Risks from Microbes on the Rise: Reasons Why and Ways To Prevent Future Epidemics

Although scientists have long known that animals could transmit infections to humans, they are increasingly concerned about animal-borne diseases. All of the recent high-profile infectious diseases in humans have been acquired from animals: mice carrying hantavirus, cows with bovine spongiform encephalopathy (BSE), chickens with avian influenza, birds and mosquitoes carrying West Nile virus, civet cats infected with severe acute respiratory syndrome (SARS)–associated coronavirus. Raised awareness of these animal-to-human diseases transmitted, called zoonotic diseases, has helped contain their spread, but factors such as changes in land use and global travel mean that these infections are an increasing threat to humans worldwide. "You're definitely going to see infections spreading more quickly across the globe. SARS is a vivid example of that," said James M. Hughes, MD, an Assistant Surgeon General and director of the Centers for Disease Control and Prevention's (CDC's) National Center for Infectious Diseases.

Zoonotic diseases are noteworthy among emerging diseases, but, in fact, Hughes said, the CDC is currently on high alert for increases in many other emerging and reemerging infectious diseases. Importation of produce from developing countries has added to the incidence of food-borne infections, including newer pathogens such as *Cyclospora* species and *Listeria monocytogenes* and better known pathogens such as *Salmonella* species and hepatitis A virus. Antibiotic misuse increasingly contributes to a growing problem of resistant pathogens. And the 2001 anthrax attacks are a frightening reminder of the potential for bioterrorism involving infectious agents such as the smallpox virus.

The CDC and other public health agencies have been playing catch-up with microbes ever since the early 1990s. From the period following World War II until then, some experts widely believed that effective vaccines and powerful antibiotics, combined with pesticide use and improved water quality and sanitation practices, would conquer infectious diseases. Public health workers and clinicians grew complacent about surveillance and susceptibility testing. Microbial research fell out of favor with the federal research establishment. But then, after marked declines after World War II, the death rate from infectious disease increased 58% between 1980 and 1992 in the United States, according to the CDC. "In spite of all of the infectious diseases that appeared in the '70s and '80s, including AIDS, toxic shock syndrome, Legionnaires disease, Lyme disease, and multidrug-resistant strains of tuberculosis, very few people paid attention," Hughes said. An Institute of Medicine report in 1992 focused attention on emerging infectious diseases. Using strong language, the report warned that far from receding, the threat from emerging diseases was actually intensifying, and it recommended dramatic, widescale changes in the health care system to improve disease recognition and control.

Steady efforts by the CDC and others have begun to rebuild the seriously deteriorated U.S. public health system. Raised awareness combined with new domestic and international communication systems and advances in technology have improved detection, prevention, and treatment of infections. The budget for the CDC's National Center for Infectious Diseases increased from $175 million in 1992 to $377 million in 2003, with most of this extra funding allocated to work on specific diseases such as West Nile and SARS. Despite this progress, the threat from emerging infectious diseases has grown in the past decade, and experts say that it will only get worse. The reason for emerging infections is multifactorial, the social and economic impact of these infections is widespread, and the solutions are often multidisciplinary. "The reality is that we've always been in a situation of global threat from emerging infectious diseases, but we're now recognizing this in a much broader fashion than we have ever before," said Carole A. Heilman, PhD, director of the division of microbiology and infectious diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health.

In 2003, the Institute of Medicine released a new report on microbial threats, *Microbial Threats to Health: Emergence, Detection, and Response*. As in 1992, the report called for raised awareness of and aggressive action against infectious diseases, this time placing greater emphasis on global surveillance and response. In this article, members of the Institute of Medicine's Forum on Microbial Threats address the issues in light of the recent reappearance of SARS and avian influenza and the first identification of BSE in U.S. cattle.

Multifactorial Causes

Why do infections appear in humans? Most of the new infections affecting humans existed for a long time in nature before something happened to put humans in contact with that infection, according to Stephen S. Morse, PhD, director of the Center for Public Health Preparedness at Columbia University in New York. According to his research, that "something" could be one of many factors. Ecologic changes and agricultural development are the most frequent reasons that infections emerge from obscurity, according to Morse. Scientists have linked Lyme disease to reforestation, which led to increased deer and deer tick populations, followed by population movement into these reforested areas, which exposed humans to the disease carriers. They have linked han-

tavirus to exposure of agriculture workers to infected field mice during the Chinese rice harvest. Hantavirus pulmonary syndrome occurred in the United States in 1993 after weather anomalies—a drought followed by weather warmer and wetter than normal during winter and spring—resulted in greater than normal numbers of field mice coming into contact with humans. Rift Valley fever, the agent for which is transmitted by a mosquito host, has occurred in areas that became inundated after construction of dams. Mosquitoes that thrive in flooded rice fields are a vector for Japanese encephalitis. Scientists have shown how infected ducks transmit influenza virus to pigs, chickens, and other animals, who may then infect humans at live animal markets and during food production processes.

