

## Infectious Diseases and Bioterrorism: Covenants in a Shrinking Globe<sup>1</sup>

*Be fertile, then, and multiply; abound on earth and subdue it.<sup>2</sup>*  
—God

Noah, his family, and the animals had just landed on dry ground and left the ark. This particular story may be of Judeo-Christian origin, but, in actuality, it is only one of the “great flood” myths of the many cultures on this globe. Legend and literature tell of what happens next. YHWH—or in the case of other traditions, the creator-god of the myth—promises never again to destroy the earth by flood. The survivor Noah and his crew of humans and animal cargo are told to repopulate the earth. The organisms that cause illness in those humans apparently heard the command as well. They’ve done well, these many millennia. They’ve adapted to the climates of the globe and circumnavigated it as hitchhikers, as we traveled. They have survived nearly all of the attempts of eradication by us, their hosts.

This tongue-in-cheek commentary on the presence of disease-causing life forms on the globe today may be humorous, but the truth of the devastation caused by them—and those who use them as weapons of terror—is no joke. We should not minimize the challenges that lie ahead as we address the very real threats to human life from our inability to live side-by-side with so many organisms that cause the infectious diseases that maim, disable, and kill. Some of us have been protected with healthy immune systems, safe food and water, good housing, sophisticated health care, and preventive vaccines. In this new era of terror, some of us will be able to rely on security and intelligence forces to monitor, detect and prevent bioterrorist acts. But not nearly enough of us have received the benefits of those measures we know protect humans from the ravages of threats we cannot even see. All of us, regardless of how privileged, are at risk of becoming ill and suffering from a substantial number of diseases for which there are no preventive or curative medicines.

How will we choose to address the disease conditions that so threaten the health of the world’s population? Will we continue to invest in public health and take the social and economic steps necessary to improve the living conditions of people on the globe? Will we support the diplomacy and peace-keeping efforts that prevent wars and the disease consequences they bring as refugees flee their homelands? How will those of us in the nations of wealth and privilege

support infectious-disease prevention efforts in the developing world? How can we best develop the technologies and reform the health systems to bring vaccines and medicines to those who need them? How can we best prepare for the anticipated global pandemic that the influenza virus so reliably causes? How will we address the horrors that can result when these organisms are used to wage war? Will we find our way to global cooperation and true public-private partnerships?

### ***Infectious Diseases Span Time and Cross Borders***

Infectious diseases cause disruption of the world's economic well being. Diseases take life and cause disability. Diseases interfere with trade, tourism and foreign investment.<sup>3</sup> This, in turn, can further destroy a country's economic viability, as it is required to spend more of its Gross Domestic Product (GDP) on health care during times when diseases are causing morbidity and mortality in the nation's workforce, keeping workers from their jobs. The more economically deprived a nation, the more widespread disease can destabilize governments, particularly newly democratic governments, as dissatisfaction with leadership creates reversions to oppressive regimes. In the past, these scenarios were playgrounds of fiction writers;<sup>4</sup> now they are ground zero of public health and safety officials.

Many of the infectious diseases that create these disruptions—plaguing plants, animals and humans—may be as old as the earth's earliest-formed microorganisms. Although they may have first attacked humans, it is believed that some we know best today—tuberculosis, for example—probably originated as zoonotic diseases; that is, in animals. When humans lived and worked in close contact with animals, were scratched or injured by animals, or when they ate poorly cooked or raw animal meat, the diseases carried by those animals may have mutated to adapt to these new human hosts.<sup>5</sup> The apparent transformation of bovine spongiform encephalopathy in cows into Creutzfeldt-Jakob disease in humans may be a modern example of that phenomenon.<sup>6</sup> A similar theory has been used to explain HIV/AIDS, which may have adapted to humans when people ate the sooty mangobey monkey (green monkey), a carrier of a simian immunodeficiency virus (SIV<sub>sm</sub>) that closely resembles HIV2.<sup>7</sup>

