system, and the mandate of the Emergency Committee is limited to providing its views to the WHO Director-General on (1) whether an event constitutes a public health emergency of international concern; (2) whether to terminate a public health emergency of international concern; and (3) the proposed issuance, modification, extension, or termination of temporary recommendations (IHR 2005, Article 48(1)). In other words, the IHR 2005 do not authorize the Emergency Committee to advise the WHO Director-General on whether she should raise the alert phase under the pandemic alert system, which itself forms no part of the IHR 2005.

### *The H1N1 Outbreak's Impact on the Virus Sharing Controversy*

During the H1N1 outbreak, affected countries shared samples of the H1N1 virus with WHO and other countries (e.g., Mexico shared virus samples with Canada and the United States) without controversies. This pattern of behavior reinforced how critical timely sharing of virus samples is for national and global efforts to understand and manage a potentially dangerous outbreak of a new pathogen. How the sharing of H1N1 viruses for global surveillance and response purposes will affect the difficult, ongoing negotiations on sharing H5N1 virus samples is not clear, but the sharing of samples of the H1N1 virus might shift the terrain enough for more productive talks at the next negotiating session to emerge.

### *The H1N1 Outbreak and Health as a Foreign Policy Issue*

The H1N1 outbreak also illustrates the elasticity that health exhibits as a foreign policy issue. The global energy, food, and economic crises that emerged in 2008 had pushed health issues down the list of foreign policy priorities until the H1N1 outbreak—another global health crisis—raised again the importance of health to foreign policy and diplomacy. And, when the H1N1 outbreak began to look more like an annual influenza epidemic rather than the dreaded 1918-1919 pandemic, the outbreak faded almost as quickly from political prominence as it had emerged.

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*The Failure to Emphasize the IHR 2005 in Global Health Proposals for the Obama Administration*

As noted earlier, the H1N1 outbreak revealed the importance of the IHR 2005 as a global health governance framework. The first global health problem the Obama Administration confronted involved a novel influenza virus handled globally through the IHR 2005. The outbreak helps highlight the failure of the Committee on U.S. Commitment to Global Health to give any serious emphasis to the threat of influenza epidemics or to the importance to the United States of the IHR 2005 in its highly touted report of December 2008.

## Conclusion

The virus sharing controversy sparked by Indonesia has been a body blow to the trajectory of global health governance, and in particular the IHR 2005. This controversy has not been fatal to the prospects of the IHR 2005, as the H1N1 outbreak demonstrates. But, in reality, nothing in the way in which the controversy has unfolded hints that this episode has any silver linings for the IHR 2005's future. In fact, as we attempt to look past the virus sharing controversy with the H1N1 outbeak in mind, we must acknowledge that the IHR 2005 face some rather daunting global trends:

- Epidemiological risks are expanding and accelerating,
- Incentives for political disagreements on how to handle such risks are increasing,
- Limitations on governance mechanisms, such as the IHR 2005 and WHO, are increasingly exposed, and
- Vulnerabilities of societies to pathogen politics are deepening.

More positively, the H1N1 outbreak has brought the IHR 2005 renewed political attention and importance because the outbreak highlighted the value of the strategies embedded in the IHR 2005 and the capability of WHO to implement it in a crisis. The H1N1 virus's comparatively mild impact did not, however, test the IHR 2005 as severely as a more virulent virus would have done. The IHR 2005's relevance to the H1N1 outbreak demonstrates that the virus sharing controversy does not represent the beginning of the end for the IHR 2005, but this controversy and the H1N1 outbreak perhaps together signal the end of the beginning for the IHR 2005's journey in global health, with potentially more difficult times ahead for the IHR 2005 as an innovative mechanism for global health governance.

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# 5

# Global Disease Surveillance and Response

## OVERVIEW

In the previous chapter, Fidler characterized surveillance as the "'center of gravity' for public health governance" and, along with Tomori, asserted that efforts toward global governance are unlikely to succeed unless the benefits afforded by surveillance are equitably distributed. The essays collected in this chapter highlight strategies to address this challenge, and that of enlisting global, multisectoral support for infectious disease surveillance and response efforts both within and beyond the purview of the International Health Regulations (IHR) 2005.

The first paper, by speaker David Bell of the Centers for Disease Control and Prevention (CDC), was originally published in the *Far Eastern Economic Review* in October 2008. Bell argues that, given the disruption of trade and tourism attributed to severe acute respiratory syndrome (SARS) and the likely far greater consequences of pandemic influenza, "business, trade, and tourism stakeholders, and those who support them, such as the insurance industry, have a strong vested interest in working with public health authorities to promote global health security." However, he observes, many representatives of trade and tourism are unfamiliar with the concept of global health security and the IHR 2005, and they may not realize how their participation in efforts to advance a global health agenda can serve their specific business interests.

Bell suggests that the private sector could be effectively (and profitably) engaged in addressing the challenge of public health capacity-building through investment, "in kind" assistance, or partnership with governmental and non-governmental public health agencies. He also proposes that an international scheme to compensate individuals or countries for economic hardships resulting



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from infectious disease outbreaks could be created as a public-private partnership involving trade and tourism stakeholders, and structured as a trust fund or insurance product. "In summary," Bell writes, "the public-health sector needs help in implementing the IHR; recognition of their importance to trade security can provide the basis for engagement of trade and tourism stakeholders."

Several important collaborations among nongovernmental organizations support infectious disease surveillance and response efforts and the larger goal of global health security. In his contribution to this chapter, Ottorino Cosivi of the World Health Organization (WHO) discusses that organization's partnerships with a broad range of organizations; the most significant of these are the World Organisation for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO), which, together with the WHO, are referred to as "the three sisters." He describes a variety of interagency collaborations to promote the early detection and control of disease at the animal-human interface, including the aforementioned Global Outbreak Alert and Response Network (GOARN), the Global Early Warning and Response System for Major Animal Diseases, Including Zoonoses (GLEWS), the International Food Safety Authorities Network (INFOSAN), and the Mediterranean Zoonoses Control Program.

"In order to address the threat of emerging zoonotic diseases, we must change the paradigm for disease prevention and focus on disease surveillance and control in animals," Cosivi observes. This is the reasoning behind the One World, One Health strategic framework, which aims to prevent and to prepare for a range of potential global health risks through collaboration at the intersection of animal and human health. Cosivi discusses the development of this framework, which evolved from lessons learned in efforts to address the threat of pandemic avian influenza and its current activities. Partners in the One World, One Health® framework currently include the WHO, FAO, OIE, the UN Children's Fund (UNICEF), and the World Bank.

A representative of another of the "three sisters," workshop speaker Alejandro Thiermann of the OIE discusses global surveillance and health security from the perspective of animal health in this chapter's third essay. Focusing on the obligation of OIE member nations to report cases of known zoonotic disease threats, as well as of any "emerging disease with significant morbidity or mortality, or zoonotic potential," Thiermann compares and contrasts the OIE's disease surveillance program with its human-health counterpart, the IHR 2005. He describes the OIE's notification requirements, how such information is conveyed to members, and how the organization collaborates with the WHO and the FAO to obtain and respond to outbreak information from unofficial sources through networks such as GOARN and GLEWS.

The OIE engages in a range of activities to build global surveillance capacity, including funding and technical assistance for countries with inadequate ability to detect and report disease threats, according to Thiermann. He also notes that, in recognition of the important role of compensation in ensuring timely and accurate

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reporting of disease threats, the OIE offers guidance for establishing compensation systems. The OIE has also founded a "virtual vaccine bank," which has supplied large quantities of vaccines to address severe outbreaks of avian influenza (in birds). "This mechanism allows countries to begin vaccinating with certified vaccines, immediately after the decision is made that vaccination is needed to control the serious outbreak, and without having to wait for the administrative process of securing the funds and identifying the supplier of vaccines," Thiermann states.

In the final essay of this chapter, workshop speaker David Nabarro of the UN reflects on his experience as that organization's coordinator for avian and human influenza and for global food security. While attempting to respond to the increasingly worrisome prospect of an avian influenza pandemic in humans, Nabarro and colleagues collaborated with stakeholders from the public, private, and volunteer sectors and found that most recognized the value of working together on disease surveillance, reporting, and response. "They found it both operationally useful and reassuring in a situation where there was considerable political urgency and need for concerted action by institutions," he writes. "They have joined together to support the evolution of an inclusive movement that enables hundreds of different stakeholders to feel at home."

From these observations, Nabarro distilled several "factors for success" and additional "incentives for success" for global health collaboration. He then explores major challenges to establishing surveillance as a foundation for global public health governance (as embodied in global efforts toward influenza pandemic preparedness, and more generally in the IHR 2005, OIE regulations, and One World, One Health® framework). In addition to the previously discussed needs for surveillance capacity-building and stakeholder engagement, Nabarro adds a third, more general necessity: creating trust, which he deems the most important incentive for participation, and one which requires active maintenance. "We need to insure against periods of mistrust that may build up in relationships that are otherwise very good," he writes. "We have to know that we are able to cope with these periods."

## OF MILK, HEALTH AND TRADE SECURITY[1]

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Centers for Disease Control and Prevention

The melamine-contaminated milk that has sickened at least 53,000 infants is the latest public-health emergency to have triggered international concern and highlighted the need for improved global cooperation to prevent, detect and con-

[1]Reprinted from *The Far Eastern Economic Review* © 2008 Review Publishing Company Limited. All rights reserved.

[2]Dr. Bell is with the Division of Viral Hepatitis at the U.S. Centers for Disease Control and Prevention in Atlanta. The opinions expressed in this paper are the author's own.

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trol health threats that may rapidly spread beyond national borders. Other recent examples include contamination of the drug heparin in 2007, the dumping of 500 tons of petrochemical waste in Abidjan, Côte d'Ivoire in 2006, and the SARS epidemic in 2003. Importantly, these health emergencies also disrupted business operations, trade and/or tourism.

The economic impact of the tainted milk is not yet known, although precautions are being taken by countries that import milk-containing products from China and rebuilding public confidence may take a long time. SARS caused a global economic loss estimated at $40 billion due to decreased trade and travel and the disruption of global supply chains. These disruptions would pale before that of a severe influenza pandemic, estimated by the World Bank to cost the global economy up to 4.8% of global GDP. According to the Unites States Congressional Research Service, trade disruptions during a pandemic could include countries banning goods from infected regions, travel bans due to protective health measures, or supply-side constraints caused by health crises in exporting countries. For these reasons, business, trade, and tourism stakeholders, and those who support them, such as the insurance industry, have a strong vested interest in working with public-health authorities to promote global health security.

An important new framework to promote global health security in the 21st century is the revised International Health Regulations (IHR), adopted by the 192 member states of the World Health Organization in 2005. Known as IHR 2005, it replaced the previous IHR 1969, which proved unable to address new health threats. The focus of the latest IHR shifted to prevention, detection, reporting and containment of "public health emergencies of international concern," or PHEICs and discouraging trade and travel restrictions disproportionate to the threat. IHR 2005 became effective in 2007, with implementation required of member states by 2012.

The IHR also promote global trade security, which may be provisionally defined as maintenance of a stable trade environment by promotion of safe and unhindered travel and transport, stability of supply and distribution chains, continuity of business operations, and safety of imports and exports. Trade security has been mentioned in the context of protecting shipping lanes and more recently, intercepting terrorist cargo disguised as freight. In the 21st century, a broader concept is needed that also addresses disruption due to public-health emergencies. For businesses, industry associations and international trade organizations and their member states, promoting IHR implementation is good risk management, since the risk of business and trade disruption is reduced in countries where the IHR are implemented.

### Overcoming Barriers

There are two major challenges to IHR implementation: technical and political/economic. Many countries, especially in the developing world, lack

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the necessary infrastructure for prevention, detection, and control of disease outbreaks, toxic spills, unsafe food and drugs, or other PHEICs. Last year, to guide global capacity-building needs in the next five years, the WHO published "IHR 2005: Areas of work for implementation." This ambitious document calls for global partnerships to "strengthen national disease prevention, surveillance, control and response systems; public-health security in travel and transport; WHO global alert and response systems; and the management of specific risks." Building public health capacity is particularly important because it will enable countries to prevent and respond to public health emergencies regardless of whether they meet the IHR definition of a PHEIC. However, resources are insufficient and political will varies in light of competing priorities.

The nontechnical challenges are even more daunting. Countries may perceive substantial economic disincentives to reporting and responding to public health threats as required by the IHR. Economic harm to tourism or export industries could result from public health measures such as travel advisories, quarantine, seizure of hazardous products, or culling of infected livestock—or simply from unjustified public fears. Mounting an emergency response will challenge the health budget of many developing countries, yet the IHR includes no provision for financial support or compensation. Countries may be reluctant to request international assistance for various reasons, including national pride, desire to obtain primary recognition for research findings related to the event, or a commercial interest in biological samples obtained in surveillance or response activities.

On the bright side, national economic interests, such as protecting tourism, can promote government actions consistent with global health security. In late 2006, the Indonesian government suspended sharing influenza virus samples with WHO due to intellectual-property issues regarding vaccine development, thus compromising the global surveillance of influenza. Yet in August 2007 samples were sent from a patient who died of avian influenza in Bali. According to the Indonesian Health Ministry, the specimens were sent to the WHO Influenza Collaborating Center at the U.S. Centers for Disease Control and Prevention in Atlanta "to prove that no mutation took place in the virus and to inform people in the world that Bali was still a safe place to visit." Although Indonesia did not resume sending specimens from elsewhere in the country, this incident illustrates that enlightened economic self-interest can be leveraged to promote health security.

The IHR are intended to avoid unjustified governmental restrictions on international trade and travel in a PHEIC, but have no enforcement mechanism and do not apply to private entities which may implement such restrictions on their own. IHR implementation is primarily the responsibility of health ministries, yet the trade and tourism sectors have much to lose in a disease outbreak and often have more influence on government policy than do health ministries. In summary, the public-health sector needs help in implementing the IHR; recognition of their importance to trade security can provide the basis for engagement of trade and tourism stakeholders.

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## A Path Forward

Many trade and tourism stakeholders may not realize they have a vested interest in IHR implementation. Many are unfamiliar with the IHR and its recent shift in focus. Others recognize the potential adverse economic impact of a health emergency, but consider early detection and control to be the responsibility of public-health authorities. Since many companies appear to believe that these events are like unpredictable and unpreventable hurricanes, their risk management strategy, if any, is limited to minimizing damage if the storm hits them. These companies may not realize the benefits of early detection and containment to their own risk-management strategy, or the daunting challenges faced by public-health authorities in implementing early measures. That is, stakeholders may have an implicit understanding of the importance of health security for trade security, but not as a goal they should pursue.

On a technical level, many companies and industries can potentially assist countries to meet the new IHR infrastructure requirements. Industries in the aviation and maritime sectors have long collaborated with public-health authorities regarding measures at points of entry, but many other trade and tourism stakeholders have an interest in promoting safe and expeditious travel and transport through these critical sites as well. Since PHEICs are most effectively detected and contained in communities rather than at borders, IHR 2005 requires, for the first time, that countries develop public-health infrastructure throughout their territories. This difficult challenge may offer an opportunity for direct private-sector engagement.

Larger companies or their nonprofit foundations could invest by providing resources to individual countries or the WHO to help countries through its IHR Implementation Plan. Investments might include funding and "in kind" assistance, e.g., supplies, facilities, expertise, and transport capacity. Small- and medium-sized firms also have a role, especially as partners in public health emergency response, e.g., in developing policies that encourage infectious employees to stay home and relaying health messages to workers and their families.

Countries are now developing their national action plans to meet IHR requirements by 2012, offering an opportunity for trade and tourism stakeholders to learn about these plans and consider investing in their success. Tabletop exercises with public-health officials and local case studies may help businesses understand their return on investment. Discussions have occurred at the World Economic Forum about roles for global business in disaster response that could help serve as a model.

Industry and political leaders should be encouraged to understand, *before* any event occurs, that it is always in their interest for public-health authorities to report and control a PHEIC rapidly, and to seek international assistance if appropriate. In the Internet age, news and rumors cannot be suppressed indefinitely. Temporary losses for a country's tourism or export industries would be preferred over taking halfway measures leading to worsening conditions or a loss of trust

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by the public and business partners at home and abroad. This message would be more influential coming from business communities and trade ministries than public-health officials.

Particularly challenging is the issue of compensation for businesses and their employees who suffer economic losses when a country complies with the IHR and WHO advice in controlling a PHEIC. Even wealthy countries will have difficulty addressing this issue. It is unrealistic to expect developing countries to bear the economic consequences of disease-control measures unassisted. The experience gained in compensating poultry farmers for culling to contain avian influenza outbreaks illustrates that such programs can be helpful when appropriately designed and implemented and that international financial and technical assistance may be required.

The availability of partial compensation to countries through an internationally supported mechanism should be established before any PHEIC, as well as procedures and criteria for disbursing aid. Ad hoc donations afterwards will be too late to influence decision making or cushion the immediate losses of businesses and workers who have little financial reserves. To promote IHR implementation, public-health and business leaders might consider establishing an international trust fund or insurance product. This could be done as a public-private partnership involving an agency such as the World Bank or WEF.

Trust funds are typically supported by a tax on specific transactions, which may be unpopular, whereas the concept truly is insurance, perhaps purchased by countries and industry consortia. Insurance premiums for many developing countries would need to be subsidized, but donors might consider this as a worthwhile investment. Insurance companies have experience in writing policies to cover many unusual eventualities and it is not inconceivable that a sound product could be designed. Many large companies already have business-interruption insurance for known risks. While commercial insurance is likely beyond the reach of many small businesses in developing countries, this approach could serve as a model for a policy to cover entire communities or perhaps critical industries and their suppliers. Conditioning the insurance on improvements in public-health and emergency management infrastructure could help justify these improvements as attractive investments, rather than costs. Many details would need to be worked out, including what losses would be covered, how claims would be adjudicated, and to whom claims would be paid. The national government might be a likely candidate, to the extent that it incurred verifiable expenses in disease control and in compensating private companies or citizens.

An initiative by major trading nations and business sector champions is needed to engage trade and tourism stakeholders to promote implementation of the revised IHR. Focusing on trade security would help avoid entanglement in more controversial health-trade issues like drug pricing. Activities may include raising awareness in business sectors and organizations like the WTO, seeking resources to help the WHO and member states strengthen core public health

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capacity, developing novel compensation mechanisms to offset economic disincentives to IHR adherence, drafting codes of good practice, and promoting evaluation of public-health interventions.

Global trade security depends on global health security, including IHR implementation. Public-health, trade and tourism stakeholders have much to gain from joining forces to promote both and much to lose from failing to recognize their common interests.

