SARS Revisited: The Challenge of Controlling Emerging Infectious Diseases at the Local, Regional, Federal, and Global Levels

[It is] an ill wind that bloweth no man to good.
John Haywood (1546)

In 1992, a blue-ribbon panel was commissioned by the Institute of Medicine of the National Academy of Sciences to advise the US government on emerging infectious diseases that posed a threat or potential threat to the health of people living in the United States and assist in the federal allocation of public health resources.1,2 Emerging infections were defined as infections caused by newly identified human pathogens—such as the Legionella bacillus,3 the reemergence of previously controlled pathogens—such as measles,4 or the appearance of anti-infective resistance—such as methicillin-resistant Staphylococcus aureus,5 the incidence of which had increased significantly within the past 2 decades or threatened to increase in the near future.

Since the outbreak of severe pneumonia in US veterans attending a convention at the Bellevue-Stratford Hotel in 1976, found 6 months later to have been caused by a previously unknown and remarkably ubiquitous waterborne bacterium, Legionella pneumophila,3 more than 3 dozen human pathogens have been identified as agents of emerging infectious diseases in the United States (Table 1).

The most recent and perhaps most fearsome emerging infections are the appearance of West Nile virus encephalitis in New York City in 1999 and its rapid spread westward6; inhalation anthrax, deriving from use of Bacillus anthracis spores as a biologic weapon against the US civilian population in 20017; the global outbreak of severe acute respiratory syndrome (SARS) in 20038; and the looming threat of pandemic influenza, especially global disease caused by the highly virulent avian subtype A (H5N1)9,10. During the past 16 months, Mayo Clinic Proceedings has published reviews of diseases caused by 3 of these emerging pathogens, West Nile virus,12 the SARS coronavirus (SARS-CoV),13 and avian influenza virus.14

Efforts to better inform readers about the consequences of emerging infectious diseases continue in this issue of the Proceedings, in which Chiang et al15 report a study of 14 cases of nosocomial SARS acquired in 3 Taipei hospitals during 2003. Most of the 14 patients, 13 of whom were followed up for at least 8 months, were health care workers, and because few had underlying diseases, all except 1 survived; thus, this study provides some of the best data on the long-term effects of SARS on the lung. The clinical features and natural history of SARS encountered by Chiang et al are similar to those reported in much larger cohorts.16,17 All their patients had fever, and most had cough and dyspnea as well; however, 79% had diarrhea, and 64% had myalgias, indicative of the severe systemic immunoinflammatory response to this unique new human infection.18,19 Similarly, all their patients had lymphopenia, and most had elevated levels of lactate dehydrogenase, now well-defined surrogate laboratory markers for patients presenting with SARS.16,17 However, Chiang et al also found that patients with a very high C-reactive protein or lactate dehydrogenase level at the outset were far more likely to have progression to a severe stage of disease requiring mechanical ventilatory support, information of value to clinicians who might be called on to manage patients with SARS in the not-too-distant future.

Most interestingly, Chiang et al show that whereas bilateral fibrotic changes were demonstrable by high-resolution computed tomographic imaging 6 to 8 months after the acute infection, most of the survivors showed near-normal spirometric lung volumes (forced vital capacity, forced expiratory volume in 1 second), albeit one third with reduced diffusion capacity, but none required home oxygen. It is likely that most of these individuals will have recovery of normal lung function. These findings are very similar to...
TABLE 1. Major Emerging Infectious Diseases in the United States, 1973-2004*