There is little information about the infectious diseases of prehistoric humans, but we do have information from the study of Egyptian and South American mummies,<sup>8</sup> along with medical case reports from early physicians.<sup>9</sup> Tuberculosis, caused by *mycobacterium tuberculosis*, is believed to have originated around 15,000 years ago, possibly by crossing the species barrier from cattle when humans drank milk from cows with *Mycobacterium bovis*.<sup>10</sup> A pre-dynastic Egyptian mummy from 3400 B.C. showed DNA evidence specific to the mycobacterium that causes Pott's disease (tuberculosis of the vertebrae), and studies of a 900-year-old Peruvian mummy indicate that tuberculosis existed in the New World long before Europeans arrived.<sup>11</sup> Early written evidence of pulmonary tuberculosis was found in the library of Assurbanipal, an Assyrian king (668-626 B.C.).<sup>12</sup> Tuberculosis was documented by Hippocrates in his "Of the Epidemics," written around 400 B.C. Hippocrates called the illness *phthisis* and identified it as the most widespread disease of the time, noting it was usually fatal. Similar documentation comes from the Roman physician Claudius Galen.<sup>13</sup> Shakespeare mentioned tuberculosis in his plays, as "consumption" in *Much Ado About Nothing*, and as

“scrofula” in *Macbeth*.

Malaria is another ancient disease. The malarial *plasmodium* parasites probably originated in Africa, possibly before the dawn of man, since fossils of mosquitoes up to 30 million years old have been found.<sup>14</sup> References to deadly fevers that were probably malaria, can be found in Indian Vedic writings of 1600 B.C., and again in the writings of Hippocrates from around 2,500 years ago. Since the medical texts of the early Mayans and Aztecs make no reference to malaria, it is reasoned that it came to them with the European military and civilian settlers who came to colonize the New World. That form of disease transmission would not be uncommon. Malaria is mentioned in military accounts as more devastating to troops than battle injuries, and it is believed that Alexander the Great spread malaria during his various far-reaching military campaigns. One of the first military expenditures of the Continental Congress was for \$300 to buy quinine to protect the troops of General Washington. During World War II, when General Douglas MacArthur commanded troops in the Southwest Pacific, he complained that it would be a long war if only one of three divisions could face the enemy while the other two were either in the acute or recovery phases of the disease.

Measles can be found in references as far back as the seventh century A.D. In the tenth century, Rhazes described the disease as more dreaded than smallpox, and there is mention of measles often occurring along with other epidemics. A smallpox and measles epidemic from 1530-45 killed nearly 1.5 million people in Mexico.<sup>15</sup> Diarrheal diseases caused by several different and distinct organisms—cholera, typhoid fever and dysentery—killed many and created major problems for soldiers in numerous battles throughout history.<sup>16</sup> Pneumonia and other acute respiratory diseases—particularly influenza—have killed millions of people worldwide through the centuries. One influenza season alone in 1918-19 killed 20 million people.<sup>17</sup>

It is no surprise, then, that man has attempted to control these diseases. Within the covenant of obligation created at Sinai, community public health measures were detailed to prevent and control the spread of disease. Some were drastic, calling for homes with mildew to be sealed for a time, re-plastered and, if the mildew did not disappear, to be dismantled and taken to a dump outside the town.<sup>18</sup> People were cleansed in prescribed ways and their clothes burned if they contracted infectious diseases.<sup>19</sup> Other methods have been mounted since that time, such as public health measures to provide safe food, pure water, uncrowded housing, and vaccinations, and many of these measures have been successful. Medicines have been used to treat the overwhelming infections caused by the offending organisms. Hospital care and oral rehydration are also used to support patients as they suffer and recover from the malady.

Mankind has attempted, as well, to eradicate infectious diseases altogether, and several are on their way out. It is projected that polio and leprosy may be conquered by 2005, and measles and hepatitis B by 2010.<sup>20</sup> A campaign for global eradication of malaria was initiated by the World Health Organization (WHO) in the mid-1950s, but by 1967 it was clear that eradication was impossible and the focus shifted to a more modest goal: control. In one of the most notable private-sector endeavors, The Carter Center embarked on a number of projects in the developing world to improve health and survival. It attacked river blindness, *trachoma*, *schistosomiasis*, and *lymphatic filariasis*, and it achieved a 97% eradication of Guinea Worm in

Asia and Africa.<sup>21</sup>

Man has been able to eradicate only one disease so far: smallpox. Though the Chinese may have attempted to stem the tide of smallpox over a thousand years ago, we in the West credit Edward Jenner, with his first vaccination in 1796, as the beginning of immunization science. It would be many years, however, before smallpox eradication would be attempted, and the successful achievement of that goal would not be announced until 1979.<sup>22</sup> With any luck, the announcement will not be premature, as some public health experts wait to see if icecap melting from global warming will lead to a renewed exposure to the smallpox some scientists believe may be trapped within the ice,<sup>23</sup> and as national security experts wait to see if smallpox will be used as a weapon in the post-World Trade Center terrorism era.