## INTERNATIONAL TECHNICAL AGENCIES WORKING AT THE HUMAN-ANIMAL INTERFACE

*Ottorino Cosivi, D.V.M.*[3]
World Health Organization

Following World Health Day in 2007 (WHO, 2007a), the *World Health Report* (WHO, 2007b) defined the concept of global health security and identified major threats to global health security. Emerging infectious diseases, particularly foodborne diseases and zoonoses,[4] figure prominently among these risks, which also include international crises and humanitarian emergencies; deliberate use of biological, chemical, and radioactive agents to cause harm; and environmental disasters. International actions to address international crises; deliberate use of biological, chemical, and radioactive agents; and environmental disasters require primarily political partnerships. Conversely, technical and scientific partnerships are required to effectively address emerging infectious diseases. Many such partnerships focus on the prevention of foodborne and zoonotic diseases as an important means to protect public health, as well as to promote the production of food of animal origin and facilitate international trade in animals and animal products.

The main message of the *2007 World Health Report* (WHO, 2007b) is that collective action is needed to address global health risks. Such collective action is embodied in the tripartite relationship of the WHO, the World Organisation for Animal Health (OIE),[5] and the Food and Agriculture Organization of the United Nations (FAO). Together, these agencies are confronting emerging zoonoses such as Rift Valley fever, which has had both dire public health and economic effects on vulnerable populations in Africa; and influenza, with efforts to address the emergence of the new influenza A (H1N1)—building on preparations under way since the emergence of H5N1 avian influenza.

[3]At the time of the submission of this paper, Dr. Cosivi was a staff member of the World Health Organization. He is now working for the Pan American Health Organization. The author alone is responsible for the views expressed in this publication and they do not necessarily represent the decisions, policy, or views of the World Health Organization or the Pan American Health Organization.

[4]A disease and/or infection that is naturally transmissible from vertebrate animals to people.

[5]The intergovernmental Office International des Epizooties (OIE), created in 1924, was renamed the World Organisation for Animal Health in 2003, but retained its historical acronym.

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The International Health Regulations (IHR) provide a framework for managing collective risks (WHO, 2009a). They emphasize that the best way to limit the public health impact of emerging diseases is by strengthening national preparedness and response activities in order to enable the early detection of health threats and the efficient implementation of response actions, thereby addressing problems at a manageable stage. At the international level, WHO's alert and response operations under IHR (see Heymann in Chapter 4) are linked to similar systems for animal health managed by the OIE and FAO.

## FAO, OIE, and WHO

WHO pursues collaborations to address emerging infectious diseases with many different organizations and partners, and at multiple levels, but for those infectious agents originating from animals and animal products its primary relationships are with the OIE and FAO. The ambitious, overarching definition employed by the WHO—that "health is a state of complete physical, mental, and social well-being, not merely the absence of disease or infirmity"—subsumes the goals of the FAO (food security and poverty alleviation) and the OIE (transparency in reporting information on animal diseases and the development of international standards for animal health and welfare). There are major structural and organizational differences among these agencies in terms of number of staff, governance, and budget. Each of the organizations brings to the table a different valuable perspective on the fight against zoonotic disease. Table 5-1 lists several important formal agreements and joint programs undertaken by the FAO, OIE, and WHO to address zoonoses.

Several different interagency frameworks for the early detection and control of zoonotic diseases build on synergies among these organizations. Some of these activities, such as the GLEWS (WHO, 2006) and INFOSAN (WHO, 2007c), support global public health surveillance, which is discussed in greater detail later. Other programs include the WHO's Global Salm-Surv and the Mediterranean Zoonoses Control Programme (MZCP), which focus on strengthening capacity for disease detection and control at the national level. The Pan American Health Organization (PAHO)/WHO Regional Office for the Americas has long been providing technical cooperation to member states in veterinary public health. Its operations have been consolidated and decentralized to the Pan American Center for Foot-and-Mouth Disease (PANAFTOSA[6]) in Rio de Janeiro, Brazil.

[6]Founded in 1951, PANAFTOSA is one of the specialized centers of the Pan American Health Organization (PAHO). Located in the Brazilian state of Rio de Janeiro, the center supports the member states of the region in the prevention, control, and eradication of zoonotic and food-borne diseases and high consequence animal diseases, primarily foot-and-mouth disease (FMD). For more information, see http://www.panaftosa.org.br/ (accessed October 23, 2009).

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**TABLE 5-1** Formal Agreements and Joint Programs to Address Zoonotic Diseases

| Parties | Date | Purpose of Agreement or Joint Program |
|---|---|---|
| WHO, FAO(a) | 1948 | Joint committees, joint missions, exchange of information, inter-secretariat committees |
| WHO, OIE(a) | 1960 (revised 2004) | Promotion and improvement of veterinary public health, and food security and safety |
| PAHO, OIE(b) | 2000 | Technical cooperation in the field of veterinary public health |
| FAO, OIE(c) | 2004 | Role of FAO, role of OIE, and joint actions |
| FAO/WHO Codex Alimentarius Commission(d) | 1963 | Develop food standards, guidelines and related texts such as codes of practice |

SOURCES: WHO (2007a), OIE (2000b; 2004c), Codex Alimentarius (2009).

There is also collaboration between WHO, OIE, and FAO to address specific health threats such as influenza, antimicrobial resistance, and laboratory biosafety challenges. With regard to avian and pandemic flu, these include WHO's interactions with the OIE/FAO animal influenza laboratory network (OFFLU), which shares information on viral strains with WHO (FAO and OIE, 2009). Efforts spearheaded by the WHO to address other health threats at the animal-human interface—from rabies to biological agents that have been associated with deliberate use to cause harm like anthrax, brucellosis, and tularemia—also draw on the additional expertise, laboratory services, and surveillance data from OIE and FAO.

WHO, FAO, and OIE hold strategic level tripartite meetings regularly. Moreover, exchange of information and technical expertise among these agencies occurs on a daily basis and has intensified considerably over the past decade.

### Collaborative Approaches Addressing Zoonoses, Food Safety, and Veterinary Public Health

#### *GLEWS*

A formalized initiative of the WHO, FAO, and OIE, GLEWS is a public and animal health early warning system intended to reduce incidence of emerging infectious diseases. Partners in GLEWS, which incorporates both agriculture and public health sectors, share information on disease outbreaks in real time and coordinate their responses, as shown in Figure 5-1. GLEWS combines and coordinates the alert and response mechanisms of the OIE, FAO, and WHO to assist in prediction, prevention, and control of emerging infectious diseases.

This international platform is among the most effective means by which these agencies currently collaborate, as was recently demonstrated when the

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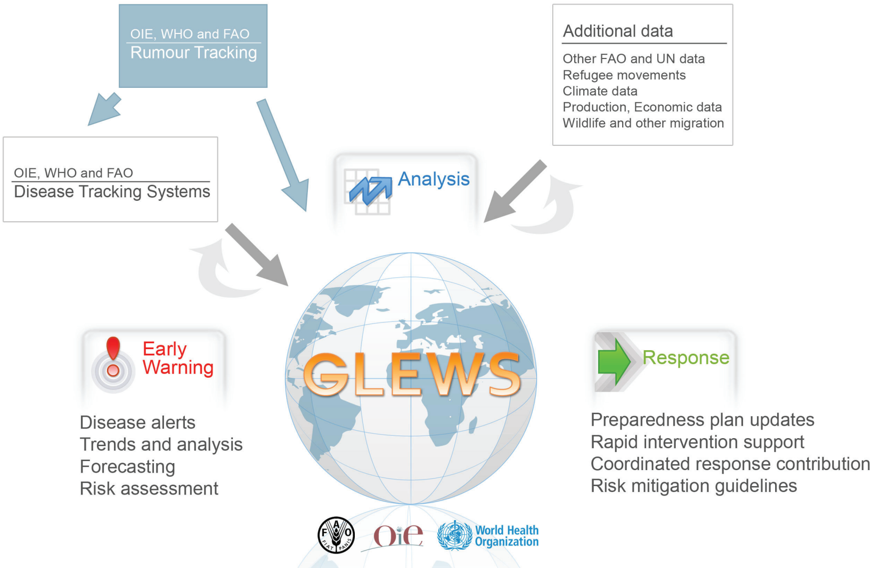


**FIGURE 5-1** Global Early Warning and Response System (GLEWS) for Major Animal Diseases, including Zoonoses.
SOURCE: OIE (2009).

Ebola Reston virus was identified in pigs and humans in the Philippines. Information was gathered and shared by the three organizations through GLEWS, which also facilitated the coordination in the communication to the public. In addition, GLEWS provides information to aid in predicting outbreaks of emerging diseases such as Rift Valley fever.

*INFOSAN*

The INFOSAN network promotes global food safety by disseminating information and fostering international collaboration. As of May 2009, 177 countries have designated more than 350 INFOSAN Emergency Contacts and INFOSAN Contact Points. As shown in Figure 5-2, INFOSAN links to all stakeholders along the "food chain"—including the private sector—and coordinates with IHR and GLEWS. This also means that emergency information related to foodborne diseases and contamination in some cases do not only reach countries through this FAO/WHO mechanism focusing of food safety authorities

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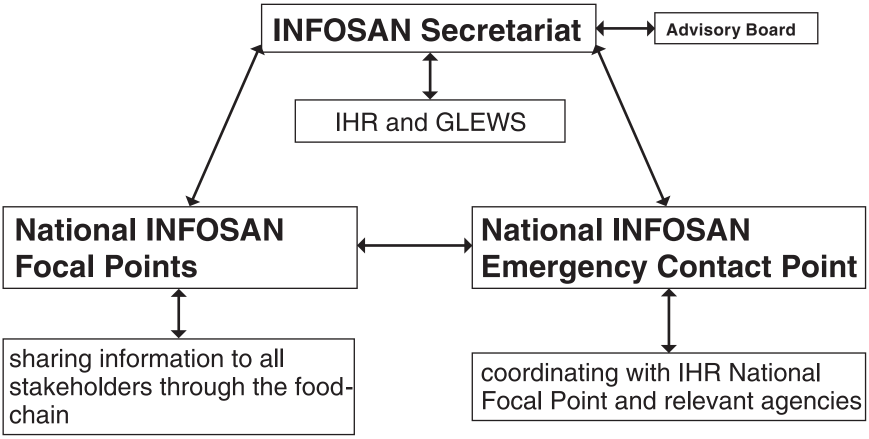


**FIGURE 5-2** INFOSAN links to all government sectors involved in food safety.
SOURCE: Reprinted from WHO (2007c) with permission from the World Health Organization.

*Global Foodborne Infections Network (GFN)*

Recognizing that food safety requires intersectoral collaboration among human health, veterinary, and food-related disciplines, the WHO developed the Global Foodborne Infections Network (GFN) (formerly known as Global Salm-Surv, GSS) in order to enhance countries' capacity to detect, respond, and prevent foodborne diseases (WHO, 2009c). The GFN promotes integrated, laboratory, and epidemiologically based foodborne disease surveillance, which is expanding to incorporate zoonotic diseases. It supports international training courses, external quality assurance programs, research projects, reference services, and communication platforms, and provides national and regional interdisciplinary intersectoral networks and national training courses through train-the-trainer concept.

*MZCP*

Created in 1978 and financed by its 13 states, the MZCP (WHO, 2009b) fosters programs and activities for the prevention, surveillance, and control of zoonoses and foodborne diseases; strengthens collaboration between public health and animal health sectors; and promotes collaboration among countries. This program has achieved significant progress in bringing together the animal health and public health communities in countries in the Mediterranean region. Its training and capacity-building activities have included intersectoral surveillance of

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zoonotic and foodborne diseases (e.g., rabies, Crimean-Congo hemorrhagic fever, and leishmaniasis), preparedness and response to zoonotic and foodborne disease emergencies (e.g., rabies, Crimean-Congo hemorrhagic fever, and leishmaniasis), and laboratory training. All of these activities are conducted jointly, on a regional basis, by public health practitioners and veterinarians.

*PANAFTOSA*

The countries of the Americas have long recognized that the health of animals and human beings are inextricably linked. In 1949, PAHO established a Veterinary Public Health (VPH) unit to bring together the animal and human health communities to address animal and zoonotic diseases of public health importance. Since 2007, PANAFTOSA has hosted PAHO's VPH project. Its main areas of intervention include emerging and neglected zoonoses (e.g., dog rabies elimination), foot-and-mouth disease, food safety and foodborne diseases (Belotto et al., 2007). More recently the neglected diseases and tropical diseases research projects have been decentralized in PANAFTOSA. PANAFTOSA acts as the Secretary of the Inter-American Meeting, at the ministerial level, on Health and Agriculture (RIMSA), the Hemispheric Committee for the Eradication of Foot-and-Mouth Disease (COHEFA), the Regional Meeting of the National Directors of Rabies Control Programs in Latin America (REDIPRA), the South American Commission for the Control of Foot-and-Mouth Disease (COSALFA), and the Pan American Commission for Food Safety (COPAIA). These advisory bodies bring together regional and international stakeholders, including member states, academia, nongovernmental organizations, development agencies, and public and private entities including agriculture, health, and the food sectors.[7]

## One World, One Health®

The concept of One World, One Health®, first defined by the Wildlife Conservation Society in 2004, has been further described by international organizations such as the FAO, the OIE, the WHO, the UN, the United Nations Children's Fund (UNICEF), and the World Bank (WB). This description was developed in response to a request made at the interministerial meeting of the December 2007 New Delhi International Ministerial Conference on Avian and Pandemic Influenza. This meeting suggested that the international community looks beyond avian flu to the next important global health risk related to the human-animal interface. In October 2008, a plan aiming at diminishing the threat and minimizing the global impact of epidemics and pandemics due to highly infectious and pathogenic emerging infectious diseases for humans and animals was presented at a follow-up International Ministerial Conference on Avian and Pandemic

[7]For more information http://www.panaftosa.org.br/ (accessed May 29, 2009).

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Influenza, Sharm El Sheikh, Egypt, October 2008. It builds on the lessons learned from the avian influenza crisis, which include:

- The economic implications of infectious disease, which range from national development to individual livelihoods;
- The role of wildlife in disease transmission;
- The necessity for control strategies based on epidemiological evidence;
- The importance of cross-sectoral and intersectoral collaboration in outbreak response;
- The crucial role of political commitment to public health; and
- The need for effective risk communication strategies.

The following six specific objectives and related activities have been determined in the document:

1. Develop international, regional, and national capacity in infectious disease surveillance, making use of international standards, tools, and monitoring processes.
2. Ensure adequate international, regional, and national capacity in public and animal health—including communication strategies—to prevent, detect, and respond to disease outbreaks.
3. Ensure functioning national emergency response capacity, as well as a global rapid response support capacity.
4. Promote interagency and cross-sectoral collaboration and partnerships.
5. Control animal influenza and other existing and potentially reemerging infectious diseases.
6. Conduct strategic research.

At the country level, an important long-term priority is the improvement of disease control capacity—including the public health, animal health, and food safety services—based on good governance compliant with IHR and OIE standards. At country and regional levels, over the short to mid term, a key goal is to establish risk-based zoonotic disease surveillance in humans and animals in order to recognize diseases at their point of origin (by identifying hotspots at the human-animal interface). The concept of global and national public goods was applied in this paper to describe further the potential future activities, as shown in Table 5-2.

## Conclusions

In order to address the threat of emerging zoonotic diseases, we must make sure the paradigm for disease prevention and focus on disease surveillance and control at the human-animal interface reflects the fact that emerging infectious

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**TABLE 5-2** Activities for Prevention and Control of Diseases at the Animal-Human-Ecosystems Interface and Their Status as a Public Good

| Activity | Disease of Low Human Epidemic Potential | Disease of Moderate to High Human Epidemic Potential |
|---|---|---|
| 1. Preparedness | | |
| Risk analysis | Global | Global |
| Preparedness plan | National/regional | Global |
| Animal vaccine development | Private[a] | Global |
| 2. Surveillance | | |
| Public health, veterinary, and wildlife | National | Global |
| Diagnostic capacity | National/global | Global |
| Managerial and policy arrangements | National/global | Global |
| 3. Outbreak control | | |
| Rapid response teams | National | National/global |
| Vaccination | National/regional | National/global |
| Cooperation among human, veterinary, and wildlife services | National | Global |
| Compensation schemes | National | Global |
| 4. Eradication plans | National/regional | Global |
| 5. Research | National/regional | Global |

[a]This may also be a global public good depending on diseases and circumstances (context).
SOURCE: Reprinted with permission from FAO et al. (2008).

diseases are dynamic risks and that their control is complex and requires a systems-based approach, with the active contribution of stakeholders from public to private sectors, and input from various disciplines such as public health, animal health and production, environment protection, conservation of wildlife. The main focus should always be the prevention of human disease but these efforts can be advanced through existing animal and human disease surveillance networks that need to be strengthened and enabled to communicate across sectors, and by defining research priorities addressing the needs of the most vulnerable regions of the world. National and regional capacity-building is key to infectious disease prevention and mitigation.

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## INTERNATIONAL ANIMAL HEALTH REGULATIONS AND THE WORLD ANIMAL HEALTH INFORMATION SYSTEM

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World Organisation for Animal Health (OIE)

The World Organisation for Animal Health (OIE)[9] is the international organization responsible for establishing international standards on animal health and zoonoses. The draft sanitary standards are presented to the 173 members for a vote and, once adopted, they are published in the Terrestrial and Aquatic Animal Health Codes[10] as well as the accompanying manuals for diagnostics and vaccines.

When the OIE was established in 1924, its two primary objectives were to provide transparency of global animal health information and to provide scientific and technical support on the prevention and control of animal diseases. Today, the OIE's mandates relate to improving animal health worldwide, which goes well beyond the notification obligations of the occurrence of animal diseases of significance. However, for the purpose of this paper, only the notification obligations by members are discussed.

The importance of credible and up-to-date animal disease information is critical to ensure transparency in the animal disease status worldwide. Therefore, the OIE has had the notification of the occurrence of significant animal diseases, including zoonoses, as one of its major objectives and a mandatory obligation for its members since its inception. The notification system has been reviewed and updated several times, and the most recent revision in 2004 was accompanied by the launching of the current World Animal Health Information System (WAHIS) platform.

Already in 1924, when the agreement on the creation of the OIE was signed, the organic rules prescribed clearly that the OIE members have an obligation to inform the OIE of changes in the epidemiology of major diseases listed by the OIE (OIE, 2006).

Under Article 4b, "the statues identify that the main objective of the OIE is to collect and bring to the attention of the governments or their sanitary services all facts and documents of general interest concerning the spread of epizootic diseases and the means used to control them" (OIE, 2006).

> Under Article 5, the statues state that the governments shall forward to the OIE, by telegram, notification of the first cases of rinderpest or FMD observed in a

[8]President, Terrestrial Animal Health Code Commission.