<table>
<thead>
<tr>
<th>Year</th>
<th>Microbial pathogen</th>
<th>Disease(s)</th>
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<tbody>
<tr>
<td>1973</td>
<td>Rotavirus</td>
<td>Diarrheal disease in infants, nosocomial gastroenteritis</td>
</tr>
<tr>
<td>1975</td>
<td>Parvovirus B19</td>
<td>Roseola in infants, aplastic anemia with chronic hemolytic anemia, polyarthritis</td>
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<tr>
<td>1976</td>
<td>Legionella pneumophila</td>
<td>Severe community-acquired and nosocomial pneumonia</td>
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<tr>
<td>1977</td>
<td>Campylobacter jejuni</td>
<td>Enteritis, Guillain-Barré syndrome</td>
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<tr>
<td>1978</td>
<td>Chloroquine-resistant Plasmodium falciparum</td>
<td>Life-threatening malaria</td>
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<tr>
<td>1978</td>
<td>Human papillomavirus</td>
<td>Genital warts, cervical cancer</td>
</tr>
<tr>
<td>1980</td>
<td>Human T-cell lymphotropic virus I/II</td>
<td>T-cell leukemia, lymphoma, tropical spastic paraparesis</td>
</tr>
<tr>
<td>1980</td>
<td>Measles virus</td>
<td>Resurgent measles in young US adults</td>
</tr>
<tr>
<td>1980</td>
<td>Borrelia burgdorferi</td>
<td>Lyme disease</td>
</tr>
<tr>
<td>1981</td>
<td>Clostridium difficile</td>
<td>Antibiotic-associated colitis</td>
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<tr>
<td>1981</td>
<td>Human immunodeficiency virus</td>
<td>AIDS</td>
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<tr>
<td>1981</td>
<td>Toxic shock syndrome toxin-1-positive Staphylococcus aureus</td>
<td>Tampon-related toxic shock syndrome</td>
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<tr>
<td>1982</td>
<td>Helicobacter pylori</td>
<td>Gastritis, peptic ulcer disease, gastric malformations</td>
</tr>
<tr>
<td>1982</td>
<td>Escherichia coli O157:H7</td>
<td>Hemorrhagic enteritis, hemolytic uremic syndrome in children, thrombotic thrombocytopenic purpura in adults</td>
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<tr>
<td>1984</td>
<td>Methicillin-resistant S aureus</td>
<td>Pandemic nosocomial infections</td>
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<tr>
<td>1987</td>
<td>Ehrlichia species</td>
<td>Severe systemic febrile illness</td>
</tr>
<tr>
<td>1987</td>
<td>Streptococcal pyrogenic exotoxin–positive Streptococcus pyogenes</td>
<td>Toxic shock syndrome deriving from necrotizing soft tissue infections or bacteremia</td>
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<tr>
<td>1989</td>
<td>Hepatitis C virus</td>
<td>Chronic hepatitis, transfusion-related infection, end-stage liver disease, hepatocellular carcinoma</td>
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<tr>
<td>1990</td>
<td>Bordetella pertussis</td>
<td>Resurgent pertussis throughout the United States</td>
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<tr>
<td>1990</td>
<td>Multidrug-resistant Mycobacterium tuberculosis</td>
<td>Lethal tuberculosis in patients with AIDS</td>
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<tr>
<td>1991</td>
<td>Vibrio cholerae O139</td>
<td>Epidemic and pandemic cholera in South America</td>
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<tr>
<td>1991</td>
<td>Vancomycin-resistant enterococci</td>
<td>Nosocomial infections</td>
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<tr>
<td>1992</td>
<td>Bartonella henselae</td>
<td>Cut-scratch disease in children, bacillary angiomatosis in patients with AIDS</td>
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<tr>
<td>1993</td>
<td>Cryptosporidium parvum</td>
<td>Acute enteritis in immunocompetent persons, chronic enteritis and wasting disease in patients with AIDS</td>
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<tr>
<td>1993</td>
<td>Hantavirus</td>
<td>Very severe pneumonia, 50% mortality</td>
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<tr>
<td>1996</td>
<td>Creutzfeldt-Jakob prion</td>
<td>Variant Creutzfeldt-Jakob disease in the United Kingdom and elsewhere, traced to epidemic bovine spongiform encephalopathy in cattle</td>
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<tr>
<td>1998</td>
<td>Methicillin-resistant S aureus</td>
<td>Pandemic community-acquired infections</td>
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<tr>
<td>1999</td>
<td>West Nile virus</td>
<td>Encephalitis, poliomyelitis-like syndrome, transfusion-related infection</td>
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<tr>
<td>2001</td>
<td>Bacillus anthracis</td>
<td>Biologic weapon used against US civilian population</td>
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<tr>
<td>2002</td>
<td>Vancomycin-resistant S aureus</td>
<td>Nosocomial infections in hemodialysis patients</td>
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<tr>
<td>2003</td>
<td>Monkeypox virus</td>
<td>Human monkeypox from contact with imported exotic rodents and US prairie dogs</td>
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<tr>
<td>2003</td>
<td>SARS-coronavirus</td>
<td>Pandemic SARS</td>
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<tr>
<td>2004</td>
<td>Avian influenza A (H5N1)</td>
<td>Life-threatening human influenza in southeastern Asia</td>
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*AIDS = acquired immunodeficiency syndrome; SARS = severe acute respiratory syndrome.

the well-documented long-term pulmonary effects of garden-variety acute respiratory distress syndrome, stemming from overwhelming pneumonia, gastric aspiration, near drowning, trauma, pancreatitis, or systemic sepsis, in which most survivors have gratifying recovery of lung function in the early years after the acute episode.20-22 Because SARS is such a unique human viral infection and induces such an unusually severe systemic inflammatory response,18,19 it will be important to closely follow survivors of severe SARS for considerably longer to be certain that latency expressed progressive pulmonary fibrosis does not occur.