Even in the absence of extraordinary circumstances, mankind today continues to confront virulent diseases. Together, six diseases cause 90% of global infectious disease deaths: tuberculosis, malaria, diarrheal diseases, acute respiratory diseases (including pneumonia and influenza), measles, and HIV/AIDS. While most of these diseases are very old, some are quite new, which means that we must also confront the reality that new diseases can emerge on the globe and strike us at any time. In the past three decades alone, thirty new infectious diseases have been identified, including rotavirus, a cause of infant diarrhea; Human Immunodeficiency Virus, a cause of HIV/AIDS; *Borrelia burgdorferi*, a cause of Lyme disease; Ebola virus, a cause of acute hemorrhagic fever; *Legionella pneumophila*, a cause of Legionnaires's disease; *Helicobacter phlori*, a cause of peptic ulcer disease; Hantavirus, a cause of adult respiratory distress; and Nipah, a cause of severe encephalitis.<sup>24</sup>

### ***The “Big Six” Take Their Toll***

*Tuberculosis* was thought to be under control until it reemerged in recent years—with a vengeance. It is the largest killer of women of childbearing age, and altogether kills nearly 1.5 million people a year. Two billion people—one in every three worldwide—have latent tuberculosis, giving the disease a large potential reservoir. Adding to the human reservoir of disease is bovine tuberculosis, which is endemic, as children and adults drink contaminated milk in many parts of the world.<sup>25</sup> What is even more frightening is the widespread emergence of drug-resistant tuberculosis strains, created when people do not take medications consistently or stop taking them altogether midway through treatment.<sup>26</sup>

*Malaria* is endemic in sub-Saharan Africa, where the disease accounts for one in five childhood deaths. Pregnant women are more likely to suffer miscarriages, give birth to low weight babies, or die from the disease. It is estimated that 300-400 million people are infected with malaria yearly, and it kills over one million people annually. After some years of control, it is currently rebounding in many developing nations.

*Measles*, the most contagious disease known to man, infects 42 million children annually. It spreads easily by wet droplets from sneezing or exhalation, and infection is immediate. Measles is a major childhood killer in developing countries and a leading cause of death among refugees and displaced persons. It kills nearly a million people every year, mostly children.

*Diarrheal diseases* also strike children and are a major cause of death in the children of developing nations, especially under the age of five. Pathogens such as *Salmonella typhi* (typhoid fever), *Shigellosis* (bacillary dysentery), *Vibrio cholerae* (cholera), and *Escherichia coli* can be contracted from contaminated water and food, usually a consequence of poverty in areas where waste disposal and facilities for hygiene are inadequate. Periodic epidemics of typhoid fever and cholera are also killers of adults, particularly the elderly and those with compromised immune systems.

*Acute respiratory infections* (ARIs), such as pneumonia and influenza, are highly contagious and kill mainly the very young, the elderly, and those with compromised immune systems. It is estimated that these ARIs are responsible for 3.5 million deaths yearly. The misuse and overuse of antibiotics contribute to growing bacterial resistance to the most common drugs used to treat these infections.

*HIV/AIDS* is the most well publicized of the major infectious diseases. It is a true pandemic. While its devastation of sub-Saharan Africa is now well known, it has also spread in other populous areas, such as China, India, and the former Soviet Union.<sup>27</sup> There are estimates of the number of HIV/AIDS-infected people worldwide, but many within the health professions believe the numbers to be much higher than what is reported. The majority of those infected with HIV/AIDS are working-age adults. The disease is fatal. While there are medications that will prolong life, the death toll and the consequences to family life and national economics and stability will be staggering in developing nations that do not have the infrastructure to promote prevention and education, provide HIV testing and clinical care, afford the medications, and ensure patient compliance.

### ***Causes Are As Old As Mankind***

Before the late Neolithic period, acquiring disease in any way—either from animals or plants, or from other humans, for that matter—was not a major problem for mankind. Hunter-gatherers lived mainly in small clans of 25 to 50 people that were well dispersed from each other. Even if an infectious disease spread within a clan, the rest of humanity was safe. As people adopted an agricultural life, however, clans grew into larger tribes, providing more human hosts in which the disease could spread and creating a more substantial impact on the economics of the community and the survival of the people.<sup>28</sup> Today, the population size and density are beyond what early man could have imagined. The worldwide population is currently six billion and is expected to rise to nine billion before it stabilizes. But population size alone is not the only driving factor in the spread of infectious diseases; other human behaviors and cultural dimensions help enable these devastating diseases to spread all the more rapidly.