[9]The need to fight animal diseases at the global level led to the creation of the Office International des Epizooties (OIE) in 1924. In May 2003, the Office became the World Organisation for Animal Health but kept its historical acronym (OIE, 2009b).

[10]See http://www.oie.int/eng/normes/mcode/en_sommaire.htm.

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> country or an area hitherto free from the infection. They must also forward, at regular intervals, bulletins prepared according to a model adopted by the International Committee (the highest authority of the OIE, comprising all member countries), giving information on the presence and distribution of the following diseases: rinderpest, rabies, FMD, glanders, contagious pleuropneumonia, dourine, anthrax, swine fever, and sheep pox.
>
> Article 5 also states that the list of diseases to which either of the foregoing provisions applies may be revised by the International Committee, subject to the approval of the governments.
>
> The governments shall also inform the OIE of the measures adopted by them to control epizootics, especially such measures enforced at their own frontiers to protect their territory against import from infected countries. As far as possible they shall furnish information in reply to inquiries sent to them by the OIE. (OIE, 2006)

This agreement is still today an obligation for members.

> Under Article 9, the statues state that all information collected by the OIE shall be brought to the attention of the participating states by means of a bulletin or by special notifications which shall be sent to them either automatically or upon request. Notification concerning the first outbreaks of rinderpest or FMD shall be forwarded immediately by telegram to the various governments and sanitary services. In addition, official reports shall be sent periodically to the participating states, giving detailed accounts of the activities of the OIE. (OIE, 2006)

The scope of Article 5 was later enlarged by covering a broader list of animal diseases, including zoonoses, and by addressing emerging diseases (even if they are not OIE-listed diseases). These changes are reflected in the Terrestrial Animal Health Code Chapter on notification, as early as 1986. The Code states that veterinary administrations shall send to the OIE notification, within 24 hours, of any new findings, even of diseases not listed under list A, which are of exceptional epidemiological significance to other countries. In May 2004, OIE members approved the creation of a single list of diseases (see Table 5-3), thereby eliminating the organization of diseases under lists A, B, and C.

Further improvements to the chapter on notification and the criteria for listing diseases were also adopted in 2004, where specific reference was made to the obligation to notify of "an emerging disease with significant morbidity or mortality, or zoonotic potential."

Currently, the Terrestrial Animal Health Code describes the notification obligations for members and provides a list of the notifiable diseases. The OIE's notification criteria are based on a decision tree (Figure 5-3) that incorporates several factors such as the ability of the pathogen for international spread, as well as

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**TABLE 5-3** Diseases Notifiable to the OIE

**Multiple species diseases**
- Anthrax
- Aujeszky's disease
- Bluetongue
- Brucellosis (*Brucella abortus*)
- Brucellosis (*Brucella melitensis*)
- Brucellosis (*Brucella suis*)
- Crimean Congo haemorrhagic fever
- Echinococcosis/hydatidosis
- Epizootic haemorrhagic disease
- Equine encephalomyelitis (Eastern)
- Foot-and-mouth disease
- Heartwater
- Japanese encephalitis
- Leptospirosis
- New world screwworm (*Cochliomyia hominivorax*)
- Old world screwworm (*Chrysomya bezziana*)
- Paratuberculosis
- Q fever
- Rabies
- Rift Valley fever
- Rinderpest
- Surra (*Trypanosoma evansi*)
- Trichinellosis
- Tularemia
- Vesicular stomatitis
- West Nile fever

**Cattle diseases**
- Bovine anaplasmosis
- Bovine babesiosis
- Bovine genital campylobacteriosis
- Bovine spongiform encephalopathy
- Bovine tuberculosis
- Bovine viral diarrhoea
- Contagious bovine pleuropneumonia
- Enzootic bovine leukosis
- Haemorrhagic septicaemia
- Infectious bovine rhinotracheitis/infectious pustular vulvovaginitis
- Lumpky skin disease
- Theileriosis
- Trichomonosis
- Trypanosomosis (tsetse-transmitted)

**Swine diseases**
- African swine fever
- Classical swine fever
- Nipah virus encephalitis
- Porcine cysticercosis
- Porcine reproductive and respiratory syndrome
- Swine vesicular disease
- Transmissible gastroenteritis

**Sheep and goat diseases**
- Caprine arthritis/encephalitis
- Contagious agalactia
- Contagious caprine pleuropneumonia
- Enzootic abortion of ewes (ovine chlamydiosis)
- Maedi-visna
- Nairobi sheep disease
- Ovine epididymitis (*Brucella ovis*)
- Peste des petits ruminants
- Salmonellosis (*S. abortusovis*)
- Scrapie
- Sheep pox and goat pox

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**TABLE 5-3** Continued

| | |
|---|---|
| **Bee diseases**<br>• Acarapisosis of honey bees<br>• American foulbrood of honey bees<br>• European foulbrood of honey bees<br>• Small hive beetle infestation (*Aethina tumida*)<br>• *Tropilaelaps* infestation of honey bees<br>• Varroosis of honey bees | **Equine diseases**<br>• African horse sickness<br>• Contagious equine metritis<br>• Dourine<br>• Equine encephalomyelitis (Eastern)<br>• Equine encephalomyelitis (Western)<br>• Equine infectious anaemia<br>• Equine influenza<br>• Equine piroplasmosis<br>• Equine rhinopneumonitis<br>• Equine viral arteritis<br>• Glanders<br>• Surra (*Trypanosoma evansi*)<br>• Venezuelan equine encephalomyelitis |
| **Mollusk diseases**<br>• Infection with *Bonamia ostreae*<br>• Infection with *Bonamia exitiosa*<br>• Infection with *Marteilia refringens*<br>• Infection with *Mikrocytos mackini*<br>• Infection with *Perkinsus marinus*<br>• Infection with *Perkinsus olseni*<br>• Infection with *Xenohaliotis californiensis* | **Avian diseases**<br>• Avian chlamydiosis<br>• Avian infectious bronchitis<br>• Avian infectious laryngotracheitis<br>• Avian mycoplasmosis (*M. gallisepticum*)<br>• Avian mycoplasmosis (*M. synoviae*)<br>• Duck virus hepatitis<br>• Fowl cholera<br>• Fowl typhoid<br>• Highly pathogenic avian influenza and low pathogenic avian influenza in poultry as per Chapter 10.4. of the *Terrestrial Animal Health Code*<br>• Infectious bursal disease (Gumboro disease)<br>• Marek's disease<br>• Newcastle disease<br>• Pullorum disease<br>• Turkey rhinotracheitis |
| **Amphibians**<br>• Infection with *Batrachochytrium dendrobatidis*<br>• Infection with ranavirus | **Lagomorph diseases**<br>• Myxomatosis<br>• Rabbit haemorrhagic disease |

*continued*

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**TABLE 5-3** Continued

| Fish diseases | Crustacean diseases |
|---|---|
| • Epizootic haematopoietic necrosis | • Taura syndrome |
| • Infectious haematopoietic necrosis | • White spot disease |
| • Spring viraemia of carp | • Yellowhead disease |
| • Viral haemorrhagic septicaemia | • Tetrahedral baculovirosis (*Baculovirus penaei*) |
| • Infectious pancreatic necrosis | • Spherical baculovirosis (*Penaeus monodon*-type baculovirus) |
| • Infectious salmon anaemia | • Infectious hypodermal and hematopoietic necrosis |
| • Epizootic ulcerative syndrome | • Crayfish plague (*Aphanomyces astaci*) Infectious myonecrosis |
| • Bacterial kidney disease (*Renibacterium salmoninarum*) | |
| • Gyrodactylosis (*Gyrodactylus salaris*) | |
| • Red sea bream iridoviral disease | |
| **Other diseases** | |
| • Camelpox | |
| • Leishmaniosis | |

SOURCE: OIE (2009a).

the ability to spread within a naïve animal population and its zoonotic potential. This decision tree is not limited to known pathogens; it also takes into account the emergence of new diseases that are potentially zoonotic and/or show an effect on naïve animal populations, and which may still not have a characterized etiologic agent. This has been recently demonstrated by the emergency notification made by Canada when it detected influenza A (H1N1) in a pig herd in Alberta. Swine influenza is a mild disease of swine and therefore not a notifiable disease by the OIE. The recent epidemiologic event of the first reported evidence of an infection in pigs with this novel strain constituted a case for emergency notification. Canada, demonstrating an efficient surveillance system and transparent reporting, immediately notified the OIE and thereby the international community became aware. Should the human infection with this pathogen be associated with severe consequences, then it would trigger the mechanism for consideration for "notifiable disease."

The new notification system also takes into account the concept of infection without necessarily having expression of clinical disease. It takes into account any change in epidemiological situations, whether it is manifested as a difference in pathogenicity or a change in host predilection, regarding known diseases within a country or zone. It also clarifies how to deal with the appearance of emerging diseases.

The events that require immediate notification (within 24 hours) are those related to the emergence of a new disease, as well as the first occurrence of a listed disease or infection in a country or zone. This also applies to the reoccurrence of a listed disease or infection in a country or zone having been previously

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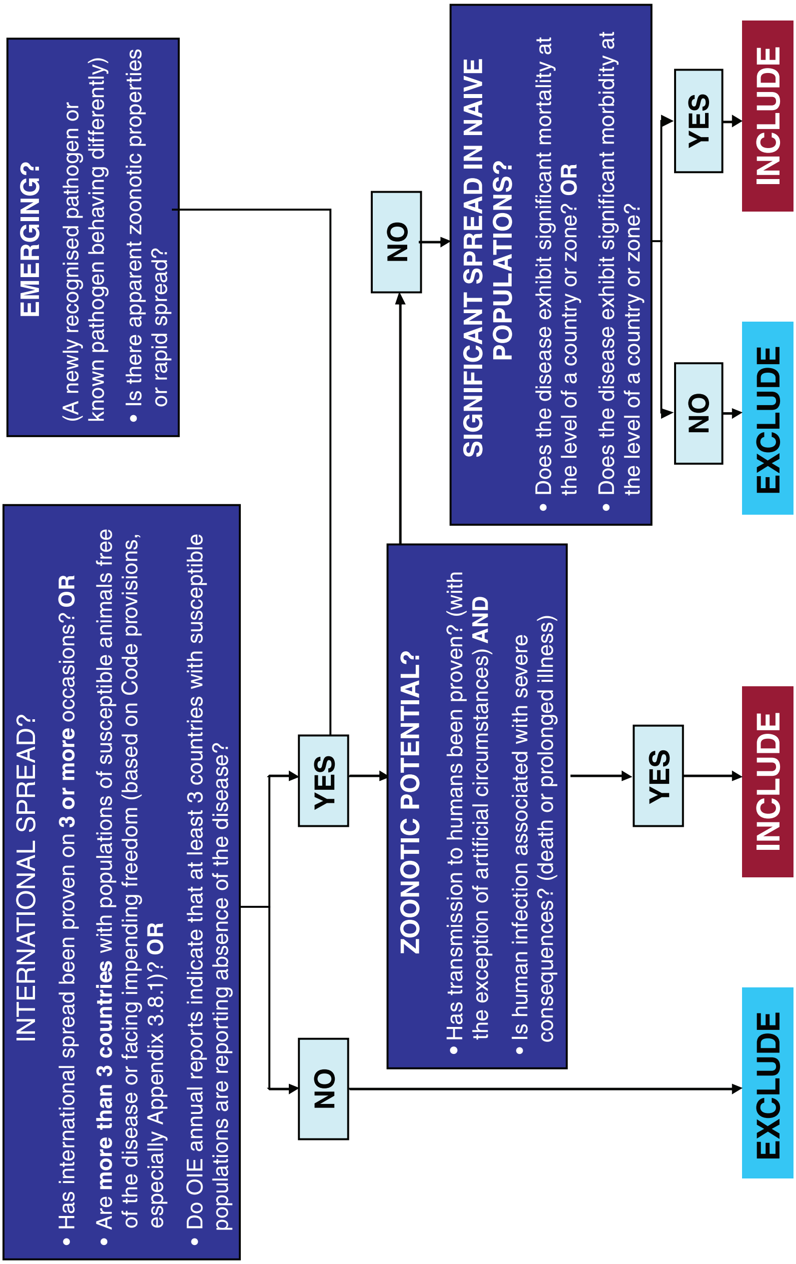


**FIGURE 5-3** OIE's disease notification criteria.
SOURCE: OIE (2008).

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declared free of such disease. It also applies to the first occurrence of a new strain of a pathogen of a listed disease, or of a previously unknown condition manifesting a significant impact on animal or public health in a country or zone.

The information received by the OIE is processed, presented in several formats, and then published on the OIE website. The immediate notifications of diseases, infections, or unusual epidemiologic events are published upon receipt, on a near-real-time basis. This is followed by weekly reports, which contain weekly updates submitted by countries on the initial notifications, until the outbreak is eliminated or the situation is such that the country or zone is declared endemic.

The OIE also publishes semiannual reports, which contain qualitative as well as quantitative information. The qualitative information describes the occurrence of the disease and the control, prophylaxis, and prevention measures being applied. The quantitative information is presented in different formats: the presence of the disease or infection within the lowest administrative division within the country (province, county, or department) monthly, and every six months; it is also presented by entire countries by month and for the six-month period. Finally, there is an annual report that summarizes country submissions not only on the listed diseases, but also provides relevant information on non-OIE-listed diseases; information on the veterinary infrastructure of the country; reports from the various reference laboratories; any relevant information to animal census conducted; the summary of human cases of zoonotic diseases; as well as any information on the production of vaccines.

Members meet their notification obligations by directly entering the related information electronically into the WAHIS web application, using a protected login and password. Only a minority of members continue to enter their information in paper form and submit it to the OIE via fax. To facilitate contact with those individuals responsible for collecting and submitting information to the OIE, each delegate (in most cases the chief veterinary officer of a given country) must identify and notify the OIE of their selected disease notification focal point.

This new notification system provides members with a simpler and more rapid method for complying with the obligation of sanitary information submissions. It also permits countries to benefit from new capabilities for accessing and retrieving valuable epidemiological information in various ready-to-use formats. The various forms of data presentation can be examined when accessing the World Animal Health Information Database (WAHID).[11] The information can be retrieved in various forms: by country, by disease, based on control measures applied, and by comparing the disease situation between two countries. There are also graphic presentations of maps depicting exceptional epidemiological events, specific disease distributions, as well as maps describing areas of control measures such as vaccinations. This information can be used to conduct risk

[11] See http://www.oie.int/wahis/.

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analysis, to prevent the spread of disease, as well as to minimize the transmission of diseases as a result of international trade.

It is true that the OIE can only publish disease information submitted officially by its members. At times, a proactive approach is required to ensure greater transparency. Mindful of this point, the OIE adopted, at its 69th General Session in May 2001, the text indicating that the Central Bureau Animal Health Information Department shall gather, analyze, and process all of the animal health information available in the OIE member countries, including that which has not been officially sent to the Office. It recognizes that such information may come from expert's reports, research work, scientific publications, international surveys, communications to other organizations, press articles, health monitoring networks on the Internet (e.g., ProMED), and so on. However, this information will not be distributed by the OIE unless it has been recognized as valid by the delegate of the country concerned.

The OIE searches, in coordination with its Collaborating Centers and partners (the FAO and the WHO), all sources of unofficial information on epidemiological events of significance and pursues all avenues to encourage rapid, transparent, and official reporting by its members. Once this information is obtained and evaluated, it is sent to the corresponding delegate, who is then asked for immediate official confirmation or denial. Thanks to the ever-increasing visibility of this unofficial information and to the negative trade implications of not transparently reporting such events, countries are responding quickly to the OIE with a confirmation or an explanation on the misinformation. During last year, more than 70 percent of the OIE requests resulted in immediate official notifications by the national authorities.

In addition to the WAHIS within the OIE, the OIE also collaborates closely with the FAO and WHO by creating a joint early warning system for major animal diseases and zoonoses, called the Global Early Warning System (GLEWS). The three organizations share the official and unofficial information received and make joint determinations on the extent and type of response required.

While the IHR 2005 of the WHO has recently received much visibility, the animal disease information system of the OIE has been long established and experienced but, nevertheless, is not that well known. Despite its long history and impressive collection and presentation of information, the benefits of the WAHIS have been known primarily by veterinary services and those engaged in international trade of animals and animal products.

There are many similarities between the OIE and the WHO systems. Among others, both systems share a common purpose and scope and a common legal basis in their obligation to notify, they both recognize the sovereign rights of their members, they establish official national focal points, they use official as well as take unofficial data into account, and they both focus on the importance of immediate notification of significant epidemiological events.

However, there are also differences between the two notification systems.

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WAHIS is not a stand-alone notification system; it is part of a complex set of obligations and standards to which members must adhere. The WAHID, with the presentation of data in various formats, aside from being an obligation provides great benefits to its members and users at large. The obligations to report are balanced by a series of mechanisms established by the OIE to assist countries in having the basic infrastructure required for a rapid and transparent reporting. Reference laboratories, in order to maintain such status within the OIE, are also required to share their findings with the OIE even in cases where the submitting country may not have done so.

It is the belief of the OIE that, in order to have a global rapid and transparent animal disease reporting system, it must create the proper incentives for all its members to actively participate. Just having a legally binding obligation to report is not likely to solve the problem of lack of reporting by most countries. The OIE has determined that the majority of countries not rapidly reporting the occurrence of notifiable diseases in their territories is because of inability and not unwillingness. Therefore, the OIE is committed to assist in the strengthening of the veterinary infrastructure of these countries unable to report. In order to provide the required assistance, the OIE has established a Global Trust Fund for Animal Health and Welfare,[12] which offers capacity-building to its members through several activities.

First, it is worth mentioning the evaluation system for veterinary services (PVS), which is used as a diagnostic tool to assess the strengths and weaknesses of veterinary infrastructures and their ability to comply with their obligations stipulated in the OIE standards. It is conducted by well-trained experts at the request of members. Of course, the assistance cannot be limited to providing diagnostic services, and therefore the OIE is following up in many of the more than 80 countries that have undergone the PVS evaluation, with a gap analysis. This gap analysis is aimed at prioritizing the areas for improvement and assistance to countries in the identification of resources required for such improvements.

The OIE also offers technical assistance in the preparation of focal points, as well as for the development or improvement of regulatory systems, essential to support the legal enforceability of international standards at a national level. Under the Trust Fund, the OIE has also supported the "twinning" program, which is aimed at establishing long-term and more guided collaborative mechanisms between established reference laboratories in developed countries and comparable institutions in developing countries. The ultimate goal is to strengthen the global network of reference laboratories capable of assisting all countries in the diagnosis and characterization of pathogens.