Between the first reports from the World Health Organization and the Centers for Disease Control and Prevention (CDC) that defined SARS as a global threat in March 200322,24 and control of the epidemic in Southeast Asia and North America 5 months later, more than 8000 persons in the Republic of China, Hong Kong, Singapore, Vietnam, Taiwan, and Canada became infected, and 774 (9.6%) died of the infection; mortality exceeded 50% in patients older than 60 years.16,17 Since the last communication on SARS in the Proceedings in April 2004, there have been extraordinary advances in our understanding of the disease in terms of its pathogenesis, epidemiology, management, and control:
Like many of the emerging human pathogens such as Borrelia burgdorferi (mice, deer), US Hantavirus (mice), West Nile virus (wild birds), variant Creutzfeldt-Jakob prions (cattle, potentially free-ranging cervids), monkeypox virus (exotic African rodents and primates, US prairie dogs), and avian influenza virus A (HSN1) (edible birds), infection by SARS-CoV can legitimately be considered a zoonosis, and wild mammals formed the initial reservoir of the virus—SARS-CoV has been isolated from palm-top civets and raccoon dogs in the live animal markets in southern China, and purveyors of these animals commonly show asymptomatic SARS-CoV seropositivity.

The genomic evidence that SARS-CoV is an animal-human recombinant is compelling, and SARS-CoV appears to have had a biologic origin remarkably similar to the human influenza A viruses and human immunodeficiency virus. Although the SARS virus originated in animals and made the leap to humans, once established in the human population, the virus has spread rapidly person-to-person, and the major reservoir of human disease is humans in the early stage of infection, before they have been diagnosed as having the virus and placed in respiratory and barrier isolation.

Elegant molecular epidemiology has traced the origins of SARS-CoV to Foshan in Guangdong Province, Southern China, from whence it spread to Beijing, then to Hong Kong, and from Hong Kong to Vietnam, Singapore, and Canada. A 65-year-old Chinese physician who traveled to Hong Kong on March 21, 2003, where he spent only 1 day, appears to have been the source of SARS-CoV that ultimately resulted in thousands of cases of SARS in 26 countries and 5 continents.

SARS-CoV is a new human pathogen to most of the world. Studies by the CDC have shown no serologic evidence of past infection in more than 400 specimens from US residents collected long before the SARS epidemic.

As a new human pathogen, there is, understandably, little if any natural immunity. Virtually all persons who became infected by SARS-CoV became symptomatic, and studies of exposed health care workers show that less than 1% to 2% of those infected experience mild or subclinical infection.

SARS spreads almost exclusively person-to-person by respiratory droplets, rarely by the airborne route: the roles of contact or fecal-oral transmission are less clear but probably occur. The puzzling large outbreak in Amoy Gardens in Hong Kong was recently traced to virus-laden aerosols generated from sewage, using sophisticated airflow-dynamic studies and computational fluid-zone modeling. However, whereas the outbreak in the Amoy Gardens complex represents distant airborne spread, distant spread is probably rare, as evidenced by the very low risk of infection in patients with no plausible face-to-face exposure to a patient with symptomatic SARS, by the effectiveness of simple isolation measures in hospitals that did not have sophisticated negative-pressure air-controlled rooms with separate roofline exhaust, and by the relatively few secondary cases on commercial airliners. In an investigation of 3 flights in which an airliner transported 1 or more symptomatic infected passengers, laboratory-confirmed cases of secondary SARS were detected on 1 flight, with the greatest risk to other passengers close to the index case (seated within 3 rows, relative risk 3.1); on 1 flight carrying 4 symptomatic infected persons, possible transmission occurred to only 1 other passenger, and no secondary illness was documented on another flight that carried 1 person with early SARS.

Simple control measures, most importantly the use of a high-quality filtration mask, ideally an N-95-type mask but even a surgical mask, combined with full-barrier precautions in a single room were highly effective in preventing spread to other patients and health care workers where it was most carefully studied, in Hong Kong, Singapore, and Canada.