Human travel is one of those behaviors. Travel has always spread infectious disease, and more of us are traveling today than ever before. Two million people cross international borders each day. Each week, a million people will leave a developing nation to travel to the industrialized world, principally to find work. In a year's time, fully 10% of the world's population will leave one country to travel to another,<sup>29</sup> and few will understand their risks of contracting disease or take precautions to prevent acquiring a transmissible disease.<sup>30</sup>

We not only travel more, we travel faster and connect more remote locales directly to the most populous areas. In 1850, there were fewer than one billion people in the world and it would take nearly a year to circle the globe. Today, any one of our more than six billion “neighbors” can travel from their home to ours, arriving on our doorstep in less than one day. In the case of our North American continent, of the 350 and 500 million visitors each year to the U.S., more than a million come each day from our closest neighbors—250,000 from Canada and 800,000 from Mexico. In less than the incubation period for many diseases, an infected person can travel across our borders, or across the globe. An infected patient or treating doctor could easily leave the area of an Ebola outbreak in Africa and arrive in another country halfway around the world before the first symptoms became evident. Likewise, one person can infect others across their own country. This happened recently within the U.S. when a patient infected airplane passengers on a flight from New York to the Midwest,<sup>31</sup> and when teenagers returning from a summer mission in Mexico spread pneumococcal pneumonia through five states, causing both illness and death.<sup>32</sup> Air travel has also made it easier for animal and insect disease vectors, such as mosquitoes, to spread over an increasingly larger area of the globe. Malaria-carrying mosquitoes have been identified in industrialized country airports “hitching” on commercial flights. Mosquitoes carrying dengue virus or yellow fever can do likewise, as can other disease-carrying insects, such as tsetse flies, which carry *trypanosomiasis*, or sleeping sickness, and sandflies, which carry *leishmaniasis*.<sup>33</sup> Ships and their commercial cargoes of equipment and food multiply the possibilities for transporting the vectors that cause disease into areas that previously had little or no incidence of the condition.

Even travel within a nation spreads disease. Every year, people leave rural areas to migrate to cities, principally for employment. Over the last century cities in both developed and developing nations have seen major growth and overcrowding. In developing nations the infrastructure of these cities has not kept pace with population growth, and public health measures, such as clean water and effective waste removal, have deteriorated. Making matters worse, many of those who emigrate are poor and live in overcrowded and substandard housing, where airborne diseases spread rapidly. Poverty and the physical environment surrounding the poor are prime areas for the growth and dispersion of harmful organisms. Open and stagnant pools of wastewater are perfect breeding grounds for insects and parasites.<sup>34</sup> But diseases are transmitted from person to person in the developed world as well, where those of us with adequate housing and sanitation frequently neglect the important, well-known and simple preventive measures, like sanitary food handling, hand washing, and vaccines.

As the population migrates to cities, economic development and land use choices have disease consequences. Destruction of forests and grasslands for agricultural use forces disease-carrying animals and insects to come into closer contact with humans. Lyme disease-infected deer, therefore, are no longer distant in forests, but are forced into suburban backyards. Rabies-infected animals search for food in neighborhood waste bins. Building dams for recreation and irrigation encourages the spread of water-breeding vectors, like mosquitoes and snails, and when grasslands are destroyed for farming, disease-carrying field mice come into closer contact with farmers and their animals. This same migration has created a market for trafficking in young girls and women who, lured by promises of factory employment or sold by families for the value of their labor, become sex-workers forced into brothels in cities, contributing to the spread of

HIV.<sup>35</sup>

Each year in the past decade, there were 40-59 wars on the globe.<sup>36</sup> Refugees fleeing fighting zones bring their diseases to new areas. The crowding and poor nutrition and sanitation in refugee camps add fuel to the fire by allowing diseases to spread rapidly. Tuberculosis, malaria, cholera, dysentery, and HIV are abundant in many refugee camps in both sub-Saharan Africa and the Middle East.<sup>37</sup> Peace-keeping troops spread disease also, as the prostitution that accompanies any military presence results in an attendant increase in sexually-transmitted diseases.<sup>38</sup> In the face of the budgetary strains of war on the nation, military spending is high and health care spending is low, even though far more people die from infectious diseases than from the consequences of combat. In the past fifty years, wartime spending globally exceeded \$864 billion. Twenty-three million people died. In that same time period, prevention spending for only three infectious diseases—AIDS, tuberculosis and malaria—was only \$15 billion, despite the fact that those diseases took the lives of more than 150 million people.<sup>39</sup>