As an additional incentive for rapid and transparent reporting, primarily at the grassroots level, the OIE provides guidance on the establishment of compensation mechanisms. As experienced during the avian influenza H5N1 crisis, it

[12] See http://www.oie.int/eng/Edito/en_edito_mars07.htm.

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has been difficult in certain situations to have active and sustained participation by local villagers and small farmers on reporting the presence of sick poultry. At times this is the most important sector in the early reporting of disease. However, it is also the sector most negatively affected by the destruction of the infected and potentially exposed chickens. The OIE believes that, unless there is an adequate compensation mechanism for these individuals, it will be difficult to have a sustained reporting system of emerging diseases.

In order to assist in the response time in cases of serious outbreaks, the OIE has also established a virtual vaccine bank. So far this has been used in cases of serious avian influenza outbreaks, whereby the OIE provides large numbers of vaccines to affected countries when so requested. This mechanism allows countries to begin vaccinating with certified vaccines immediately after the decision is made that vaccination is needed to control the serious outbreak, and without having to wait for the administrative process of securing the funds and identifying the supplier of vaccines. Depending on the country and the situation, the country may then be asked to reimburse the OIE for the vaccines. This service is currently being considered to assist developing countries affected by other significant animal diseases.

In conclusion, the recent avian influenza crisis, as well as other emerging and reemerging disease outbreaks, has shown that disease notification cannot be dealt with in isolation: obligations must be accompanied by incentives and benefits. Unless all countries are in a position to rapidly detect and report significant epidemiological events, animal and public health worldwide will be at risk from the appearance of a pandemic or any other devastating disease. Therefore, countries must be assisted in the strengthening of their animal health governance so that all countries, regardless of their status and trade ability, are in a position to detect and report the emergence of significant diseases. At the national level, there must be a paradigm shift from a traditional focus on protection at the borders and restrictions on trade toward the encouragement of the creation of a global surveillance system, as a global public good, that should benefit all countries and should globally minimize the impact of the emergence of a new disease.

As stated earlier, the OIE publishes the animal disease information only after receiving official confirmation from its delegate. The record shows that members have been very quick to respond positively by officially confirming or denying the validity of information when approached by the OIE with information from unofficial sources. However, on a few recent occasions, the OIE took the responsibility to publish unofficial information on the occurrence of important animal diseases and before it was confirmed by the authorities of the affected country.

In theory, the WHO could legally intervene under IHR 2005, even in cases where the information has not been officially provided by the national authorities. However, it is highly unlikely that this would be done with any frequency in cases where the information is not yet in the public domain. The current inability of

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the international community to intervene in serious situations such as the cholera epidemic in Zimbabwe, which is now spreading to neighboring countries, serves as an example.

The international organizations have shown a great spirit of collaboration, evidenced recently in response to the avian influenza crisis. However, to be prepared for future challenges, whether coming from avian influenza or a new emerging disease, the international community as well as leadership at the national level will have to improve and broaden their spirit of interdependence and collaboration.

## INCENTIVES AND DISINCENTIVES TO TIMELY DISEASE REPORTING AND RESPONSE: LESSONS FROM THE INFLUENZA CAMPAIGN[13]

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United Nations

### International Health Regulations 2005 as the Framework for Action

During the past few years, we have witnessed the agreement and application of the revised International Health Regulations (IHR 2005). This is an important intergovernmental framework and series of instruments for collective responses to infectious disease and other public health threats. The proper implementation of the IHR 2005 depends on the full participation of national authorities and other stakeholders. Some of them question the extent to which systems for global governance on health reflect the interests of poor people and their nations: they question the value of globalized thinking and working.

### United Nations System Influenza Coordination

A word on my own involvement in this field: I worked at the WHO in various roles between 1999 and 2005. In September 2005, I was asked by the late J. W. Lee, the then WHO Director-General, and Kofi Annan, the then Secretary-General of the United Nations, to move to New York. My remit was to help different parts of the United Nations (UN) system react to increasing political concern among heads of state and government, particularly from Southeast Asia, about the potential political, societal, and economic impacts of a severe influenza pandemic.

I was asked to establish a temporary mechanism to ensure that the capacities of the whole UN system (technical human health and agriculture bodies, as well

[13]I acknowledge the contribution of my many colleagues in UN systems agencies to the development of these ideas. The responsibility for the way in which I have presented them is mine alone.

[14]Senior UN System Coordinator for Avian and Human Influenza.

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as our full range of social, political, and economic bodies) is made available, in a coherent way, to the governments of our member states.

### Agreement on the Science

In 2005, there was broad agreement on the scientific basis of work being undertaken on avian and pandemic influenza: outstanding research questions were also clear. These include a better understanding of risks associated with the movement of highly pathogenic avian influenza among poultry (particularly in ducks); the relative roles of wild birds, trade, and cross-border movements in spreading H5N1 among birds; and the behavioral patterns that increase risks for human infection still needing some work.

The WHO, FAO, and OIE had established clear strategies for national actions to be undertaken: stamping out highly pathogenic avian influenza (HPAI) when identified, through quick and thorough action; reducing the threat to poultry through introducing biosecurity; monitoring wild birds and charting their movements so that, where possible, wild birds that might be infected with this virus could be separated from domestic birds; reducing the risk of human sporadic cases by limiting the degree to which humans would be in contact with infected birds; and then preparing to contain and mitigate the next influenza pandemic when it happens.

This was to be done within the context of two key areas of standards: the OIE Animal Health standards and the revised IHR.

### Impetus for Coordinated Implementation

The challenge for us in late 2005 was to ensure that governments gave these strategies the impetus necessary for their implementation, leading to the control of HPAI and preparedness for an influenza pandemic. The technical work had to be taken forward within the momentum of the emerging political environment. The Association of Southeast Asian Nations (ASEAN), the United States, the European Union, Canada, and Japan took political initiatives as well.

Within the UN System Influenza Coordination Office, we sought to align different international institutions—including the World Bank, the international organizations of the UN, the regional development banks, other international, regional, and local research bodies—to encourage the collective pursuit of international norms and standards, with the specialized organizations (WHO, FAO, and the OIE) charting a path for the rest of the UN system and the myriad of other organizations becoming engaged in work on avian and pandemic influenza.

From the start, most of those who were involved in this work demonstrated unity of purpose and synergy of action. In general, coordination between the bilateral donors—the foundations, national governments, regional bodies, and

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international nongovernmental groups (including the Red Cross and Red Crescent movement)—was strong.

### The Evolution of an Accountable Movement

We have subsequently sought to identify the incentives that brought many disparate groups to work together. Finance was important, and the partnership has mobilized more than US$3 billion in assistance for avian and human influenza actions between 2005 and 2009. But this, on its own, cannot explain the extent to which national authorities have worked together on these issues. The funds that have been pledged are primarily made available to governments, which have moved comparatively slowly.

An International Partnership on Avian and Pandemic Influenza was established as a basis for this cooperation. Other partnerships were organized at the regional level through the European Union, Asia-Pacific Economic Cooperation (APEC), ASEAN, and other regional groupings. Few of these partnerships were formal: most had real impact on the alignment and ways of working of their members.

We concluded that most of the groups working together in synergy on this issue recognized its value. They found it both operationally useful and reassuring in a situation where there was considerable political urgency and need for concerted action by institutions. Stakeholders from the public, private, and voluntary sectors have valued the opportunity for coherence, joint working, and participation. They have worked together on disease surveillance, reporting, and response. They have joined together to support the evolution of an inclusive movement that enables hundreds of different stakeholders to feel at home. (WHO's GOARN is an example of such collaboration: staff from institutions in the network are ready—at short notice—to assist countries with laboratory and epidemiological investigations.) Pandemic preparedness work has moved forward over the past four years thanks to the efforts of this broader movement, which has been tracked through annual global progress reports using information from countries. These reports, which have involved the full range of UN system agencies and the World Bank, have served as the basis for collective accountability. The reports reveal that, over the four-year period, there has been more rapid reporting of HPAI and more effective, sustained responses to outbreaks of the disease in poultry. The OIE is now pursuing the elimination of H5N1 in the next few years.

### Factors for Success

The annual reports identify seven factors for success: (1) consistent political commitment; (2) resources and capacity to go to scale in response to a threat; (3) interdisciplinary working (particularly animal health and human health); (4) predictable, prompt, fair, and sustained compensation schemes for those who

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lose property or animals as a result of control measures; (5) strong engagement of the public sector, the private sector, and voluntary agencies; (6) clear and unambiguous communication of reliable information (and sharing of uncertainty as appropriate); and (7) the need for a viable and scientific response strategy. Experiences with SARS and other diseases suggest that if information is kept from people they will not feel empowered to be part of the response.

What are the incentives for success? First is the availability of good-quality and accessible information about HPAI outbreaks—based on good mapping of issues, tracking of progress, and risk analysis. Information has been synthesized and made available to those who need it through the efforts of international organizations in response to the needs of their primary clients. WHO provides data to ministries of health and their institutions; and the World Tourism Organization, the International Civil Aviation Organization, the International Monetary Fund, and the International Organization for Migration have provided similar services. This interaction enabled people with a stake in pandemic preparations to feel that they are informed and are part of the global effort.

These information networks have had practical implications. Thanks to the link between the World Tourism Organization and WHO, tourism operating companies have immediate access to available information about the location of disease outbreaks that might mean they have to move either their customers or their staff out of harm's way. Similarly, by knowing what is happening in and around different airports, the International Civil Aviation Organization has helped airport managers to handle these problems. Access to intelligence and its use through agreed procedures facilitates effective preparation: the information itself is an incentive for participation.

A second incentive is the ready availability of instruments and assets needed for effective action. These include the GOARN within WHO and the FAO-OIE Crisis Management Center for Animal Health, which provide a backbone for solidarity and international action. This encourages countries and other stakeholders to be engaged; they know that dependable systems exist that can help them.

A third incentive is the existence of the right legal codes (and means for enforcement) at the country level—for controlling movements of animals, for ensuring compensation when animals have to be killed, and for enabling the consistent nationwide implementation of public health functions (especially in decentralized political systems).

A fourth incentive is the widespread appreciation, among the public, of the pandemic threat and the need to be prepared. Unfortunately, it has not proved easy to sustain the appreciation that animals, and ways in which they are cared for, can pose a risk not only for their own health but also for human health, a risk that can be reduced by changed behavior. The information and compensation needed to encourage behavior changes are often not sufficient. Why do H5N1 deaths in Egypt remain despite the most intense communication campaigns and engagement of all governors in the country?

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A fifth incentive is an empowered civil service—people in government who feel that they are in a position to take the initiative in the face of a disease threat. They sometimes do not believe that their own authorities, or international authorities, are working in their interests. This is a challenge. H5N1—or other diseases—will not be controlled through compulsion and sanctions. It does not work. People start to hide, they do not explain, and they do their best to avoid involvement. So it is absolutely essential to build the necessary trust for effective action.

### Continuing Challenges

There are a number of continuing challenges for our collective effort to control HPAI caused by the H5N1 virus and to prepare for pandemics.

The first is the lack of adequate systems and capacities for data collection and surveillance, laboratory services, and analysis. This applies to both animal and human health.

The second is the reality that some key groups (in some countries) are not fully engaged into the movement for pandemic preparedness. How do you ensure that workers in the poultry industry see it in their collective self-interest to work together with the nongovernmental organizations, researchers, and governments on control and prevention of HPAI? This requires a continuous effort to build and sustain a movement, which will wither away if it is not persistently supported and kept going.

The third challenge is to maintain trust. Committed professionals from countries in Southeast Asia worked with the Rockefeller Foundation to build the Mekong Basin Disease Surveillance Program over many years. This covers several different disease issues. It has generated trust between technicians across borders, and it has survived and continues to do well, despite occasional difficulties at the ministerial or high political level. Similar systems are being established between Bangladesh, India, and Nepal following their HPAI outbreaks in 2008 and 2009.

We are all involved in this effort to build trust. We should ask ourselves from time to time whether we are contributing to trust as effectively as we could.

### Conclusion

In conclusion, we who are involved in this work tend to want to implement the most appropriate (or "right") actions. These norms must be well publicized, continuously reinforced in a very positive, embracing, and open way, and backed with good-quality literature. They include the following:

- *Strong political leadership*. This is the wind in our sails—we move along more easily with it than when it is absent. We have to do our best to sustain the political leadership.

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- *A well-structured legal context* has value and helps us to move forward with confidence.
- *Engaging all stakeholders*—government, private sector, particularly poultry producers, civil society, research groups, the Red Cross, and civil defense.
- *Ensuring that our work leads to benefits for all.* It doesn't have to be a direct linkage, but there has to be some sign that benefits will be there, and they will be shared fairly.
- *Building trust and being skilled at handling mistrust when it exists* (because not all relationships are characterized by trust at all times). We need to insure against periods of mistrust that may build up in relationships that are otherwise very good and we have to know that we are able to cope with these periods.
- *Providing compensation for those who are putting themselves out to do extra work,* be it tracking cases of H5N1 in poultry or doing extra surveillance for humans that are affected. That doesn't just apply to individuals; it applies to countries.

Getting the incentives right is worthwhile so that pandemic preparations are successfully put in place. The reward may well be that when the next severe influenza pandemic strikes, millions of people survive who might otherwise be expected to die. That is the ultimate incentive.

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# Appendix A

# Agenda

**Globalization, Movement of Pathogens (and Their Hosts) and the Revised International Health Regulations**

December 16-17, 2008
Keck Building, Room 100
500 Fifth Street, NW
Washington, DC

## DAY 1: DECEMBER 16, 2008

8:30-9:00 Registration and Continental Breakfast

9:00-9:15 Welcoming Remarks: David Relman, M.D., Chair, and Margaret A. "Peggy" Hamburg, M.D., Vice-Chair, Forum on Microbial Threats

### Session I
### Overview of Globalization and Its Impact on Public and Environmental Health

Moderator: James M. Hughes, M.D.

9:15-9:45 Migration and Development: Past, Present, and Future
Mark J. Miller, Ph.D.
University of Delaware



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| | |
|---|---|
| 9:45-10:15 | People, Borders, and Disease—Health Disparities in a Mobile World<br>Brian Gushulak, M.D.<br>Office of the Director General (Canada), Singapore |
| 10:15-10:45 | Public Health, Global Governance, and the Revised International Health Regulations<br>David Heymann, M.D.<br>World Health Organization |
| 10:45-11:00 | Break |
| 11:00-11:30 | Viral Sovereignty, Global Governance, and the IHR—The Case of H5N1 Virus Sharing Controversy and Its Larger Implications for Global Disease Surveillance<br>David P. Fidler, J.D.<br>Indiana University School of Law |
| 11:30-12:00 | Incentives and Disincentives to Timely Disease Reporting and Response: Lessons from the Influenza Campaign<br>David Nabarro, M.D.<br>United Nations |
| 12:00-12:45 | Discussion |
| 12:45-1:30 | Break and lunch; continued discussion of Session 1 |

**Session II**
**The Global Exchange of People and Disease**

Moderator: Rima Khabbaz, M.D.

| | |
|---|---|
| 1:30-2:00 | Global Travel and Emerging Infections<br>Mary E. Wilson, M.D.<br>Harvard University School of Public Health |
| 2:00-2:30 | Armed Conflict and Infectious Disease<br>Barry S. Levy, M.D., M.P.H.<br>Tufts University School of Medicine |
| 2:30-3:00 | Global Trade Security and the International Health Regulations<br>David M. Bell, M.D.<br>Centers for Disease Control and Prevention |

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| | |
|---|---|
| 3:00-3:30 | Globalization of the Food Supply: Time for Change in Approach<br>David Acheson, M.D.<br>Food and Drug Administration |
| 3:30-4:00 | Break |
| 4:00-4:30 | Asian Tigers, Polka Fever, Yellow Jack, West Nile Virus . . . Its Globalization, Not Global Warming!<br>Paul Reiter, Ph.D.<br>Institute Pasteur |
| 4:30-5:00 | Quantitative Glimpses of Emerging Pathogens as Invasive Species<br>Andrew Dobson, Ph.D.<br>Princeton University |
| 5:00-5:45 | Discussion |
| 5:45-6:00 | Summary remarks<br>David Relman, M.D. |
| 6:00 | Adjourn Day 1 |
| 6:30-9:30 | Working dinner for Forum members, speakers, and staff |

**DAY 2: DECEMBER 17, 2008**

| | |
|---|---|
| 8:30-9:00 | Registration and Continental Breakfast |
| 9:00-9:15 | Summary of Day 1: Margaret A. "Peggy" Hamburg, M.D. |

**Session III**
**Movement of Animal Diseases—Globally and Locally**

Moderator: Lonnie King, D.V.M.

| | |
|---|---|
| 9:15-9:45 | Risky Trade and Emerging Infections: The Sequel<br>Ann Marie Kimball, M.D., M.P.H.<br>APEC Emerging Infections Network |
| 9:45-10:15 | Animal Health Regulations<br>Alejandro B. Thiermann, D.V.M., Ph.D.<br>World Organisation for Animal Health (OIE)/<br>U.S. Department of Agriculture |

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10:15-10:45 Break

10:45-11:15 Public Health Impact of Trade in Animals
Nina Marano, D.V.M., M.P.H., Dipl ACVPM
Centers for Disease Control and Prevention

11:15-12:00 Discussion

12:00-12:45 Break and lunch; continued discussion of Session III

**Session IV**
**Novel Approaches to Disease Surveillance and Response**
**(Normative vs. Reality)**

Moderator: James LeDuc, Ph.D.

12:45-1:15 WHO Activities in Relation to the OIE
Ottorino Cosivi, D.V.M.
World Health Organization

1:15-1:45 Capacity Building Under the IHR to Address Public Health Emergencies of International Concern
May C. Chu, Ph.D.
World Health Organization

1:45-3:00 Panel Discussion of the "Intent" of the IHRs and the "Realities" of Their Implementation

- Oyewale "Wally" Tomori, D.V.M., Ph.D., Redeemer's University, Nigeria
- May C. Chu, Ph.D.
- David M. Bell, M.D.
- David P. Fidler, J.D.