Changes in human demographics, human behavior, and international travel and commerce are additional key factors in emerging infections, Morse said. Mass movement of people into and between urban areas has exposed more people to infections that were once found only in rural areas. Closer living and working environments in urban areas, such as apartment buildings, office complexes, and hospitals, can further facilitate faster disease spread. So does more efficient worldwide travel. Infections move quickly across borders, sometimes even before symptoms develop, as do antibiotic-resistant bacteria. Starting with the spread of yellow fever in the 18th and 19th centuries, ships inhabited by mosquitoes and other arthropods have carried infections to previously unexposed areas. Bilge water released from freighters recently spread strains of cholera to previously cholera-free regions. Human behavior can further affect disease spread, as occurs with sexually transmitted diseases, Morse said, and technology that allows immune-compromised and elderly humans to live longer increases the chances of contracting, and transmitting, infections.

Modern agricultural practices and food production techniques contribute to the emergence of infectious diseases. Over the past 2 decades, Michael T. Osterholm, PhD, MPH, director of the Center for Infectious Disease Research and Policy at the University of Minnesota in Minneapolis, Minnesota, has studied the role of food-borne diseases on human health. Osterholm has tracked the rapid changes in what Americans eat and where food comes from and how it is produced. The recent outbreak of hepatitis A linked to infected green onion is just part of an ever-escalating problem, he said. "We chase the sun around the world today so that produce is always available on our grocery shelves. In doing that, we are in some instances growing it in third-world country conditions where there's greater exposure to infected potable water sources, illnesses carried by migrant workers, and so on. If you were to travel to one of those countries, we'd tell you to boil it, peel it, or don't eat it. Today you can go to a grocery store shelf and buy it, and in many cases it's the same as buying it in the country where it was grown," said Osterholm, who has advocated food irradiation because washing produce does not always decontaminate it. He noted recent cases of foodborne illness caused by previously unknown pathogens: raspberries and lettuce that spread *Cyclospora* infection; unpasteurized apple juice that spread *Escherichia coli* O157:H7; raw poultry, meat, and unpasteurized milk that spread *Campylobacter* species. In addition, we continue to experience outbreaks of foodborne illness caused by more familiar pathogens such as *Salmonella* and *Listeria* species. Now scientists have identified civet cats, which the Chinese eat during the winter months, as the SARS–coronavirus host.

Looking forward, many experts are concerned about the continued emergence of arthropod-borne infections across the globe. Osterholm notes that the occurrence of West Nile virus in the United States in 1999 and seasonal reappearance have not stimulated efforts to ward off the spread of additional arthropod-borne infections to the United States. "If Rift Valley fever or Japanese encephalitis were introduced into this country, they would make West Nile virus seem as if it were a minor cold. And we have virtually no system in place today to address that. The same airplane cargo holds, commerce shipments, and livestock that were bringing mosquitoes into this country 5 years ago are bringing them in today. It's only a matter of time," Osterholm said. Arthropods carrying the agent for Rift Valley fever recently caused outbreaks in countries previously free of the disease. An outbreak of Rift Valley fever in a rural area of Egypt in 2003 resulted in 45 infections, including 17 deaths, and an outbreak in Yemen in 2000 resulted in 653 suspected infections, including 80 deaths.

Widespread Social and Economic Impact

Waiting to respond to infections until after they occur has serious negative social and economic implications. China, Canada, and other countries that experienced SARS outbreaks lost almost all tourism- and transport-based revenue for weeks or months. Canada documented millions of dollars of lost revenue due to a quarantine that kept workers at home and severely reduced daily activities such as bus travel, theater going, and restaurant dining. Furthermore, the response to SARS isolated people in infected countries from the rest of the world or led to their being unwelcome when they tried to travel abroad. SARS also stressed the countries' health care system, and medical costs soared during the disease outbreak.

Bovine spongiform encephalopathy has severely affected the economy in countries with documented infections. In England in 1996, the link between BSE and new-variant Creutzfeldt–Jakob disease led to an immediate 40% decline in domestic beef sales and a 25% decline in the price of beef. Beef export sales fell off completely, and many slaughterhouses closed temporarily, according to the British Ministry of Agriculture, Fisheries and Food. The

overall economic impact of the recent identification of BSE in cattle in the United States remains to be determined, but some countries have banned U.S. beef. In any case, the economic fallout from BSE is undoubtedly far more costly than stricter BSE prevention measures, Osterholm noted.

On a smaller scale, periodic disease outbreaks from bacteria-contaminated produce, milk, meat and poultry have led to the recall of millions of pounds of food and widespread fears about infection. Disease outbreaks may be costly even when they pose no threat of food contamination. A 1998 outbreak of cholera in Tanzania led to a European Union ban on imports from Tanzania, even though subsequent investigation showed little or no risk for cholera transmission at any time. The ban cost Tanzania $36 million, according to the World Health Organization.