War not only spreads disease; disease is a weapon of war.<sup>40</sup> Mongol soldiers in the 1300s used bodies of dead plague victims as cannon balls. Shot over the walls of a fort in Genoa, they infected the retreating troops, who carried the disease back to Sicily and from there to the rest of Europe. Lord Cornwallis attempted to spread smallpox throughout New York during the Revolutionary War. General George Washington ordered letters received from Boston dipped in vinegar to kill germs he suspected were being used to contaminate fighting forces. One hundred years later, a Southern sympathizer would attempt to spread yellow fever through northern cities using clothing infected with the disease from an epidemic in Bermuda. Smallpox was also used by Spanish conquistadors and the U.S. army to subdue Native Americans.

Mankind has attempted to manage these disease conditions. Public health measures to assure good sanitation, housing, and vaccines are essential to disease control, as are surveillance, reporting, and management of outbreaks, including drastic measures like quarantine. There is no better way to start—after these basic public health measures are in place—than with education, though this is lacking in many parts of the world. The best contemporary example can be found in HIV/AIDS. Even today, misinformation, bias, and ignorance about its transmission exist in the developed and developing worlds alike. This causes discrimination and violence against persons with AIDS, sometimes resulting in the denial of care. Sometimes—as in Africa, where it is believed that sex with a virgin will rid a man of HIV—ignorance has resulted in violence and rape of young girls, which actually further spreads the disease.<sup>41</sup> Sometimes—as in the case of Buddhist monks in Myanmar, who share razors to shave heads,<sup>42</sup> or in rural areas of China, where the sale of blood contributed to the growing HIV epidemic<sup>43</sup>—ignorance hampers efforts to prevent practices that are not intended to be harmful, but are.

Frequently, education is minimal because the infrastructure for communicating with the nation is poor. Health care system weaknesses cannot do other than mirror the poverty and economic conditions of the region. Government leadership is sometimes lacking and native healers, long trusted but rarely able to stem the tide of the severe infectious diseases attacking the population, cannot fill the vacuum left by inadequate facilities, limited caregivers, and unavailable medicines. An exception is the currently widespread use of anti-microbials, where

the cure might someday be worse than the diseases due to the increase in resistant pathogens caused by the misuse and overuse of drugs. In many developing nations, these drugs are available over-the-counter and can be used at the discretion of the patient. Sometimes they are used as replacements for vaccines that are intended to prevent the diseases. Further, these drugs are misused in both the developed and developing worlds when patients do not take a full course of prescribed treatment. Both misuse and overuse can lead to the emergence of resistant pathogens, a factor in nosocomial (hospital-acquired) infections. This problem is increasing globally and has serious national defense implications.<sup>44</sup>

### ***Bigger Challenges Need Expansive Covenants***

Those of us in the U.S. can no longer enjoy the illusions that we are protected in this country by our wealth, public health systems, and distance from these diseases. Health isolationism is, frankly, an unhealthy practice. In addition to the moral issues, there are practical ones. Even with the best that medicine has to offer available to us here, diseases that circumnavigate the world will show up in our cities and visit our schools, theme parks,<sup>45</sup> homes, and hospitals. They will stress our health care system, deprive us of productive work and school time, cost us money, and, in some cases, take our lives or leave us with short- and long-term disabilities.

Intrigue surrounds the specter of bioterrorism today. Which nations have the capacity to spread anthrax or smallpox to the U.S. or throughout the world? Who might contaminate the food supply with botulism? From where might the next threat emerge? Might it be from a domestic source? Or are our only enemies those of hostile nations?