3:00-3:45 Discussion

3:45-4:00 Concluding Remarks/Meeting Adjourns

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# Appendix B

# Acronyms

| | |
|---|---|
| AFP | Acute Flaccid Paralysis |
| AFRO | World Health Organization Regional Office for Africa |
| AIDS | Acquired Immune Deficiency Syndrome |
| AMRO | World Health Organization Regional Office for the Americas |
| ANPRM | Advance Notice of Proposed Rulemaking |
| APEC | Asia-Pacific Economic Cooperation |
| ARO | Alert Response Operations |
| ASEAN | Association of Southeast Asian Nations |
| BATMN | Boston Area Travel Medicine Network |
| BCTF | Bushmeat Crisis Task Force |
| BSE | Bovine Spongiform Encephalopathy |
| BTV | Bluetongue Virus |
| CBD | Convention on Biological Diversity |
| CDC | Centers for Disease Control and Prevention |
| CHIKV | Chikungunya virus |
| CSIRO | Commonwealth Scientific and Industrial Research Organization |
| DENV | Dengue Virus |
| EIS | Events Information Site |
| EMRO | World Health Organization Regional Office for Eastern Mediterranean |
| EMS | Event Management System |



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| | |
|---|---|
| EU | European Union |
| EURO | World Health Organization Regional Office for Europe |
| FAO | Food and Agriculture Organization of the United Nations |
| FDA | Food and Drug Administration |
| GDP | Gross Domestic Product |
| GLEWS | Global Early Warning and Response System for Major Animal Diseases |
| GOARN | Global Outbreak and Response Network |
| GPHIN | Global Public Health Information Network |
| HIV | Human Immunodeficiency Virus |
| HPAI | Highly Pathogenic Avian Influenza |
| IDSR | Integrated Disease Surveillance and Response |
| IHR | International Health Regulations |
| IOM | Institute of Medicine |
| LEMIS | U.S. Fish and Wildlife Department's Law Enforcement Management |
| MDR | Multidrug Resistance |
| MZCP | Mediterranean Zoonoses Control Programme |
| NAFTA | North American Free Trade Agreement |
| NFP | National Focal Point |
| NGO | Nongovernmental organization |
| NHPs | nonhuman primates |
| NIC | National Intelligence Council |
| NRC | National Research Council |
| OASIS | Organization for the Advancement of Structured Information Standards |
| OECD | Organisation for Economic Co-operation and Development |
| OFFLU | OIE/FAO Animal Influenza Laboratory Network |
| OIC | Organization of Islamic Conferences |
| OIE | World Organization for Animal Health (Office International des Epizooties) |
| PAHO | Pan American Health Organization |
| PANAFTOSA | Pan American Center for Foot-and-Mouth Disease |
| PEP | Post-exposure Prophylaxis |

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| | |
|---|---|
| PERV | Porcine Endogenous Retrovirus |
| PHEICs | Public Health Emergencies of International Concern |
| | |
| SARS | Severe Acute Respiratory Syndrome |
| SEARO | World Health Organization Regional Office for South-East Asia |
| SPS | Sanitary and Phytosanitary |
| | |
| TRIPS | Trade-Related Aspects of Intellectual Property Rights |
| | |
| UN | United Nations |
| UNESCO | United Nations Educational, Scientific, and Cultural Organization |
| UNICEF | United Nations Children's Fund |
| UNWTO | United Nations World Tourism Organization |
| USDA | Unites States Department of Agriculture |
| USDA/APHIS | U.S. Department of Agriculture, Animal and Plant Health Inspection Service |
| | |
| VFR | Visiting Friends and Relatives |
| | |
| WEF | World Economic Forum |
| WHA | World Health Assembly |
| WHO | World Health Organization |
| WNV | West Nile Virus |
| WPRO | World Health Organization Regional Office for Western Pacific |
| WTO | World Trade Organization |
| | |
| XDR | Extensive Drug Resistance |

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# Appendix C

# Glossary

**Animal Husbandry:** The science of breeding, feeding, and care of domestic animals; includes housing and nutrition (http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=mesh&list_uids=68000822&dopt=Full).

**Anophelines:** A genus of mosquitoes that includes all mosquitoes that transmit malaria to humans (http://www.merriam-webster.com).

**Anthroponotic:** Transmission from human to human and potentially from human to animal.

**Antibiotic:** Class of substances that can kill or inhibit the growth of some groups of microorganisms. Used in this report to refer to chemicals active against bacteria. Originally antibiotics were derived from natural sources (e.g., penicillin from molds), but many currently used antibiotics are semisynthetic and modified with additions of man-made chemical components. See *Antimicrobials.*

**Antibiotic Resistance:** Property of bacteria that confers the capacity to inactivate or exclude antibiotics or a mechanism that blocks the inhibitory or killing effects of antibiotics.

**Antimicrobials:** Class of substances that can destroy or inhibit the growth of pathogenic groups of microorganisms, including bacteria, viruses, parasites, and fungi.

**Arboviral Diseases:** Shortened form of arthropod-borne virus. Any of a group of viruses that are transmitted to humans and animals by mosquitoes, ticks, and



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sand flies; they include such agents as yellow fever and eastern, western, and Venezuelan equine encephalitis viruses.

**Arthralgia:** (Joint pain) or stiffness without joint swelling (http://wonder.cdc.gov/wonder/help/vaers/reportable.htm).

**Arthropod:** As used in this report, refers to insects and ticks, many of which are medically important as vectors of infectious diseases.

**Arthropod-borne:** Capable of being transmitted by insect and tick (arthropod) vectors.

**Asymptomatic:** Presenting no symptoms of disease.

**Autopsy:** Systematic examination of the body of a deceased person by a qualified pathologist. The body is inspected for the presence of disease or injury; specimens of the vital organs and/or body fluids may be taken for microscopic, chemical, or other tests.

**Bacteria:** Microscopic, single-celled organisms that have some biochemical and structural features different from those of animal and plant cells.

**Biological weapons:** A harmful biological agent (such as a pathogenic microorganism or a neurotoxin) used as a weapon to cause death or disease usually on a large scale (http://www.merriam-webster.com).

**Biota:** The animal and plant life of a given region (http://www.epa.gov/OCEPAterms/bterms.html).

**Bioterrorism:** Terrorism involving use of biological warfare agents (as disease causing viruses or herbicides).

**Botulism:** A rare but serious paralytic illness caused by a nerve toxin. Symptoms of botulism include double vision, blurred vision, drooping eyelids, slurred speech, difficulty swallowing, dry mouth, and muscle weakness. The illness can cause paralysis, respiratory failure, and death (http://www.fsis.usda.gov/Fact_Sheets/Frozen_Fully_Cooked_Products_&_Botulism/index.asp).

**Bushmeat:** Wildlife species which are hunted in the "bush," or forests (http://www.wcs-congo.org/01ecosystemthreats/02bushmeat/104whatisbushmeat.html).

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**Chemoprophylaxis:** The use of drugs or biologics taken by asymptomatic persons to reduce the risk of developing a disease (http://odphp.osophs.dhhs.gov/pubs/guidecps/text/ii_met~1.txt).

**Communicable Disease:** An infectious disease transmissible (as from person to person) by direct contact with an affected individual or the individual's discharges or by indirect means (as by a vector).

**Disease:** As used in this report, refers to a situation in which infection has elicited signs and symptoms in the infected individual; the infection has become clinically apparent.

**Emerging infections:** Any infectious disease that has come to medical attention within the last two decades or for which there is a threat that its prevalence will increase in the near future (IOM, 1992). Many times, such diseases exist in nature as zoonoses and emerge as human pathogens only when humans come into contact with a formerly isolated animal population, such as monkeys in a rain forest that are no longer isolated because of deforestation. Drug-resistant organisms could also be included as the cause of emerging infections since they exist because of human influence. Some recent examples of agents responsible for emerging infections include human immunodeficiency virus, Ebola virus, and multidrugresistant *Mycobacterium tuberculosis,* and H1N1 influenza A.

**Emerging infectious diseases:** Infections that are rapidly increasing in incidence or geographic range.

**Emigration:** To leave one's usual country of residence to settle in another.

**Encephalitis:** An acute inflammatory disease of the brain due to direct viral invasion or to hypersensitivity initiated by a virus or other foreign protein.

**Endemic:** Present in a community or common among a group of people; said of a disease prevailing continually in a region.

**Enteric:** Of, relating to, or affecting the intestines.

**Enzootic:** A disease of low morbidity that is constantly present in an animal community.

**Epidemic:** The condition in which a disease spreads rapidly through a community in which that disease is normally not present or is present at a low level.

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**Epidemiology:** Study of the distribution and determinants of health-related states or events in specified populations. Epidemiology is the basic quantitative science of public health.

**Epizootic:** A disease of high morbidity that is only occasionally present in an animal community.

**Eradication:** Reduction of the worldwide incidence of a disease to zero as a result of deliberate efforts (http://www.cdc.gov/mmwr/preview/mmwrhtml/su48a7.htm).

**Etiologic agent:** The organism that causes a disease.

**Etiological:** Of or pertaining to causes or origins (www.dictionary.com).

**Etiology:** Science and study of the causes of diseases and their mode of operation.

**Extensively Drug Resistant Tuberculosis (XDR-TB):** A relatively rare type of MDR-TB. XDR-TB is defined an *M. tuberculosis* isolate that is resistant to isoniazid and rifampin plus any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin; for more information see http://www.cdc.gov/tb/pubs/tbfactsheets/mdrtb.htm).

**Flavivirus:** Any of a group of arboviruses that contain a single strand of RNA, are transmitted by ticks and mosquitoes, and include the causative agents of dengue, Japanese B encephalitis, and yellow fever.

**Food Contamination:** Poisonous or deleterious substances, such as chemical contaminants, which may or ordinarily render it harmful to health (http://www.fda.gov/Food/FoodSafety/FoodContaminantsAdulteration/default.htm).

**Foodborne Diseases:** Disease caused by consuming contaminated foods or beverages. Many different disease-causing microbes, or pathogens, can contaminate foods, so there are many different foodborne infections. In addition, poisonous chemicals, or other harmful substances can cause foodborne diseases if they are present in food (http://www.cdc.gov/ncidod/dbmd/diseaseinfo/foodborneinfections_g.htm).

**Genomics:** The study of all the genes in a person, as well as interactions of those genes with each other and with that person's environment (http://www.cdc.gov/genomics/faq.htm).

**Globalization:** The increased interconnectedness and interdependance of peoples and countries, is generally understood to include two interrelated elements: the

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opening of borders to increasingly fast flows of goods, services, finance, people and ideas across international borders; and the changes in institutional and policy regimes at the international and national levels that facilitate or promote such flows (http://www.who.int/trade/glossary/story043/en/index.html).

**Hantavirus:** A group of viruses that cause hemorrhagic fever and pneumonia. Hantaviruses are transmitted to humans by contact direct or indirectly with the saliva and excreta of rodents such as deer mice, field mice, and ground voles.

**Heparin:** A blood-thinning drug (http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM112597).

**Herd immunity:** A reduction in the probability of infection that is held to apply to susceptible members of a population in which a significant proportion of the individuals are immune because the chance of coming in contact with an infected individual is less.

**Host:** Animal or plant that harbors or nourishes another organism.

**Immigration:** To arrive and take up permanent residence in a country other than one's usual county of residence.

**Immune-Competence:** The ability of the immune system to respond appropriately to an antigenic stimulation (http://medical-dictionary.thefreedictionary.com/immune+competence).

**Immunologically Compromised:** A condition (caused, for example, by the administration of immunosuppressive drugs or irradiation, malnutrition, aging, or a condition such as cancer or HIV disease) in which an individual's immune system is unable to respond adequately to a foreign substance.

**Incubation Period:** The time from the moment of inoculation (exposure to the infecting organism) to the appearance of clinical manifestations of a particular infectious disease (http://agclass.nal.usda.gov/agt/mtwdk.exe?k=default&l=60&w=47104&n=1&s=5&t=2).

**Infection:** The invasion of the body or a part of the body by a pathogenic agent, such as a microoganism or virus. Under favorable conditions the agent develops or multiplies, the results of which may produce injurious effects. Infection should not be confused with disease.

**Inoculum:** Collective term for microorganisms or their parts (spores, mycelial fragments, etc.) which are capable of infection or symbiosis when transferred to

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a host (http://agclass.nal.usda.gov/agt/mtwdk.exe?k=default&l=60&w=837&n=1&s=5&t=2).

**Insectivorous Mammals (insectivores):** Small mammals (shrews and moles) with short, dense fur, five clawed toes on each foot, and small eyes and ears. As the name implies, insectivores eat many insects and their larvae, however, they also eat many other invertebrates. They are land-dwellers, burrowers, and some spend much of their life in water (http://www.dcnr.alabama.gov/watchable-wildlife/what/Mammals/Insectivores/).

**Intellectual Property:** Property (as an idea, invention, or process) that derives from the work of the mind or intellect; *also* an application, right, or registration relating to this (http://www.merriam-webster.com/dictionary/Intellectual%20Property).

**Intermediate Host:** A host which is normally used by a parasite in the course of its life cycle and in which it may multiply asexually but not sexually (http://www.merriam-webster.com/dictionary/intermediate%20host).

**International Health Regulations (IHR):** An international legal instrument that is binding on 194 countries across the globe, including all the member states of WHO. Their aim is to help the international community prevent and respond to acute public health risks that have the potential to cross borders and threaten people worldwide. The IHR, which entered into force on June 15, 2007, require countries to report certain disease outbreaks and public health events to WHO. Building on the unique experience of WHO in global disease surveillance, alert and response, the IHR define the rights and obligations of countries to report public health events, and establish a number of procedures that WHO must follow in its work to uphold global public health security (http://www.who.int/topics/international_health_regulations/en/).

**Iron Curtain:** The political, military, and ideological barrier erected by the Soviet Union after World War II to seal off itself and its dependent eastern European allies from open contact with the West and other noncommunist areas (http://www.britannica.com/EBchecked/topic/294419/Iron-Curtain).

**Latency:** Delay between exposure to a disease-causing agent and manifestation of the disease (onset of infectiousness) (http://www.cdc.gov/niosh/docs/2000-127/chartbk9.htm).

**Microbe:** A microorganism or biologic agent that can replicate in humans (including bacteria, viruses, protozoa, fungi, and prions).

**Microbial Threat:** Microbes that lead to disease in humans.

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**Microbiology:** A branch of biology dealing especially with microscopic forms of life.

**Migration:** The regular, usually seasonal, movement of all or part of an animal population to and from a given area (http://www.britannica.com/EBchecked/topic/381854/migration).

**Mitigation**: Initiatives that reduce the risk from natural and man-made hazards.

**Melamine:** An industrial chemical that can cause health problems such as kidney disease (http://wwwn.cdc.gov/travel/content/in-the-news/melamine-china.aspx).

**Morbidity:** Diseased condition or state.

**Mortality:** The quality or state of being mortal; the number of deaths in a given time or place; the proportion of deaths to population.

**Multiple Resistance or Multi-Drug Resistance Tuberculosis (MDR-TB):** Property of bacteria that are resistant to more than one antibiotic. In this report, MDR refers to Tuberculosis that is resistant to at least two of the best anti-tuberculosis drugs, isoniazid and rifampin. These drugs are considered first-line drugs and are used to treat all individuals with tuberculosis (for more information, see http://www.cdc.gov/tb/pubs/tbfactsheets/mdrtb.htm).

**Mutation:** Genetic change that can occur either randomly or at an accelerated rate through exposure to radiation or certain chemicals (mutagens) and may lead to change in structure of the protein coded by the mutated gene.

**Myalgia:** Muscle pain.

**Necropsy:** An autopsy performed on an animal.

**Notifiable Disease:** Disease physicians are required to report to state health departments.

**Oviposit:** To lay eggs, especially by means of an ovipositor (a tube in many female insects that extends from the end of the abdomen and is used to lay eggs) (http://www.thefreedictionary.com/ovipositor).

**Paleolithic Period:** Ancient cultural stage, or level, of human development, characterized by the use of rudimentary chipped stone tools (http://www.britannica.com/EBchecked/topic/439507/Paleolithic-Period).

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**Pandemic:** Occurring over a wide geographic area and affecting an exceptionally high proportion of the population.

**Paracetamol (acetaminophen):** A drug used in the treatment of mild pain, such as headache and pain in joints and muscles, and to reduce fever. The drug inhibits prostaglandin synthesis in the central nervous system. Overdoses can cause fatal liver damage (http://www.britannica.com/EBchecked/topic/3205/acetaminophen).

**Paramyxoviridae:** Important pathogens of humans and a common cause of respiratory disease in children (http://virus.stanford.edu/paramyxo/paramyxo.html). In this report, Paramyxoviridae is used to refer to the Nipah virus, a newly emerging zoonosis that causes severe disease in both animals and humans. The natural host of the virus are fruit bats of the Pteropodidae Family, Pteropus genus (http://www.who.int/csr/disease/nipah/en/index.html).

**Parasite:** An organism that lives in or on and takes its nourishment from another organism. A parasite cannot live independently. Parasitic diseases include infections by protozoa, helminths, and arthropods (http://www.medterms.com/script/main/art.asp?articlekey=4769).

**Patency:** In this report patency refers to the patent period—the period between acquisition of the parasite and the time when eggs, larvae, or microfilariae are shed (http://books.google.com/books?id=oKSEhVMVrJ4C&pg=PA3&lpg=PA3&dq=patency+and+parasites&source=bl&ots=Wh45JBXqGB&sig=oYApNDLeVhJ3mQZCGCqi2hNNlZE&hl=en&ei=ac1gSoqdItqBtgfEv5XRDA&sa=X&oi=book_result&ct=result&resnum=4).

**Pathogen:** Organism capable of causing disease.

**Pathogenic:** Capable of causing disease.

**Pathology:** The branch of medicine concerned with disease, especially its structure and its functional effects on the body (http://www.biology-online.org/dictionary/Pathology).

**Phylogeny:** The connections between all groups of organisms as understood by ancestor/descendant relationships (http://www.ucmp.berkeley.edu/exhibit/introphylo.html).

**Physiochemical:** Of or relating to physiological chemistry.

**Prevalence:** Total number of cases (new as well as previous cases) of a disease in a given population at a point in time.

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**Prions:** A newly discovered type of disease-causing agent, neither bacterial nor fungal nor viral, and containing no genetic material. A prion is a protein that occurs normally in a harmless form. By folding into an aberrant shape, the normal prion turns into a rogue agent. It then co-opts other normal prions to become rogue prions. They have been held responsible for a number of degenerative brain diseases, including Mad Cow disease, Creutzfeldt-Jakob disease, and possibly some cases of Alzheimer's disease.

**Prophylaxis:** Measures designed to preserve health (as of an individual or of society) and prevent the spread of disease (http://www.merriam-webster.com/dictionary/prophylaxis).

**Public Health:** The art and science of dealing with the protection and improvement of community health by organized community effort and including preventive medicine and sanitary and social health.

**Quarantine:** The enforced isolation or restriction of free movement imposed to prevent the spread of a contagious disease.

**Quinolones:** Class of purely synthetic antibiotics that inhibit the replication of bacterial DNA; includes ciprofloxacin and fluoroquinolone.

**Radiological Agents:** Materials that emit radiation that can harm living organisms (http://books.google.com/books?id=XdXpn6NH2GcC&pg=PA363&lpg=PA363&dq=radiological+agents&source=bl&ots=5CneVzp3-e&sig=Z6Y8qF9prbJx7hdI510dNRGBj_Q&hl=en&ei=edFgSpq8MaCwtgeM16zWDA&sa=X&oi=book_result&ct=result&resnum=2).