Patients with early SARS do not pose a risk to others until they become symptomatic and start to cough, but there is considerable variability in contagiousness, probably based on the quantity of virus in the respiratory secretions and the degree of coughing. Very close proximity to an infected patient who is coughing heavily poses the greatest risk. It appears that most spread of the virus can be linked to “super spreaders,” and most infected persons are probably not very contagious. The risk of acquisition of SARS-CoV is far higher in the hospital than in the community.

The mean incubation period of SARS is approximately 6 days (range, 2-10 days) and is considerably longer than that for most other human respiratory viral infections, such as the common cold or influenza A, which permits case-contact investigations and quarantine of exposed contacts before those destined to become infected and contagious can spread the disease to others.

Because so few persons develop clinical SARS more than 10 days after exposure, there is no need to extend quarantine of exposed persons beyond 10 days.

Fever is so ubiquitous in SARS that monitoring the body temperature of quarantined contacts and health care workers caring for patients with SARS is a sensitive and specific method for detection of early infection, especially for health care workers before they become symptomatic and contagious. All health care workers caring for patients with suspected or proven SARS should be monitored 3 to 4 times daily; fever constitutes grounds for quarantine and diagnostic studies.
• To control SARS, early diagnosis is essential. Clinical predictors for SARS, based on study of large cohorts of patients in Hong Kong, suggest that fever, myalgia, malaise, an abnormal chest radiograph, lymphopenia, thrombocytopenia, and, most importantly, previous contact with a patient with SARS are each associated with a greatly increased likelihood of SARS. In contrast, in a newly symptomatic patient older than 65 years or younger than 18 years without a plausible face-to-face exposure who has a cough productive of sputum, abdominal pain, sore throat, rhinorrhea, or leukocytosis, SARS is unlikely.

• Modern-day virology has shifted rapidly during the past decade, from tissue cultures and serologic techniques to detection of the viral genome in clinical specimens by nucleic acid amplification techniques, such as polymerase chain reaction (PCR) or, for RNA viruses, reverse transcriptase–PCR (RT-PCR). Highly sensitive and specific RT-PCR assays were developed in most of the countries afflicted by SARS, most notably in Hong Kong, Singapore, and Canada, and were invaluable in early confirmation of SARS-CoV infection. The sensitivity of second-generation assays has been as high as 80% in the first 3 days of SARS-CoV infection. The sensitivity of second-generation assays has been as high as 80% in the first 3 days of illness. Whereas a PCR assay developed at the CDC was given immediate Investigational Device Exemption approval by the Food and Drug Administration, no commercial PCR assay has yet been licensed for clinical use in the United States.

If SARS returns and spreads in the United States, it will be essential that reliable real-time PCR assays are available in US hospitals. Public health laboratories are not clinical service laboratories and are unlikely to be able to meet the need if SARS reappears on a major scale. Private companies should be given access to clinical strains of SARS-CoV and, if available, clinical specimens from infected patients in order to test and validate commercial assays that hopefully will be as accurate as, perhaps more accurate than, the current CDC assay.

• Ribavirin was used empirically in many patients with SARS in southeast Asia with the impression that it was effective therapeutically; however, in vitro studies have shown that SARS-CoV is not susceptible to ribavirin at concentrations achievable clinically. Hence, it is unlikely that the drug is active therapeutically. Uncontrolled trials suggest that interferon alfa may be of benefit. There are a number of compounds and antiviral drugs with in vitro activity against SARS-CoV, including interferon alfa, interferon beta, and glycyrrhizin (licorice-root extract). Theoretical RNA virus targets, such as protease inhibitors and fusion inhibitors, also need to be assessed for efficacy. If SARS returns on a major scale, it will be essential that the efficacy of antiviral drugs, such as commercial interferons, is tested in randomized, double-blind trials.

• Whereas uncontrolled studies of treated cohorts in Asia have suggested that using moderate doses of corticosteroids, 1 to 2 mg/kg of a prednisone-equivalent daily, at the first evidence of severe SARS, specifically hypoxemia, may improve survival, corticosteroid therapy for SARS has had serious adverse effects, and a single randomized trial of preemptive pulse corticosteroid therapy did not show benefit. If SARS returns, it will also be essential that efforts are made to determine the efficacy of corticosteroids in a large prospective, randomized, double-blind trial.