In many cases, the enemy is the disease itself, and one that we have, for too long, ignored is influenza. Misperceived as a “mild” and “unimportant” disease, it is truly a killer of many. Influenza—commonly called “flu”—is one of the oldest and most common diseases known to man. It may also be one of the fastest killers. Influenza was first described by Hippocrates in 412 B.C. The disease today still affects large sections of the population each year. Its ability to kill comes from the ability of the virus to mutate quickly, often producing new strains against which humans have no immunity. Influenza epidemics occur nearly every year and in most countries. In the United States, annual influenza epidemics and associated complications are associated with 4 million to 24 million healthcare visits, 314,000 hospitalizations, and 20,000 to 40,000 deaths. These effects, in turn, drive the estimated \$4.6 billion in spending each year in the United States on influenza-related direct medical costs, with the total costs upwards of \$12 billion per year.<sup>46</sup>

There are two major types of influenza viruses known: *type A* and *type B*. These are further classified into subtypes on the basis of two surface antigens: *hemagglutinin [H]* and *neuraminidase [N]*. Both types of the virus undergo continual antigenic change (*antigenic drift*), resulting in new strains. The constant development of antigenic variants through antigenic drift is the basis for the seasonal epidemics and the reason why the influenza virus is carefully tracked worldwide and the vaccine updated annually. In addition, *influenza type A* viruses are more unstable than *type B* and can undergo a more dramatic, abrupt type of antigenic change called



*antigenic shift*. In antigenic shift, which occurs when there is an exchange of genetic material between two different influenza viruses, a large proportion, or even all, of the world's population lacks the immunity to the new virus. In this circumstance, a pandemic can result in which disease spreads quickly and causes even greater illness and death.<sup>47</sup> An epidemic is bad, but a pandemic is far worse. The first well-described influenza-like pandemic occurred in 1580.<sup>48</sup> Since that time, 31 influenza pandemics have been documented, with three occurring in recent memory: 1918, 1957, and 1968.

When pandemic influenza occurs, mortality rates can be staggering. During the “Spanish Flu” pandemic of 1918-1920 (*A/Spain/[H1N1]*) at least 20 million people died from influenza, including 500,000 in the United States. In addition, 20 to 40% of the worldwide population became severely ill with a virus that was especially quick to kill. Many people who felt well in the morning became sick by noon and were dead by nightfall. Those who did not succumb to the disease within the first few days often died of complications caused by bacterial illnesses, such as pneumonia. During the Asian flu pandemic of 1957 (*A/Asia/[H2N2]*), more than a million people died worldwide, about 70,000 in the United States. The Hong Kong flu of 1968 (*A/Hong Kong/[H3N2]*) also killed more than a million people worldwide, including 34,000 in the U.S. These last two pandemics together caused an estimated \$32 billion in economic damages worldwide due to medical expenses and productivity losses.<sup>49</sup> Another pandemic is highly likely, if not inevitable, according to the experts.<sup>50</sup> The Spanish Flu of 1918 circled the globe in a number of months, but any new pandemics are predicted to spread much more quickly given population density and rapid travel.

Based on rates of illnesses and complications observed in the previous pandemics, preliminary estimates from the Centers for Disease Control and Prevention (CDC) indicate that the next pandemic could kill as many as 60 million people worldwide.<sup>51</sup> In the United States, the potential impact is estimated to be between 89,000 to 207,000 deaths; 314,000 to 734,000 hospitalizations; 18 to 42 million outpatient visits; and 20 to 47 million additional illnesses. The estimated economic impact would be \$71.3 to \$166.5 billion, excluding disruptions to commerce and society.<sup>52</sup>

One of the most recent and worrisome influenza events occurred in Hong Kong in 1997. The virus infected eighteen people, killing six of them—a high death rate for an infectious disease. The outbreak highlighted the success of the global influenza surveillance network at the time, which is one important indication of a global covenant.<sup>53</sup> It all started in May, when a three-year-old boy with influenza-like illness was treated with salicylates and later died of complications consistent with Reye's syndrome. The laboratory diagnosis included the isolation of *influenza type A*, but the specific strain or subtype could not be further characterized with reagents distributed by WHO for diagnosis of human influenza viruses. Within days, infectious disease experts from around the world converged to investigate. Within weeks, tissue samples were forwarded to the CDC in Atlanta, to England's National Institute of Medical Research (NIMR) at Mill Hill, London, and to the Dutch National Institute of Health and the Environment (NIHE) in Amsterdam, the Netherlands. By August the virus was characterized as an *H5N1* subtype.