**Recombine:** The process by which the combination of genes in an organism's offspring becomes different from the combination of genes in that organism (http://www.bio-medicine.org/biology-definition/Genetic_recombination/).

**Reservoir:** Any person, animal, arthropod, plant, soil, or substance (or combination of these) in which an infectious agent normally lives and multiplies, on which it depends primarily for survival, and in which it reproduces itself in such manner that it can be transmitted to a susceptible vector.

**Resistance:** See *Antibiotic Resistance.*

**Rickettsial Disease:** Caused by organisms within the genus of rickettsiae. Rickettsiae comprise a group of microorganisms that phylogenetically occupy a position between bacteria and viruses (http://emedicine.medscape.com/article/968385-overview).

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***Salmonella*:** A group of bacteria that cause typhoid fever, food poisoning, and enteric fever from contaminated food products.

**Salmonellosis:** An infection with bacteria called *Salmonella*. Most persons infected with *Salmonella* develop diarrhea, fever, and abdominal cramps 12 to 72 hours after infection. The illness usually lasts 4 to 7 days, and most persons recover without treatment (http://www.cdc.gov/nczved/dfbmd/disease_listing/salmonellosis_gi.html).

**Serotype:** The characterization of a microorganism based on the kinds and combinations of constituent antigens present in that organism; a taxonomic subdivision of bacteria based on the above.

**Species Barrier:** Difficulty or impossibility for an infectious agent to pass from one species to another (due to differences between species) (http://www.cite-sciences.fr/lexique/definition1.php?lang=an&id_expo=15&id_habillage=28&iddef=406&idmot=179).

**Stem Cell:** A cell that has the potential to develop into many different cell types in the body during early life and growth (http://stemcells.nih.gov/info/basics/basics1.asp).

**Surge Capacity:** A measurable representation of a health care system's ability to manage a sudden or rapidly progressive influx of patients within the currently available resources at a given point in time (http://www.acep.org/practres.aspx?id=29506).

**Surveillance:** Used in this workshop summary to refer to data collection and recordkeeping to track the emergence and spread of disease-causing organisms such as antibiotic-resistant bacteria.

**Syndrome:** A group or recognizable pattern of symptoms or abnormalities that indicate a particular trait or disease (http://www.genome.gov/glossary.cfm?key=syndrome).

**Temporal Barrier:** A barrier which blocks the movement of the entire population of an organism some of the time (http://wdfw.wa.gov/hab/ahg/shrg/11-shrg_fish_passage_restoration.pdf).

**Transmission**: Process by which a pathogen passes from a source of infection to a new host.

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**Universal Precautions:** The use of gloves, protective garments, and masks, when handling potentially infectious or contaminated materials (http://www.who.int/csr/disease/hepatitis/whocdscsrlyo20022/en/index5.html#guidelines).

**Vaccine:** A preparation of living, attenuated, or killed bacteria or viruses, fractions thereof, or synthesized or recombinant antigens identical or similar to those found in the disease-causing organisms, that is administered to raise immunity to a particular microorganism.

**Vector:** A carrier, especially an arthropod, that transfers an infective agent from one host (which can include itself) to another.

**Vector-borne:** Transmitted from one host to another by a vector.

**Viral Sovereignty:** Deadly viruses are the sovereign property of individual nations even though they cross borders and could pose a pandemic threat to all the world's peoples. Coined by Indonesia's minister of health, Siti Fadilah Supari (http://www.whothailand.org/LinkFiles/Media_AI25Sep08.pdf).

**Viremia:** The presence of virus in the blood of a host.

**Virulence:** The ability of any infectious agent to produce disease. The virulence of a microoganism (such as a bacterium or virus) is a measure of the severity of the disease it is capable of causing.

**Wheat Gluten:** The mixture of proteins, including gliadins and glutelins, found in wheat grains, which are not soluble in water and which give wheat dough its elastic texture (http://www.thefreedictionary.com/gluten).

**Xenotransplantation:** Any procedure that involves the transplantation, implantation, or infusion into a human recipient of either (a) live cells, tissues, or organs from a nonhuman animal source, or (b) human body fluids, cells, tissues or organs that have had *ex vivo* contact with live nonhuman animal cells, tissues or organs (synonym: *xenogeneic transplantation*) (http://www.fda.gov/BiologicsBloodVaccines/Xenotransplantation/default.htm).

**Zoonotic Infection:** Infection that causes disease in human populations but can be perpetuated solely in nonhuman host animals (e.g., bubonic plague); may be enzootic or epizootic.

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# Appendix D

# Forum Member Biographies

**David A. Relman, M.D.** (*Chair*), is professor of medicine (infectious diseases and geographic medicine) and of microbiology and immunology at Stanford University School of Medicine, and chief of the infectious disease section at the Veterans Affairs (VA) Palo Alto Health Care System. Dr. Relman received his B.S. in biology from the Massachusetts Institute of Technology and his M.D. from Harvard Medical School. He completed his residency in internal medicine and a clinical fellowship in infectious diseases at Massachusetts General Hospital, Boston, after which he moved to Stanford for a postdoctoral fellowship in 1986 and joined the faculty there in 1994. His research focus is on understanding the structure and role of the human indigenous microbial communities in health and disease. This work brings together approaches from ecology, population biology, environmental microbiology, genomics, and clinical medicine. A second area of investigation explores the classification structure of humans and nonhuman primates with systemic infectious diseases, based on patterns of genome-wide gene transcript abundance in blood and other tissues. The goals of this work are to understand mechanisms of host-pathogen interaction, as well as predict clinical outcome early in the disease process. His scientific achievements include the description of a novel approach for identifying previously unknown pathogens; the characterization of a number of new human microbial pathogens, including the agent of Whipple's disease; and some of the most in-depth analyses to date of human indigenous microbial communities. Among his other activities, Dr. Relman currently serves as chair of the Board of Scientific Counselors of the National Institutes of Health (NIH) National Institute of Dental and Craniofacial Research, is a member of the National Science Advisory Board for Biosecurity, and advises a number of U.S. government departments and agencies on matters



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related to pathogen diversity, the future life sciences landscape, and the nature of present and future biological threats. He was cochair of the Committee on Advances in Technology and the Prevention of Their Application to Next Generation Biowarfare Threats for the National Academy of Sciences (NAS). He received the Squibb Award from the Infectious Diseases Society of America (IDSA) in 2001, the Senior Scholar Award in Global Infectious Diseases from the Ellison Medical Foundation in 2002, an NIH Director's Pioneer Award in 2006, and a Doris Duke Distinguished Clinical Scientist Award in 2006. He is also a fellow of the American Academy of Microbiology.

**Margaret A. Hamburg, M.D.** (*Vice Chair*),[1] was the founding vice president, Biological Programs, at the Nuclear Threat Initiative, a charitable organization working to reduce the global threat from nuclear, biological, and chemical weapons, and ran the program for many years. She currently serves as senior scientist for the organization. She completed her internship and residency in internal medicine at the New York Hospital-Cornell University Medical Center and is certified by the American Board of Internal Medicine. Dr. Hamburg is a graduate of Harvard College and Harvard Medical School. Before taking on her current position, she was the assistant secretary for planning and evaluation, U.S. Department of Health and Human Services (HHS), serving as a principal policy adviser to the secretary of HHS, with responsibilities including policy formulation and analysis, the development and review of regulations and legislation, budget analysis, strategic planning, and the conduct and coordination of policy research and program evaluation. Prior to this, she served for nearly six years as the commissioner of health for the City of New York. As chief health officer in the nation's largest city, her many accomplishments included the design and implementation of an internationally recognized tuberculosis control program that produced dramatic declines in tuberculosis cases, the development of initiatives that raised childhood immunization rates to record levels, and the creation of the first public health bioterrorism preparedness program in the nation. She currently serves on the Harvard University Board of Overseers. She has been elected to membership in the Institute of Medicine (IOM), the New York Academy of Medicine, and the Council on Foreign Relations and is a fellow of the American Association for the Advancement of Science (AAAS) and the American College of Physicians.

**David W. K. Acheson, M.D., F.R.C.P.,** is assistant commissioner for food protection in the U.S. Food and Drug Administration (FDA). Dr. Acheson graduated from the University of London Medical School in 1980 and, following training in internal medicine and infectious diseases in the United Kingdom, moved to the

[1]Until June 9, 2009. Dr. Hamburg is currently the Commissioner of the Food and Drug Administration.

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New England Medical Center and Tufts University in Boston in 1987. As an associate professor at Tufts University, he undertook basic molecular pathogenesis research on foodborne pathogens, especially Shiga toxin-producing *Escherichia coli*. In 2001, Dr. Acheson moved his laboratory to the University of Maryland Medical School in Baltimore to continue research on foodborne pathogens. In September 2002, Dr. Acheson accepted a position as chief medical officer at the FDA Center for Food Safety and Applied Nutrition (CFSAN). In January 2004, he also became the director of CFSAN's Food Safety and Security Staff, and in January 2005, the staff was expanded to become the Office of Food Safety, Defense, and Outreach. In January 2007, the office was further expanded to become the Office of Food Defense, Communication, and Emergency Response. On May 1, 2007, Dr. Acheson assumed the position of FDA assistant commissioner for food protection to provide advice and counsel to the commissioner on strategic and substantive food safety and food defense matters. Dr. Acheson has published extensively and is internationally recognized both for his public health expertise in food safety and for his research in infectious diseases. Additionally, Dr. Acheson is a fellow of both the Royal College of Physicians (London) and the IDSA.

**Ruth L. Berkelman, M.D.,** is the Rollins Professor and director of the Center for Public Health Preparedness and Research at the Rollins School of Public Health, Emory University, in Atlanta. She received her A.B. from Princeton University and her M.D. from Harvard Medical School. Board certified in pediatrics and internal medicine, she began her career at the Centers for Disease Control and Prevention (CDC) in 1980 and later became deputy director of the National Center for Infectious Diseases (NCID). She also served as a senior adviser to the director of CDC and as assistant surgeon general in the U.S. Public Health Service. In 2001 she came to her current position at Emory University, directing a center focused on emerging infectious diseases and other urgent threats to health, including terrorism. She has also consulted with the biologic program of the Nuclear Threat Initiative and is most recognized for her work in infectious diseases and disease surveillance. She was elected to the IOM in 2004. Currently a member of the Board on Life Sciences of the National Academies, she also chairs the Board of Public and Scientific Affairs at the American Society of Microbiology (ASM).

**Enriqueta C. Bond, Ph.D.,** is president Emeritus of the Burroughs Wellcome Fund. She received her undergraduate degree from Wellesley College, her M.A. from the University of Virginia, and her Ph.D. in molecular biology and biochemical genetics from Georgetown University. She is a member of the IOM, the AAAS, the ASM, and the American Public Health Association. Dr. Bond chairs the Academies' Board on African Science Academy Development and serves on the Report Review Committee for the Academies. She serves on the board and

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executive committee of the Hamner Institute, the board of the Health Effects Institute, the board of the James B. Hunt Jr. Institute for Educational Leadership and Policy, the council of the National Institute of Child Health and Human Development, and the NIH Council of Councils. In addition Dr. Bond serves on a scientific advisory committee for the World Health Organization (WHO) Tropical Disease Research Program. Prior to being named president of the Burroughs Wellcome Fund in 1994, Dr. Bond served on the staff of the IOM beginning in 1979, becoming its executive officer in 1989.

**Roger G. Breeze, Ph.D.,** received his veterinary degree in 1968 and his Ph.D. in veterinary pathology in 1973, both from the University of Glasgow, Scotland. He was engaged in teaching, diagnostic pathology, and research on respiratory and cardiovascular diseases at the University of Glasgow Veterinary School from 1968 to 1977 and at Washington State University College of Veterinary Medicine from 1977 to 1987, where he was professor and chair of the Department of Microbiology and Pathology. From 1984 to 1987 he was deputy director of the Washington Technology Center, the state's high-technology sciences initiative, based in the College of Engineering at the University of Washington. In 1987, he was appointed director of the U.S. Department of Agriculture's (USDA's) Plum Island Animal Disease Center, a Biosafety Level 3 facility for research and diagnosis of the world's most dangerous livestock diseases. In that role he initiated research into the genomic and functional genomic basis of disease pathogenesis, diagnosis, and control of livestock RNA and DNA virus infections. This work became the basis of U.S. defense against natural and deliberate infection with these agents and led to his involvement in the early 1990s in biological weapons defense and proliferation prevention. From 1995 to 1998, he directed research programs in 20 laboratories in the Southeast for the USDA Agricultural Research Service before going to Washington, DC, to establish biological weapons defense research programs for the USDA. He received the Distinguished Executive Award from President Clinton in 1998 for his work at Plum Island and in biodefense. Since 2004 he has been chief executive officer of Centaur Science Group, which provides consulting services in biodefense. His main commitment is to the Defense Threat Reduction Agency's Biological Weapons Proliferation Prevention Program in Europe, the Caucasus, and Central Asia.

**Steven J. Brickner, Ph.D.,** is an independent consultant based in southeastern Connecticut. He received his Ph.D. in organic chemistry from Cornell University, and completed an NIH postdoctoral research fellowship at the University of Wisconsin–Madison. He is co-inventor of Zyvox® (linezolid), a leading antibiotic with annual worldwide sales first exceeding US$1 billion in 2008. He initiated the oxazolidinone research program at Upjohn and led the team that discovered linezolid and an earlier clinical candidate, eperezolid. Linezolid is the first member of any entirely new class of antibiotics to reach the market in the more than

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35 years since the discovery of the first quinolone. Dr. Brickner is a corecipient of the Pharmaceutical Research and Manufacturers of America (PhRMA) 2007 Discoverers Award, and the 2007 American Chemical Society Award for Team Innovation. He was named the 2002-2003 Outstanding Alumni Lecturer, College of Arts and Science, Miami University (Ohio). Dr. Brickner is a synthetic organic/medicinal chemist with over 25 years of research experience focused entirely on the discovery of novel antibacterial agents during his prior tenure at Upjohn, Pharmacia & Upjohn, and Pfizer. He is an inventor or co-inventor on 21 U.S. patents and has published over 30 peer-reviewed scientific papers, particularly on the oxazolidinones and novel azetidinones. An internationally recognized drug discoverer with over 20 invited speaker presentations, he has been a member of the IOM Forum on Microbial Threats since 1997 and is on the Editorial Advisory Board of *Current Pharmaceutical Design* and the Faculty of 1000 Biology. In February 2009, he established SJ Brickner Consulting, LLC, which primarily offers consulting services on all aspects of medicinal chemistry and drug design related to the discovery and development of new antibiotics.

**John E. Burris, Ph.D.,** became president of the Burroughs Wellcome Fund in July 2008. He is the former president of Beloit College. Prior to his appointment at Beloit in 2000, Dr. Burris served for eight years as director and CEO of the Marine Biological Laboratory in Woods Hole, Massachusetts. From 1984 to 1992 he was at the National Research Council/National Academies, where he served as the executive director of the Commission on Life Sciences. A native of Wisconsin, he received an A.B. in biology from Harvard University in 1971, attended the University of Wisconsin–Madison in an M.D.-Ph.D. program, and received a Ph.D. in marine biology from the Scripps Institution of Oceanography at the University of California–San Diego in 1976. A professor of biology at the Pennsylvania State University from 1976 to 1985, he held an adjunct appointment there until coming to Beloit. His research interests were in the areas of marine and terrestrial plant physiology and ecology. He has served as president of the American Institute of Biological Sciences and is or has been a member of a number of distinguished scientific boards and advisory committees including the Grass Foundation; the Stazione Zoologica "Anton Dohrn" in Naples, Italy; the AAAS; and the Radiation Effects Research Foundation in Hiroshima, Japan. He has also served as a consultant to the National Conference of Catholic Bishops' Committee on Science and Human Values.

**Gail H. Cassell, Ph.D.,** is currently vice president, Scientific Affairs, and Distinguished Lilly Research Scholar for Infectious Diseases, Eli Lilly and Company, in Indianapolis, Indiana. She is the former Charles H. McCauley Professor and chairman of the Department of Microbiology at the University of Alabama Schools of Medicine and Dentistry at Birmingham, a department that ranked first in research funding from NIH during her decade of leadership. She obtained her

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B.S. from the University of Alabama in Tuscaloosa and in 1993 was selected as one of the top 31 female graduates of the twentieth century. She obtained her Ph.D. in microbiology from the University of Alabama at Birmingham and was selected as its 2003 Distinguished Alumnus. She is a past president of the ASM (the oldest and single-largest life sciences organization, with a membership of more than 42,000). She was a member of the NIH Director's Advisory Committee and a member of the Advisory Council of the National Institute of Allergy and Infectious Diseases (NIAID) of NIH. She was named to the original Board of Scientific Councilors of the CDC Center for Infectious Diseases and served as chair of the board. She recently served a three-year term on the Advisory Board of the director of the CDC and as a member of the HHS secretary's Advisory Council of Public Health Preparedness. Currently she is a member of the Science Board of the FDA Advisory Committee to the Commissioner. Since 1996 she has been a member of the U.S.–Japan Cooperative Medical Science Program responsible for advising the respective governments on joint research agendas (U.S. State Department–Japan Ministry of Foreign Affairs). She has served on several editorial boards of scientific journals and has authored more than 250 articles and book chapters. Dr. Cassell has received national and international awards and an honorary degree for her research in infectious diseases. She is a member of the IOM and is currently serving a three-year term on the IOM Council, its governing board. Dr. Cassell has been intimately involved in the establishment of science policy and legislation related to biomedical research and public health. For nine years she was chairman of the Public and Scientific Affairs Board of the ASM; she has served as an adviser on infectious diseases and indirect costs of research to the White House Office of Science and Technology Policy (OSTP); and she has been an invited participant in numerous congressional hearings and briefings related to infectious diseases, antimicrobial resistance, and biomedical research. She has served two terms on the Liaison Committee for Medical Education (LCME), the accrediting body for U.S. medical schools, as well as other national committees involved in establishing policies for training in the biomedical sciences. She has just completed a term on the Leadership Council of the School of Public Health of Harvard University. Currently she is a member of the Executive Committee of the Board of Visitors of Columbia University School of Medicine, the Board of Directors of the Burroughs Wellcome Fund, and the Advisory Council of the School of Nursing of Johns Hopkins.