• Advancing age (>50 years) and coexisting illness—especially diabetes or heart failure—greatly increase the likelihood of severe SARS (requiring mechanical ventilatory support) and the risk of death. Inexplicably, SARS is usually very mild in children, who do not appear to be very contagious. Also, maternal-fetal transmission does not appear to occur.

• While coronaviruses are more resistant than most other respiratory viruses, SARS-CoV appears to be susceptible to the commercial microbicides used for surface decontamination in hospitals.

• Most importantly, outbreaks in Hong Kong, Singapore, Vietnam, Canada, and elsewhere in the world were successfully controlled, but only by an intensive, coordinated effort in which the national public health authorities worked very closely with the regional public health agencies and, especially, hospital infection control officers and clinicians caring for patients with SARS. The measures needed for control of SARS are clear: (1) earliest detection of cases, having at-risk individuals isolated and queried about their face-to-face contacts during the 10 to 14 days before the onset of illness; (2) expeditious contact tracing, with uncompromising home quarantine for all contacts of suspect and proven cases; and (3) stringent isolation of symptomatic suspect and proven cases, focusing most heavily on techniques to prevent droplet and airborne spread (eg, single negative-pressure rooms, ideally with separate roofline exhaust or filtration of outlet air; fit-tested high-filtration mask respirators and a face shield or goggles or a powered air-purifying system for all health care workers and others entering the room of the case, as well as the use of nonsterile gloves and gowns to prevent contact transmission). The value of border screening and temperature monitoring of travelers is questionable.

The resources needed to control an outbreak in a city or a country are huge. In North America, the Toronto outbreak consisted of 246 documented cases in 4 hospitals. To control SARS in Toronto required home quarantine of more than 23,000 contacts and an informational hotline that handled more than 300,000 calls; the economic cost of the epidemic to the city and the city and provincial govern-
ments was estimated at $1.13 billion (Canadian). The long-term psychological impact of SARS on patients, families, and health care workers was also very substantial.\textsuperscript{72-74}

- Efforts are now under way to test candidate SARS vaccines.\textsuperscript{75}

The national tragedy of September 11, 2001, was followed by the most serious instance of bioterrorism involving the US civilian population in history, the spread of anthrax through the US mail.\textsuperscript{7} These events coincided with growing awareness that weaponized smallpox virus almost certainly yet exists in the world, with strong suspicion that the former Soviet Union,\textsuperscript{76,77} as well as countries that have sponsored international terrorism, such as Iran and North Korea,\textsuperscript{77,78} retained smallpox virus as a potential weapon. The unthinkable has become plausible: weaponized smallpox virus in the hands of international terrorist groups. As a consequence, the federal government has undertaken major steps to greatly improve emergency preparedness at all levels, especially the capacity to respond to the use of biologic agents such as smallpox or anthrax as weapons against the civilian population as well as our military (Table 2).\textsuperscript{79,80} Billions of dollars have been appropriated to improve the capacity of public health and clinical laboratories to reliably detect infectious agents that might represent biologic weapons; to improve the likelihood that emergency department physicians and all primary care providers could recognize anthrax, smallpox, and other infectious diseases that might denote bioterrorism; to establish and coordinate surveillance programs at the regional, state, and federal levels; and to train more than a million public protection personnel and greatly improve preparedness of the 7000 US hospitals.\textsuperscript{81} At my center, we have spent hundreds of person-hours identifying and retrofitting a 35-bed patient-care unit for the potential accommodation of patients with smallpox or other highly contagious infections such as SARS or pandemic influenza caused by a new strain. This local effort has focused on air control and negative-pressure isolation rooms, which have the capacity for supporting mechanical ventilation, and developing comprehensive guidelines for health care workers who would staff the unit.

For the first time in our generation, there has been a major injection of federal dollars into the public health sector at the state, regional, and municipal levels.\textsuperscript{81} The challenge will be to provide sustained support, rather than a limited bolus of supplemental funding.

Hopefully all this effort will never be needed to control smallpox—or an even more terrifying engineered pathogen\textsuperscript{76,82}—that might be used as a biologic weapon. If it is not, the effort will not have been wasted because it is likely that all the planning and resource allocation will prove invaluable for controlling the spread of natural emerging pathogens, such as SARS-CoV or a new strain of influenza virus, which are probably far more likely to pose a serious threat to human and animal health in the United States and worldwide.