It was the influenza surveillance and warning system that noted the occurrence and alerted public health officials. In conjunction with the French *Institut National de la Santé et de la Recherche Médicale*, WHO maintains a global surveillance system, FluNet.<sup>54</sup> This system runs 24 hours per day via the Internet and links 110 WHO Influenza Centers in 83 countries. The centers communicate electronically, allowing each one to enter data remotely and to access real-time epidemiologic and virologic information. In addition, there are four other Collaborating Centers for Reference and Research on Influenza located in Australia, Japan, England and the United States. The global influenza surveillance monitors how influenza viruses vary within and between countries and continents during an influenza season, and it ensures both the collection of viral isolates for rapid characterization and the assessment of the epidemiological activity in the participating countries. This surveillance is critical in monitoring antigenic drift and shift.<sup>55</sup> Using this information, governments determine which strains require protections within the supply of the country's influenza vaccine and companies manufacture, in very short timeframes, the vaccine to those specifications. Vaccine in hand, public and private health care providers immunize susceptible groups.

Although the disease has occurred in chickens in subsequent years, officials have taken the appropriate actions, and the world is fortunate that the Hong Kong outbreak has not spread, initiating the long-anticipated, much-feared pandemic. Still, a pandemic is predicted and planning for the event is underway within this country and in international health care settings.

### ***Managing Bioterrorism: Disease as a Weapon of War***

In 1997, experts from around the world arrived in Hong Kong within days of the alerts about the new influenza strain. Their responses were prompt; cooperation was evident. A global infrastructure was in place and succeeded in alerting all nations to the possibility of the anticipated pandemic. Political will, public health readiness, and press coverage—perhaps generated by the impact of prior pandemics—has helped us achieve better global health protection from influenza. Does influenza pandemic planning now provide us with a road map for considering global covenants regarding infectious disease—and particularly those that are intentionally inflicted? If we are going to respond now to threats of uncontrolled, serious disease—whether induced unintentionally intentionally—can we use influenza as a model to address the seriousness of the challenges that lie ahead?

Perhaps influenza is the best of all models. On one hand, the experts say that a pandemic is a near-certainty, and so on those grounds, the effort to plan, protect and educate the public is a worthwhile investment to make. On the other hand, the unknowns of an intentional spread of disease are speculative, and securing the political will to plan for and fund the necessary infrastructure will therefore be difficult. Influenza pandemic planning with bioterrorism in mind may be the best and most successful alternative.

Engaging in planning for the intentional infection with deadly disease will require substantial education of the public and policy makers. Bioterrorism has yet to take its toll in modern times, but its potential is not new to the public health and safety community. Historical public health studies have charted the course of plagues through Europe and Asia, going back

thousands of years. The experts are well aware of infectious diseases and their consequences. However, the notion that these disease epidemics could have killed 25 million people in the mid-1300s—which was 30-50% of the European population at the time—is staggering to the modern imagination. Even those in political and leadership positions who may deal with similar scenarios today are unprepared for the types of disruption in economics, politics, religion, agriculture, and science that was caused then by the Black Death.<sup>56</sup> Yet, we will inevitably face some of those same consequences in our time—if not from bioterrorism, then from HIV/AIDS.<sup>57</sup>

Understanding how diseases can be transmitted, how they have been used in wartime,<sup>58</sup> how they have been used in domestic terrorism already, is key to grasping the urgency of addressing bioterrorism today. Since attempts at bioterrorism have been foiled<sup>59</sup> and incidents have been rare, they seem too remote for serious attention. As time passes and memories of Postal Service anthrax incidents of 2001 fade, it will be difficult to maintain the momentum needed to successfully plan and prepare for possible future attacks. What today seems *possible*, tomorrow may seem *improbable* and next year may seem *impossible*. Because of their planning, experts today know about the most likely diseases that would be employed in an attack. They also know our current national vulnerabilities, have created scenarios to anticipate the impact on the nation's health, and have proposed programs to improve our readiness.

Despite these plans, it has been difficult, unfortunately, to secure the funding necessary for the infrastructure required for readiness. As a result, public health surveillance and communication systems are weak, laboratory facilities and manpower are insufficient, vaccines are not available in adequate types and supply, and coordination across the myriad of local, state, and national agencies had been untested—at least until September 11. The WHO encouraged world leaders to plan, Presidential Decision Directives guided federal agencies, and the CDC coordinated with states, but, in the opinion of many experts, we are still woefully unprepared for an attack. The execution of the Postal Service contamination might have been a surprise; our failure to adequately respond to it was not. If there is a positive side to this event, it is that the nation's political leaders and the public now know what public health experts have known for decades about the risks of serious infectious disease. Will the nation now be more willing to invest in those services and systems at a level sufficient to protect us in the event of a future attack?