**Mark Feinberg, M.D., Ph.D.,** is vice president for medical affairs and policy in global vaccine and infectious diseases at Merck & Co., Inc., and is responsible for global efforts to implement vaccines to achieve the greatest health benefits, including efforts to expand access to new vaccines in the developing world. Dr. Feinberg received a bachelor's degree magna cum laude from the University of Pennsylvania in 1978 and his M.D. and Ph.D. degrees from Stanford University School of Medicine in 1987. His Ph.D. research at Stanford was supervised

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by Dr. Irving Weissman and included time spent studying the molecular biology of the human retroviruses—HTLV-I (human T-cell lymphotrophic virus, type I) and HIV—as a visiting scientist in the laboratory of Dr. Robert Gallo at the National Cancer Institute. From 1985 to 1986, Dr. Feinberg served as a project officer for the IOM Committee on a National Strategy for AIDS. After receiving his M.D. and Ph.D. degrees, Dr. Feinberg pursued postgraduate residency training in internal medicine at the Brigham and Women's Hospital of Harvard Medical School and postdoctoral fellowship research in the laboratory of Dr. David Baltimore at the Whitehead Institute for Biomedical Research. From 1991 to 1995, Dr. Feinberg was an assistant professor of medicine and microbiology and immunology at the University of California, San Francisco (UCSF), where he also served as an attending physician in the AIDS-oncology division and as director of the virology research laboratory at San Francisco General Hospital. From 1995 to 1997, Dr. Feinberg was a medical officer in the Office of AIDS Research in the Office of the Director of the NIH, the chair of the NIH Coordinating Committee on AIDS Etiology and Pathogenesis Research, and an attending physician at the NIH Clinical Center. During this period, he also served as executive secretary of the NIH Panel to Define Principles of Therapy of HIV Infection. Prior to joining Merck in 2004, Dr. Feinberg served as professor of medicine and microbiology and immunology at the Emory University School of Medicine, as an investigator at the Emory Vaccine Center, and as an attending physician at Grady Memorial Hospital. At UCSF and Emory, Dr. Feinberg and colleagues were engaged in the preclinical development and evaluation of novel vaccines for HIV and other infectious diseases and in basic research studies focused on revealing fundamental aspects of the pathogenesis of AIDS. Dr. Feinberg also founded and served as the medical director of the Hope Clinic of the Emory Vaccine Center—a clinical research facility devoted to the clinical evaluation of novel vaccines and to translational research studies of human immune system biology. In addition to his other professional roles, Dr. Feinberg has also served as a consultant to, and a member of, several IOM and NAS committees. Dr. Feinberg currently serves as a member of the National Vaccine Advisory Committee and is a member of the Board of Trustees of the National Foundation for Infectious Diseases. Dr. Feinberg has earned board certification in internal medicine; he is a fellow of the American College of Physicians, a member of the Association of American Physicians, and the recipient of an Elizabeth Glaser Scientist Award from the Pediatric AIDS Foundation and an Innovation in Clinical Research Award from the Doris Duke Charitable Foundation.

**Capt. Darrell R. Galloway, M.S.C., Ph.D.,** is chief of the Medical Science and Technology Division for the Chemical and Biological Defense Directorate at the Defense Threat Reduction Agency. He received his baccalaureate degree in microbiology from California State University in Los Angeles in 1973. After completing military service in the U.S. Army as a medical corpsman from 1969

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to 1972, Captain Galloway entered graduate school and completed a doctoral degree in biochemistry in 1978 from the University of California, followed by two years of postgraduate training in immunochemistry as a fellow of the National Cancer Institute (NCI) at the Scripps Clinic and Research Foundation in La Jolla, California. Captain Galloway began his Navy career at the Naval Medical Research Institute in Bethesda, Maryland, where he served as a research scientist working on vaccine development from 1980 to 1984. In late 1984, Captain Galloway left active service to pursue an academic appointment at Ohio State University, where he is now a tenured faculty member in the Department of Microbiology. He also holds appointments at the University of Maryland Biotechnology Institute and the Uniformed Services University of the Health Sciences. He has an international reputation in the area of bacterial toxin research and has published more than 50 research papers on various studies of bacterial toxins. In recent years, Captain Galloway's research has concentrated on anthrax and the development of DNA-based vaccine technology. His laboratory has contributed substantially to the development of a new DNA-based vaccine against anthrax that has completed the first phase of clinical trials. Captain Galloway is a member of the ASM and has served as president of the Ohio branch of that organization. He received an NIH Research Career Development Award. In 2005, Captain Galloway was awarded the Joel M. Dalrymple Award for significant contributions to biodefense vaccine development.

**S. Elizabeth George, Ph.D.,** is deputy director, Biological Countermeasures Portfolio Science and Technology Directorate, Department of Homeland Security. Until it merged into the new department in 2003, she was program manager of the Chemical and Biological National Security Program in the Department of Energy's National Nuclear Security Administration's Office of Nonproliferation Research and Engineering. Significant accomplishments include the design and deployment of BioWatch, the nation's first civilian biological threat agent monitoring system, and PROTECT, the first civilian operational chemical detection and response capability deployed in the Washington, DC, area subway system. Previously, she spent 16 years at the U.S. Environmental Protection Agency (EPA), Office of Research and Development, National Health and Ecological Effects Research Laboratory, Environmental Carcinogenesis Division, where she was branch chief of the Molecular and Cellular Toxicology Branch. She received her B.S. in biology in 1977 from Virginia Polytechnic Institute and State University and her M.S. and Ph.D. in microbiology in 1979 and 1984, respectively, from North Carolina State University. From 1984 to 1986, she was a National Research Council (NRC) fellow in the laboratory of Dr. Larry Claxton at EPA. Dr. George is the 2005 chair of the Chemical and Biological Terrorism Defense Gordon Research Conference. She has served as councillor for the Environmental Mutagen Society and president and secretary of the Genotoxicity and Environmental Mutagen Society. She holds memberships in the ASM and the AAAS

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and is an adjunct faculty member in the School of Rural Public Health, Texas A&M University. She is a recipient of the EPA Bronze Medal and Scientific and Technological Achievement Awards and the Department of Homeland Security (DHS) Under Secretary's Award for Science and Technology. She is the author of numerous journal articles and has presented her research at national and international meetings.

**Jesse L. Goodman, M.D., M.P.H.,** is director of the FDA's Center for Biologics Evaluation and Research, which oversees medical, public health, and policy activities concerning the development and assessment of vaccines, blood products, tissues, and related devices and novel therapeutics, including cellular and gene therapies. He moved to the FDA full-time in 2001 from the University of Minnesota, where he was professor of medicine and director of the Division of Infectious Diseases. A graduate of Harvard College, he received his M.D. from the Albert Einstein College of Medicine; did residency and fellowship training at the Hospital of the University of Pennsylvania and at the University of California, Los Angeles (UCLA), where he was also chief medical resident; and is board certified in internal medicine, oncology, and infectious diseases. He trained in the virology laboratory of Jack Stevens at UCLA and has had an active laboratory program in the molecular pathogenesis of infectious diseases. In 1995, his laboratory isolated the etiologic agent of human granulocytic ehrlichiosis and subsequently characterized fundamental events involved in the infection of leukocytes, including their cellular receptors. He is editor of the book *Tick Borne Diseases of Humans* published by ASM Press in 2005, and is a staff physician and infectious diseases consultant at the NIH Clinical Center and the National Naval Medical Center-Walter Reed Army Medical Center, as well as adjunct professor of medicine at the University of Minnesota. He is active in a wide variety of clinical, public health, and product development issues, including pandemic and emerging infectious disease threats; bioterrorism preparedness and response; and blood, tissue, and vaccine safety and availability. In these activities, he has worked closely with CDC, NIH, and other HHS components, academia, and the private sector, and he has put into place an interactive team approach to emerging threats. This model was used in the collaborative development and rapid implementation of nationwide donor screening of the U.S. blood supply for West Nile virus. He has been elected to the American Society for Clinical Investigation (ASCI) and to the IOM.

**Eduardo Gotuzzo, M.D.,** is principal professor and director at the Instituto de Medicina Tropical Alexander von Humbolt, Universidad Peruana Cayetan Heredia in Lima, Peru, as well as chief of the Department of Infectious and Tropical Diseases at the Cayetano Heredia Hospital. He is also an adjunct professor of medicine at the University of Alabama, Birmingham, School of Medicine. Dr. Gotuzzo is an active member of numerous international societies and has

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been president of the Latin America Society of Tropical Disease (2000-2003), the IDSA Scientific Program (2000-2003), the International Organizing Committee of the International Congress of Infectious Diseases (1994 to present), president-elect of the International Society for Infectious Diseases (1996-1998), and president of the Peruvian Society of Internal Medicine (1991-1992). He has published more than 230 articles and chapters as well as six manuals and one book. Recent honors and awards include being named an honorary member of the American Society of Tropical Medicine and Hygiene in 2002, an associate member of the National Academy of Medicine in 2002, an honorary member of the Society of Internal Medicine in 2000, and a distinguished visitor at the Faculty of Medical Sciences, University of Cordoba, Argentina, in 1999. In 1988 he received the Golden Medal for Outstanding Contribution in the Field of Infectious Diseases awarded by Trnava University, Slovakia.

**Jo Handelsman, Ph.D.,** is a Howard Hughes Medical Institute professor in the Departments of Bacteriology and Plant Pathology and chair of the Department of Bacteriology at the University of Wisconsin (UW)–Madison. She received her Ph.D. in Molecular Biology from the UW–Madison in 1984 and joined the faculty of UW–Madison in 1985. Her research focuses on the genetic and functional diversity of microorganisms in soil and insect gut communities. She is one of the pioneers of functional metagenomics, an approach to accessing the genetic potential of unculturable bacteria in environmental samples. In addition to her research program, Dr. Handelsman is nationally known for her efforts to improve science education and increase the participation of women and minorities in science at the university level. She cofounded the Women in Science and Engineering Leadership Institute at UW–Madison, which has designed and evaluated interventions intended to enhance the participation of women in science. Her leadership in women in science led to her appointment as the first President of the Rosalind Franklin Society and her service on the National Academies' panel that wrote the 2006 report, *Beyond Bias and Barriers: Fulfilling the Potential of Women in Academic Science and Engineering*, which documented the issues of women in science and recommended changes to universities and federal funding agencies. In addition to more than 100 scientific research publications, Dr. Handelsman is coauthor of two books about teaching: *Entering Mentoring* and *Scientific Teaching*. Dr. Handelsman is the editor-in-chief of *DNA and Cell Biology* and the series, Controversies in Science and Technology, and a member of the National Academy of Sciences Board on Life Sciences and the IOM Forum on Microbial Threats. She is a National Academies Mentor in the Life Sciences, a fellow in the American Academy of Microbiology and the AAAS, Director of the Wisconsin Program for Scientific Teaching, and codirector of the National Academies Summer Institute on Undergraduate Education in Biology. In 2008 she received the Alice Evans Award from the ASM in recognition of her mentoring, and in 2009 she received the Carski Award from the ASM in recognition of her

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teaching contributions, and in 2009, Seed Magazine named her "A Revolutionary Mind" in recognition of her unorthodox ideas.

**Carole A. Heilman, Ph.D.,** is the director of the Division of Microbiology and Infectious Diseases (DMID) at NIAID, a component of NIH-HHS. As director of DMID she has responsibility for scientific direction, oversight, and management of all extramural research programs on infectious diseases (except AIDS) within NIH. In addition, since 2001 Dr. Heilman has played a critical role in launching and directing NIAID's extramural biodefense research program. Previously, Dr. Heilman served as deputy director of NIAID's Division of AIDS for three years. Dr. Heilman has a Ph.D. in microbiology from Rutgers University. She did her postdoctoral work in molecular virology at the National Cancer Institute (NCI) and continued at the NCI as a senior staff fellow in molecular oncology. She moved into health science administration in 1986, focusing on respiratory pathogens, particularly vaccine development. She has received numerous awards for scientific management and leadership, including three HHS Secretary's Awards for Distinguished Service for her contributions to developing pertussis, biodefense, and AIDS vaccines.

**David L. Heymann, M.D.,** is currently chair of the Health Protection Agency, United Kingdom, and head of the Global Health Security Programme at Chatham House, London. Until April 2009, he was assistant director-general for Health Security Environment and representative of the director-general for Polio Eradication at WHO. Prior to that, from July 1998 until July 2003, he was executive director of the WHO Communicable Diseases Cluster, which included WHO's programmes on infectious and tropical diseases, and from which the public health response to SARS was mounted in 2003. From October 1995 to July 1998, he was director of the WHO Programme on Emerging and Other Communicable Diseases, and prior to that was the chief of research activities in the WHO Global Programme on AIDS. Dr. Heymann has worked in the area of public health for the past 35 years, 25 of which were on various assignments from the U.S. Centers for Disease Control and Prevention (CDC), and 10 of which have been with WHO. Before joining WHO, Dr. Heymann worked for 13 years as a medical epidemiologist in sub-Saharan Africa (Cameroon, Côte d'Ivoire, Malawi, and the Democratic Republic of Congo, formerly Zaire) on assignment from the CDC in CDC-supported activities. These activities aimed at strengthening capacity in surveillance of infectious diseases and their control, with special emphasis on the childhood immunizable diseases including measles and polio, African hemorrhagic fevers, poxviruses, and malaria. While based in Africa, Dr. Heymann participated in the investigation of the first outbreak of Ebola in Yambuku (former Zaire) in 1976, then again investigated the second outbreak of Ebola in 1977 in Tandala, and in 1995 directed the international response to the Ebola outbreak in Kikwit for WHO. Prior to assignments in Africa he was assigned for two years to

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India as a medical epidemiologist in the WHO Smallpox Eradication Programme. Dr. Heymann's educational qualifications include a B.A. from the Pennsylvania State University, an M.D. from Wake Forest University, a diploma in tropical medicine and hygiene from the London School of Hygiene and Tropical Medicine, and practical epidemiology training in the two-year Epidemic Intelligence Service (EIS) of CDC. He is a member of the IOM; and has been awarded the 2004 Award for Excellence of the American Public Health Association, the 2005 Donald Mackay Award from the American Society for Tropical Medicine and Hygiene, and the 2007 Heinz Award on the Human Condition. Dr. Heymann has been visiting professor at Stanford University, the University of Southern California, and the George Washington University School of Public Health; has published over 145 scientific articles on infectious diseases and related issues in peer-reviewed medical and scientific journals; and has authored several chapters on infectious diseases in medical textbooks. He is currently the editor of the 19th edition of the *Control of Communicable Diseases Manual*, a joint publication of the American Public Health Association and WHO.

**Phil Hosbach** is vice president, New Products and Immunization Policy, at Sanofi Pasteur. The areas under his supervision are new product marketing, state and federal government policy, business intelligence, bids and contracts, medical communications, public health sales, and public health marketing. His current responsibilities include oversight of immunization policy development. He acts as Sanofi Pasteur's principal liaison with CDC. Mr. Hosbach graduated from Lafayette College in 1984 with a degree in biology. He has 20 years of pharmaceutical industry experience, including the past 17 years focused solely on vaccines. He began his career at American Home Products in clinical research in 1984. He joined Aventis Pasteur (then Connaught Labs) in 1987 as clinical research coordinator and has held research and development positions of increasing responsibility, including clinical research manager and director of clinical operations. Mr. Hosbach also served as project manager for the development and licensure of Tripedia, the first diphtheria, tetanus, and acellular pertussis (DTaP) vaccine approved by the FDA for use in U.S. infants. During his clinical research career at Aventis Pasteur, he contributed to the development and licensure of seven vaccines, and he has authored or coauthored several clinical research articles. From 2000 through 2002, Mr. Hosbach served on the board of directors for Pocono Medical Center in East Stroudsburg, Pennsylvania. Since 2003 he has served on the board of directors of Pocono Health Systems, which includes Pocono Medical Center.

**James M. Hughes, M.D.** (*Vice Chair*),[2] is professor of medicine and public health at Emory University's School of Medicine and Rollins School of Public

[2]Current Vice Chair.

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Health, serving as director of the Emory Program in Global Infectious Diseases, associate director of the Southeastern Center for Emerging Biological Threats, and senior adviser to the Emory Center for Global Safe Water. He also serves as senior scientific adviser for infectious diseases to the International Association of National Public Health Institutes funded by the Bill and Melinda Gates Foundation. Prior to joining Emory in June 2005, Dr. Hughes served as director of the NCID at the CDC. Dr. Hughes received his B.A. and M.D. degrees from Stanford University and completed postgraduate training in internal medicine at the University of Washington, infectious diseases at the University of Virginia, and preventive medicine at the CDC. After joining the CDC as an EIS officer in 1973, Dr. Hughes worked initially on foodborne and waterborne diseases and subsequently on infection control in health-care settings. He served as director of CDC's Hospital Infections Program from 1983 to 1988, as deputy director of NCID from 1988 to 1992, and as director of NCID from 1992 to 2005. A major focus of Dr. Hughes' career has been on building partnerships among the clinical, research, public health, and veterinary communities to prevent and respond to infectious diseases at the national and global levels. His research interests include emerging and reemerging infectious diseases; antimicrobial resistance; foodborne diseases; health-care-associated infections; vector-borne and zoonotic diseases; rapid detection of and response to infectious diseases and bioterrorism; strengthening public health capacity at the local, national, and global levels; and prevention of water-related diseases in the developing world. Dr. Hughes is a fellow of the AAAS, the American College of Physicians, and the IDSA, a member of IOM, and a councillor of the American Society of Tropical Medicine and Hygiene.

**Stephen A. Johnston, Ph.D.,** is currently director of the Center for Innovations in Medicine in the Biodesign Institute at Arizona State University. His center focuses on formulating and implementing disruptive technologies for basic problems in health care. The center has three divisions: Genomes to Vaccines, Cancer Eradication, and DocInBox. Genomes to Vaccines has developed high-throughput systems to screen for vaccine candidates and is applying them to predict and produce chemical vaccines. The Cancer Eradication group is working on formulating a universal prophylactic vaccine for cancer. DocInBox is developing technologies to facilitate presymptomatic diagnosis. Dr. Johnston founded the Center for Biomedical Inventions (also known as the Center for Translation Research) at the University of Texas–Southwestern, the first center of its kind in the medical arena. He and his colleagues have developed numerous inventions and innovations, including the gene gun, genetic immunization, TEV (tobacco etch virus) protease system, organelle transformation, digital optical chemistry arrays, expression library immunization, linear expression elements, and others. He also was involved in transcription research for years, first cloning *Gal4* and later discovering functional domains in transcription factors and the connection of

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the proteasome to transcription. He has been professor at the University of Texas Southwestern Medical Center at Dallas and associate and assistant professor at Duke University. He has been involved in several capacities as an adviser on biosecurity since 1996 and is a member of the WRCE SAB and a founding member of BioChem 20/20.