A Multidisciplinary Solution

Increasingly, efforts to block emerging diseases must take place on a global scale since stopping a disease outbreak in one country can prevent its spread to other countries. David Heymann, MD, executive director of the communicable diseases division at the World Health Organization in Geneva, Switzerland, listed the 3 keys to global health security: 1) containing known infectious diseases, 2) detecting and responding to unexpected infectious diseases, and 3) improving preparedness and public health infrastructure in countries worldwide. Implementing these measures can be difficult in countries that lack the resources or the political motivation to conduct disease surveillance, detection, and response, Heymann noted. "If SARS has done anything, hopefully it has called the world's attention to the importance of a global alert and response network. The existing WHO-coordinated Global Outbreak Alert and Response Network serves as a backup for national systems that are not yet able to ensure timely disease detection and response," Heymann said.

Experts have called upon the United States to step up global disease monitoring efforts, and public health agencies are working to respond, according to Hughes. But the United States still lacks a strong public health infrastructure. The number of trained public health workers is too small to support expanded infection prevention and control measures, according to Hughes. Furthermore, systems to promote communication between clinicians and veterinarians and public health officials are rudimentary. For instance, veterinarians noted the widespread death of crows weeks before a physician reported 2 unusual cases of encephalitis to public health officials at the New York City health department. The clinician's early communication with the public health department improved identification of later West Nile infections in patients, but the dead birds were an early warning sign that might have led to anticipation of the epidemic and perhaps earlier implementation of measures to contain it. "These kinds of situations just beg collaborative efforts," Hughes said.

In an effort to strengthen communication and shore up gaps in disease detection, public health agencies are calling on health care providers, laboratory workers, and other field staff to participate in emerging infections surveillance and reporting. In recent years, the CDC has established several provider-based sentinel networks to track conditions that are likely to be seen by clinicians but that may be missed by traditional surveillance approaches. These networks include the Infectious Diseases Society of America Emerging Infections Network (IDSA EIN), a network facilitated primarily through IDSA membership and including more than 800 infectious disease physicians; EMERGEncy ID Net, an interdisciplinary, multicenter, emergency department–based network; the Global Emerging Infections Sentinel Network (GeoSentinel), a network of travel clinics under the auspices of the International Society of Travel Medicine; and the Border Infectious Disease Surveillance (BIDS) project, a binational surveillance system for infectious diseases along the United States–Mexico border. Other information-sharing systems, such as ProMED-mail, an online disease monitoring program, assist local, national, and international organizations in disseminating reports of infectious disease outbreaks, including preliminary and unofficial reports. A report on ProMED-mail contained what proved to be the earliest description of a SARS case in China, according to Hughes. Subscribers to this list-serve are, in effect, part of an early warning network for emerging infections. These subscribers, as well as many of the sentinel network participants, are practicing physicians and researchers who voluntarily monitor disease outbreaks and communicate noteworthy emerging diseases information with their colleagues and the CDC.

The federal government has allocated additional public health funding for state and local health agencies, but cuts in local and state budgets often offset these gains. State and local health departments employ fewer epidemiologists now than 10 years ago, when the supply of trained personnel was already too low. Furthermore, Osterholm said, the country's schools of public health receive little funding to support students who want to enter the field. "This is the same workforce that we're going to have to count on in a crisis," Osterholm said. The recent Institute of Medicine report called for the creation of interdisciplinary academic centers that address microbial threats to health and facilitate workforce training in epidemiologic and infectious disease prevention and control, but the government has not yet allocated any funding for these centers.

Bioterrorism preparedness, at least, has provided a boost to public health. For instance, the country's rejuvenated laboratory response network now incorporates more than 100 laboratories that have the equipment, reagents, and secure communication capacity to work on high-priority bioterrorism

threat agents. While intended for bioterrorism preparedness, these laboratories helped with SARS surveillance in the United States. Also, increased funding of bioterrorism-related research has advanced understanding of microbes.

Looking forward, most experts believe that the United States is better prepared today than it was 3 years ago—before the anthrax attacks and before SARS—to protect and respond to infectious disease threats. They credit the gains to continued pressure from scientific and medical organizations such as the Institute of Medicine, as well as from the media. Further progress, the experts agree, will depend on the political will to sustain efforts to develop all levels of the public health infrastructure and to support research that leads to new diagnostic and surveillance systems, new vaccines, and new treatment regimens. Even with all of these improvements, "you can always create scenarios that would overwhelm the capacity of the public health system," Hughes said. What would have happened if the SARS event had happened in Chicago or Minneapolis instead of Toronto? The United States' capacity to respond would likely have been as effective as Toronto's, requiring quarantines and a large number of hospital beds and stretching the entire country's resources, Osterholm said. Now imagine a SARS outbreak that occurred in Chicago, Atlanta, Philadelphia, and Minneapolis all at the same time. "That might be too much. The United States must determine what it needs in order to respond to and prevent a problem of this scope," Osterholm said. Although preventing all infectious disease outbreaks remains an impossible goal, the health care system can stop many more than it prevents now. "With emerging infectious diseases, the situation is pay now, or pay later," he said. "Real investment now could save us big money down the road." And a lot of human suffering, too.

–Jennifer Fisher Wilson
Science Reporter, *Annals of Internal Medicine*

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E-mail: jenwilson@acponline.org.