The greatest and most immediate threat is the long-overdue reappearance of pandemic influenza A. The leading and most dreaded candidate for the new pandemic subtype is avian influenza A (H5N1), recently reviewed in this journal,\textsuperscript{14} which was first recognized in a large poultry outbreak in the live-animal markets of Hong Kong in 1997, where the virus had acquired the capacity to spread from infected birds to humans and killed 6 of 18 infected persons.\textsuperscript{83} To control the outbreak, authorities killed nearly 2 million chickens to eliminate the reservoir of infection.

Since that time there have been contained outbreaks of different subtypes of avian influenza—H9N2, H7N2, and H7N7—that have caused disease in poultry, with secondary infections reported among pigs and humans, but infrequent and mild human disease, such as conjunctivitis or mild influenza-like illness.\textsuperscript{14} There was only 1 human death among 89 cases in a large H7N7 outbreak in the Netherlands in 2003.\textsuperscript{84}

In January 2003, a highly pathogenic strain of avian influenza A (H5N1) was identified in South Korea and
spread rapidly over the succeeding months to 7 other Asian countries, Cambodia, China and Hong Kong, Indonesia, Japan, Laos, Thailand, and Vietnam. To date, there have been 43 confirmed cases in humans, nearly all in children or young adults; 31 (72%) have proved fatal. More than 100 million edible birds have been slaughtered by governmental authorities.

All species of domestic birds appear to be susceptible to the H5N1 strain, which is probably transmissible to all species of wild birds, some of which migrate transcontinentally. The epidemic A (H5N1) strain appears to be gaining virulence and was recently shown to have acquired the capacity of infecting mammalian species, domestic cats and wild felines within zoos and pigs. Most alarmingly, there is growing evidence that person-to-person spread can occur, albeit yet rarely. The epidemic strain further shows high-level resistance to amantadine and rimantadine but is thus far susceptible to neuraminidase inhibitors, such as oseltamivir or zanamivir. If the strain acquires recombinant genes that facilitate human infection and person-to-person transmission, pandemic disease could prove more catastrophic than the great H1N1 influenza epidemic of 1918.

Even more concerning has been the challenge of developing an avian influenza vaccine. Current influenza vaccines are unlikely to provide any protection against the new H5N1 avian strain. The standard method for manufacturing influenza vaccines, growing the vaccine strain in chicken embryos, does not work because the avian A (H5N1) strain is so virulent that it kills the embryo before there is sufficient virus to harvest. Novel genetic techniques, under way in the United Kingdom, will be needed to alter the strain’s phenotypic features so that it can be grown in sufficient quantities in fertilized eggs and an effective vaccine can be constructed. Vaccine manufacturers are understandably reluctant to make the investment to develop and manufacture a new vaccine, particularly in large quantities, when there is uncertainty whether the avian strain will indeed spread and necessitate administration of hundreds of millions of doses. Similarly, the sole manufacturer of the only oral neuraminidase inhibitor likely to be effective against avian influenza (oseltamivir) has very limited production capacity, and less than 2 million doses are currently available in US pharmaceutical stocks; the director of the CDC has stated that it would be desirable to have at least 100 million doses available.

In summary, 22 cases of cutaneous or inhalation anthrax traced to domestic bioterrorism and the global SARS outbreak represent ill winds that have blown considerable good. The greatly expanded US federal effort to improve national preparedness for bioterrorism has strengthened public health at every level, and whereas we are far from being able to consider the United States as fully prepared, we are better prepared than only 3 years ago. The recent US epidemic of monkeypox, traced to importation of infected exotic African rodents and the burgeoning domestic trade in US prairie dogs, could be considered a live tabletop exercise—with a relatively innocuous pathogen—for the recognition and containment of smallpox.

Similarly, the global SARS emergence has proved the enormous power of modern-day molecular biology to identify and characterize new pathogens, to detect clinical infections far more rapidly than in the past, and to quickly unravel the epidemiology of new infectious diseases—the scientific foundation for strategic control. The SARS outbreak was contained only by unprecedented international cooperation under the leadership of the World Health Organization and successful coordination within the affected countries between national and regional public health agencies and health care providers. Controlling the next influenza pandemic, especially if it is caused by a highly virulent subtype such as the current A (H5N1) avian influenza virus, will require even greater international collaboration and vertical coordination in public health within the involved countries. It will also require an unprecedented commitment by the industrialized countries of the world to meet the needs of afflicted developing countries with limited public health resources. We are all in this together: it is in every country’s self-interest to work collaboratively toward a common goal—the prevention of communicable disease and improvement of health of every citizen of the world.

Knowing is not enough; we must apply.
Willing is not enough; we must do.

Goethe

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