**Kent Kester, M.D.,** is currently the Commander of the Walter Reed Army Institute of Research (WRAIR) in Silver Spring, MD. Dr. Kester holds an undergraduate biology degree from Bucknell University (1982) and an M.D. from Jefferson Medical College (1986). He completed his internship and residency in Internal Medicine at the University of Maryland Hospital/Baltimore VA Medical Center (1989) and a fellowship in Infectious Diseases at the Walter Reed Army Medical Center (1995). A malaria vaccine researcher with over 50 authored or coauthored scientific manuscripts and book chapters, Dr. Kester has played a major role in the development of the candidate falciparum malaria vaccine known as RTS,S, having safely conducted the largest number of experimental malaria challenge studies ever attempted to date. Dr. Kester's previous military medical research assignments have included director of the WRAIR Malaria Serology Reference Laboratory; chief, Clinical Malaria Vaccine Development Program; chief of the WRAIR Clinical Trials Center; and director of the WRAIR Division of Regulated Activities. He currently is a member of the Steering Committee of the NIAID/USUHS Infectious Disease Clinical Research Program, as well as multiple NIAID Safety Monitoring Committees. He also serves as the consultant to the U.S. Army Surgeon General in Medical Research and Development. Board-certified in both internal medicine and infectious diseases, Dr. Kester is also a fellow of both the American College of Physicians and the Infectious Disease Society of America. He holds faculty appointments at both the Uniformed Services University of the Health Sciences and the University of Maryland School of Medicine.

**Gerald T. Keusch, M.D.,** is associate provost and associate dean for global health at Boston University and Boston University School of Public Health. He is a graduate of Columbia College (1958) and Harvard Medical School (1963). After completing a residency in internal medicine, fellowship training in infectious diseases, and two years as an NIH research associate at the Southeast Asia Treaty Organization (SEATO) Medical Research Laboratory in Bangkok, Thailand, Dr. Keusch joined the faculty of the Mt. Sinai School of Medicine in 1970, where he established a laboratory to study the pathogenesis of bacillary dysentery and the biology and biochemistry of Shiga toxin. In 1979 he moved to Tufts Medical School and New England Medical Center in Boston to found the Division of Geographic Medicine, which focused on the molecular and cellular biology of tropical infectious diseases. In 1986 he integrated the clinical infectious diseases program into the Division of Geographic Medicine and Infectious

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Diseases, continuing as division chief until 1998. He has worked in the laboratory and in the field in Latin America, Africa, and Asia on basic and clinical infectious diseases and HIV/AIDS research. From 1998 to 2003, he was associate director for international research and director of the Fogarty International Center at NIH. Dr. Keusch is a member of ASCI, the Association of American Physicians, the ASM, and the IDSA. He has received the Squibb (1981), Finland (1997), and Bristol (2002) awards of the IDSA. In 2002 he was elected to the IOM.

**Rima F. Khabbaz, M.D.,** is director of the National Center for Preparedness, Detection, and Control of Infectious Diseases at CDC. She became director of NCID at CDC in December 2005 and led its transition to the current centers. She is a graduate of the American University of Beirut, Lebanon, where she obtained both her bachelor's degree in science and her medical doctorate degree. She trained in internal medicine and completed a fellowship in infectious diseases at the University of Maryland in Baltimore. She is also a clinical associate professor of medicine (infectious diseases) at Emory University. She began her CDC career in 1980 as an epidemic intelligence service officer in the Hospital Infections Program. She later served as a medical epidemiologist in CDC's Retrovirus Diseases Branch, where she made major contributions to defining the epidemiology of non-HIV retroviruses (HTLV-I and II) in the United States and developing guidance for counseling HTLV-infected persons. Following the hantavirus pulmonary syndrome outbreak in the southwestern United States in 1993, she led CDC's efforts to set up national surveillance for the syndrome. Prior to becoming director of NCID, she was acting deputy director and, before that, associate director for epidemiologic science, NCID. Additional positions held at CDC include associate director for science and deputy director of the Division of Viral and Rickettsial Diseases. She played a leading role in developing CDC's blood safety programs and its food safety programs related to viral diseases. She also had a key role in CDC's responses to outbreaks of new and/or reemerging viral infections including Nipah, Ebola, West Nile, SARS, and monkeypox. She led CDC's field team to the nation's capital during the public health response to the anthrax attack of 2001. She is a fellow of the IDSA, a member of the American Epidemiologic Society, the ASM, and the Council of State and Territorial Epidemiologists. She served on FDA's Blood Product Advisory Committee and on its Transmissible Spongiform Encephalopathy Advisory Committee. She also served on IDSA's Annual Meeting Scientific Program Committee and serves on the society's National and Global Public Health Committee. She is a graduate of the National Preparedness Leadership Initiative at Harvard University and of the Public Health Leadership Institute at the University of North Carolina.

**Lonnie J. King, D.V.M.,** the tenth dean of the College of Veterinary Medicine at The Ohio State University in September 2009. Dr. King most recently directed the National Center for Zoonotic, Vector-Borne and Enteric Diseases at the Centers

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for Disease Control. He served Michigan State University as dean for 10 years and prior to that spent 19 years with the U.S. Department of Agriculture in the Animal and Plant Health Inspection Service. As the nation's chief veterinarian, he worked extensively in global trade agreements and has testified before Congress on issues of emerging diseases and animal health. A member of the Institute of Medicine, Dr. King is board certified by the American College of Veterinary Preventive Medicine. He received his bachelor's degree and Doctor of Veterinary Medicine degree from Ohio State, a Master's degree in epidemiology from the University of Minnesota, and a Master's degree in public administration from American University. A expert in "One Health" and the emergence of new diseases, he is a highly sought-after speaker regarding the convergence of human and animal health.

**Stanley M. Lemon, M.D.,** is the John Sealy Distinguished University Chair and director of the Institute for Human Infections and Immunity at the University of Texas Medical Branch (UTMB) at Galveston. He received his undergraduate A.B. degree in biochemical sciences from Princeton University summa cum laude and his M.D. with honors from the University of Rochester. He completed postgraduate training in internal medicine and infectious diseases at the University of North Carolina at Chapel Hill and is board certified in both. From 1977 to 1983 he served with the U.S. Army Medical Research and Development Command, followed by a 14-year period on the faculty of the University of North Carolina School of Medicine. He moved to UTMB in 1997, serving first as chair of the Department of Microbiology and Immunology, then as dean of the School of Medicine from 1999 to 2004. Dr. Lemon's research interests relate to the molecular virology and pathogenesis of the positive-stranded RNA viruses responsible for hepatitis. He has had a long-standing interest in antiviral and vaccine development and has served as chair of FDA's Anti-Infective Drugs Advisory Committee. He is the past chair of the Steering Committee on Hepatitis and Poliomyelitis of the WHO Programme on Vaccine Development. He is past chair of the NCID-CDC Board of Scientific Counselors and currently serves as a member of the U.S. Delegation to the U.S.–Japan Cooperative Medical Sciences Program. He was cochair of the NAS Committee on Advances in Technology and the Prevention of Their Application to Next Generation Biowarfare Threats, and he recently chaired an IOM study committee related to vaccines for the protection of the military against naturally occurring infectious disease threats.

**Edward McSweegan, Ph.D.,** is a program officer at NIAID. He graduated from Boston College with a B.S. in biology in 1978. He has an M.S. in microbiology from the University of New Hampshire and a Ph.D. in microbiology from the University of Rhode Island. He was an NRC associate from 1984 to 1986 and did postdoctoral research at the Naval Medical Research Institute in Bethesda, Maryland. Dr. McSweegan served as a AAAS diplomacy fellow in the U.S. State Department from 1986 to 1988, where he helped to negotiate science and technology agree-

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ments with Poland, Hungary, and the former Soviet Union. After moving to NIH, he continued to work on international health and infectious disease projects in Egypt, Israel, India, and Russia. Currently, he manages NIAID's bilateral program with India, the Indo–U.S. Vaccine Action Program, and he represents NIAID in the HHS Biotechnology Engagement Program with Russia and related countries. He is a member of AAAS, the ASM, and the National Association of Science Writers. He is the author of numerous journal and freelance articles.

**Stephen S. Morse, Ph.D.,** is professor of epidemiology and founding director of the Center for Public Health Preparedness at the Mailman School of Public Health of Columbia University. He returned to Columbia in 2000 after four years in government service as program manager at the Defense Advanced Research Projects Agency, where he codirected the Pathogen Countermeasures Program and subsequently directed the Advanced Diagnostics Program. Before coming to Columbia, he was assistant professor of virology at the Rockefeller University in New York, where he remains an adjunct faculty member. He is the editor of two books, *Emerging Viruses* (Oxford University Press, 1993; paperback, 1996), which was selected by American Scientist for its list of 100 Top Science Books of the 20th Century, and *The Evolutionary Biology of Viruses* (Raven Press, 1994). He was a founding section editor of the CDC journal *Emerging Infectious Diseases* and was formerly an editor-in-chief of the Pasteur Institute's journal *Research in Virology*. Dr. Morse was chair and principal organizer of the 1989 NIAID-NIH Conference on Emerging Viruses, for which he originated the term and concept of emerging viruses/infections. He has served as a member of the IOM-NAS Committee on Emerging Microbial Threats to Health, chaired its Task Force on Viruses, and was a contributor to the resulting report *Emerging Infections* (1992). He was a member of the IOM Committee on Xenograft Transplantation. Dr. Morse also served as an adviser to WHO and several government agencies. He is a fellow of the New York Academy of Sciences and a past chair of its microbiology section, a fellow of the American Academy of Microbiology of the American College of Epidemiology, and an elected life member of the Council on Foreign Relations. He was the founding chair of ProMED, the nonprofit international Program to Monitor Emerging Diseases, and was one of the originators of ProMED-mail, an international network inaugurated by ProMED in 1994 for outbreak reporting and disease monitoring using the Internet. Dr. Morse received his Ph.D. from the University of Wisconsin–Madison.

**Michael T. Osterholm, Ph.D., M.P.H.,** is director of the Center for Infectious Disease Research and Policy and director of the NIH-sponsored Minnesota Center for Excellence in Influenza Research and Surveillance at the University of Minnesota. He is also professor at the School of Public Health and adjunct professor at the Medical School. Previously, Dr. Osterholm was the state epidemiologist and chief of the acute disease epidemiology section for the Minnesota

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Department of Health. He has received numerous research awards from NIAID and CDC. He served as principal investigator for the CDC-sponsored Emerging Infections Program in Minnesota. He has published more than 300 articles and abstracts on various emerging infectious disease problems and is the author of the best-selling book *Living Terrors: What America Needs to Know to Survive the Coming Bioterrorist Catastrophe*. He is past president of the Council of State and Territorial Epidemiologists. He currently serves on the IOM Forum on Microbial Threats. He has also served on the IOM Committee to Ensure Safe Food from Production to Consumption, and on the IOM Committee on the Department of Defense Persian Gulf Syndrome Comprehensive Clinical Evaluation Program, and as a reviewer for the IOM report *Chemical and Biological Terrorism: Research and Development to Improve Civilian Medical Response*.

**George Poste, Ph.D., D.V.M.,** is director of the Biodesign Institute and Del E. Webb Distinguished Professor of Biology at Arizona State University. From 1992 to 1999, he was chief science and technology officer and president, Research and Development, of SmithKline Beecham (SB). During his tenure at SB, he was associated with the successful registration of 29 drug, vaccine, and diagnostic products. He is chairman of Orchid Cellmark. He serves on the board of directors of Monsanto and Exelixis. He is a distinguished fellow at the Hoover Institution at Stanford University. He is a member of the Defense Science Board of the U.S. Department of Defense and of the IOM Forum on Microbial Threats. Dr. Poste is a board-certified pathologist, a fellow of the Royal Society, and a fellow of the Academy of Medical Sciences. He was awarded the rank of Commander of the British Empire by Queen Elizabeth II in 1999 for services to medicine and for the advancement of biotechnology. He has published more than 350 scientific papers; has coedited 15 books on cancer, biotechnology, and infectious diseases; and serves on the editorial board of several technical journals.

**John C. Pottage, Jr., M.D.,** has been vice president for Global Clinical Development in the Infectious Disease Medicine Development Center at GlaxoSmithKline since 2007. Previously he was senior vice president and chief medical officer at Achillion Pharmaceuticals in New Haven, Connecticut. Achillion is a small biotechnology company devoted to the discovery and development of medicines for HIV, hepatitis C virus (HCV), and resistant antibiotics. Dr. Pottage initially joined Achillion in May 2002. Prior to Achillion, Dr. Pottage was medical director of Antivirals at Vertex Pharmaceuticals. During this time he also served as an associate attending physician at the Tufts New England Medical Center in Boston. From 1984 to 1998, Dr. Pottage was a faculty member at Rush Medical College in Chicago, where he held the position of associate professor, and also served as the medical director of the Outpatient HIV Clinic at Rush-Presbyterian-St. Luke's Medical Center. While at Rush, Dr. Pottage was the recipient of several teaching

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awards and is a member of the Mark Lepper Society. Dr. Pottage is a graduate of St. Louis University School of Medicine and Colgate University.

**Gary A. Roselle, M.D.,** received his medical degree from the Ohio State University School of Medicine in 1973. He served his residency at the Northwestern University School of Medicine and his infectious diseases fellowship at the University of Cincinnati School of Medicine. He is program director for infectious diseases for the Department of Veterans Affairs Central Office in Washington, DC, as well as the chief of the medical service at the Cincinnati VA Medical Center. He is a professor of medicine in the Department of Internal Medicine, Division of Infectious Diseases, at the University of Cincinnati College of Medicine. Dr. Roselle serves on several national advisory committees. In addition, he is currently heading the Emerging Pathogens Initiative for the VA. He has received commendations from the under secretary for health for the VA and the secretary of VA for his work in the Infectious Diseases Program for the VA. He has been an invited speaker at several national and international meetings and has published more than 90 papers and several book chapters.

**Kevin Russell, M.D., M.T.M.&H., F.I.D.S.A. CAPT MC USN,** graduated from the University of Texas Health Science Center San Antonio Medical School in 1990; after a family practice internship he was accepted into the Navy Undersea Medicine program. He was stationed in Panama City, Florida, at the Experimental Diving Unit where he worked in diving medicine research from 1991 to 1995. After a preventive medicine residency with a masters in tropical medicine and hygiene, he was transferred to Lima, Peru, where he became head of the Virology Laboratory. His portfolio included febrile illness (largely arboviral in origin) and HIV surveillance studies in eight different countries of South America, as well as prospective dengue transmission studies. In 2001, he moved back to the states and became the director of the Respiratory Disease Laboratory at the Naval Health Research Center in San Diego, California. Febrile respiratory illness surveillance in recruits of all services was expanded into shipboard populations, Mexican border populations, support for outbreaks, and deployed settings. Validation and integration of new and emerging advanced diagnostic capabilities, utilizing the archives of specimens maintained at the laboratory, became a priority. A BSL-3-Enhanced is currently nearing completion. Projects expanded in 2006 to clinical trials support as Dr. Russell became the principal investigator for the Navy site in the FDA Phase 3 adenovirus vaccines trial, and more recently to support the Phase 4 post-marketing trial of the recently FDA-approved ACAM2000 Smallpox vaccine. Dr. Russell recently became director of the Department of Defense Global Emerging Infections Surveillance and Response System (DoD-GEIS).

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ing the legislative and regulatory affairs of this 42,000-member organization, the largest single biological science society in the world. Previously, she held positions as assistant director of public affairs for ASM; as ASM coordinator of the U.S.–U.S.S.R. Exchange Program in Microbiology, a program sponsored and coordinated by the NSF and the U.S. Department of State; and as a freelance editor and writer. She received her baccalaureate, cum laude, from the University of Massachusetts and is a graduate of the George Washington University programs in public policy and in editing and publications. She is a member of Women in Government Relations, the American Society of Association Executives, and AAAS. She has coauthored articles on research funding, biotechnology, biodefense, and public policy issues related to microbiology.

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**Terence Taylor** is director of the Global Health and Security Initiative and president and director of the International Council for the Life Sciences (ICLS). He is responsible for the overall direction of the ICLS and its programs, which have the goal of enhancing global biosafety and biosecurity. From 1995 to 2005, he was assistant director of the International Institute for Strategic Studies (IISS), a leading independent international institute, and president and executive director of its U.S. office (2001-2005). He studies international security policy, risk analysis, and scientific and technological developments and their impact on political and economic stability worldwide. He was one of IISS's leading experts on issues associated with nuclear, biological, and chemical weapons and their means of delivery. In his previous appointments, he has had particular responsibilities for issues affecting public safety and security in relation to biological risks and advances in the life sciences. He was one of the commissioners to the United Nations Special Commission on Iraq, for which he also conducted missions as a chief inspector. He was a science fellow at the Center for International Secu-

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rity and Cooperation at Stanford University, where he carried out, among other subjects, studies of the implications for government and industry of the weapons of mass destruction treaties and agreements. He has also carried out consultancy work for the International Committee of the Red Cross (ICRC) on the implementation and development of the laws of armed conflict and serves as a member of the Editorial Board of the *ICRC Review*. He has served as chairman of the World Federation of Scientists' Permanent Monitoring Panel on Risk Analysis. He was a career officer in the British Army on operations in many parts of the world, including counterterrorist operations and United Nations peacekeeping. His publications include monographs, book chapters, and articles for, among others, Stanford University, the World Economic Forum, Stockholm International Peace Research Institute (SIPRI), the Crimes of War Project, the *International Herald Tribune*, the *Wall Street Journal*, the *International Defence Review*, the *Independent* (London), *Tiempo* (Madrid), the *International and Comparative Law Quarterly*, the *Washington Quarterly*, and other scholarly journals, including unsigned contributions to IISS publications.

**Murray Trostle, Dr.P.H.,** is a foreign service officer with the U.S. Agency for International Development (USAID), presently serving as the deputy director of the Avian and Pandemic Influenza Preparedness and Response Unit. Dr. Trostle attended Yale University, where he received a master's in public health in 1978, focusing on health services administration. In 1990, he received his doctorate in public health from UCLA. His research involved household survival strategies during famine in Kenya. Dr. Trostle has worked in international health and development for approximately 38 years. He first worked overseas in the Malaysian national malaria eradication program in 1968 and has since focused on health development efforts in the former Soviet Union, Africa, and Southeast Asia. He began his career with USAID in 1992 as a postdoctoral fellow with AAAS. During his career he has worked with a number of development organizations such as the American Red Cross, Project Concern International, and the Center for Development and Population Activities. With USAID, Dr. Trostle has served as director of the child immunization cluster, where he was chairman of the European Immunization Interagency Coordinating Committee and the USAID representative to the Global Alliance on Vaccines and Immunization. Currently, Dr. Trostle leads the USAID Infectious Disease Surveillance Initiative as well as the Avian Influenza Unit.

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