A truly global covenant to protect and care for the world's people as they live, work, and travel more often and in closer proximity to one another is needed. If one is to emerge, then we in the U.S. and other developed nations must become more aware and take more definitive action. If we cannot respond out of compassion and social justice, then enlightened self-interest will do. But act, we must. There are no “developing-world” diseases. There are only global diseases. Despite our wealth, education, and privilege, we and our children will be exposed to these diseases through global commerce, education, and entertainment. Despite our immigration and border controls, we will suffer the consequences of the presence of these diseases in other countries. Despite our own relative domestic tranquility, the harsh realities of disease-driven destabilization in other countries will impact our lives. Despite our best efforts, bioterrorism may be the most devastating weapon our enemies will use against us—or others—and the impact will be felt in our own communities.

## *The Global Village Needs an Expanded Covenant*

The *New York Times* recently reflected on the dilemma of our living side-by-side with microbes:

Microbes, are, after all, members of the most ancient, zealous and Darwinically gilded 24-7 delivery consortium. They travel by land, sea, air, nose, blows, glove, love, sewage, steorage, rat backs, hat racks, uncooked burritos, overlooked mosquitoes.<sup>60</sup>

The poetry of this statement should not distract us from the deadliness of the illnesses cause by microbes. We will certainly face them as a nation—and a world—in the coming years. So what actions should we take? Charting the course is underway in government and private sector groups, and a consensus is emerging. To better prepare for the future we need to learn from simulations like *Dark Winter* and from the reality of outbreaks as they have occurred.<sup>61</sup> What these lessons have taught us is that our public health infrastructure—at local, state, national, and global levels—is tattered and our lost confidence in its ability to protect us is justified. It needs improved communication systems, more laboratories and personnel, additional disease surveillance capability, and stockpiles of drugs and vaccines for at least the most predictable of our needs. We also need improvements in public education and awareness about the appropriate use of antibiotics and encouragement for the wider acceptance of vaccines. Health care professionals need education to better diagnose infectious disease and identify unusual patterns of illness, even in small populations and clear protocols for treating patients when these diseases strike. Additional research on infectious diseases is needed to develop control strategies, drugs, or vaccines as a national defense strategy. Since many of the disease killers today are caused by organisms that can be controlled if we make the appropriate investments, eradication is also a necessary component of any strategy.

Not all our needs lie within the purview of the health sector, however. The policy, ethical, and legal foundation must be laid now, during these times of heightened awareness and relative tranquility, to address the complex issues of personal rights in an era of disease and bioterrorism. In 1893, Muncie, Indiana, suffered a suspected smallpox outbreak. The diagnosis of the disease, and therefore the government recommendations for quarantines, were questioned by the local community. Army guards patrolled neighborhoods, violators were jailed, and several public health officers were shot.<sup>62</sup> In Boston in 1902, public health officers ordered smallpox immunizations, fined or jailed those who refused to comply, and forcibly immunized others using squads of special police.<sup>63</sup> Is this our likely future as well? Now—not when the crisis is upon us—is the time to consider what we will require of the public in terms of quarantines and what rights to personal choice and privacy they will have. Likewise, we should consider now the implications for post-crisis malpractice and product-liability litigation in the context of treatment administered by overtaxed clinicians with incomplete information and resources.

Those of our healers who work in public health will plan for, and respond to, the challenges of global infectious disease and bioterrorism acts within their current environment; and herein is another challenge. Health care today—here and abroad—is stressed. Much like a physician uses “stress tests” to detect the weaknesses in the patient’s body, infectious diseases and bioterrorism are the “stress tests” of the health infrastructure. The limits of knowledge,

information, surveillance, personnel, facilities, and treatments are, now more than ever, clear to us. This is true of our mental health care systems as well as those for our physical health. Our vulnerabilities are showing, and they promise to worsen over time.

How will it be possible to address these issues? It will be possible through a sustainable effort of both public and private sectors. It will be possible through the coordination of local, state, national and international alliances of health and other sector leaders. It will be possible if all the parties involved—patients, healers and communities—embrace a global covenant.

- For patients, this will mean becoming educated about, and practitioners of, those behaviors that prevent the spread of disease. We will have to wash our hands, use antibiotics correctly—and only when necessary—and be willing to take vaccines. We will have to take curative medicines—such as those for tuberculosis—in compliance with recommendations.
- For healers, this will mean developing and maintaining the capacity to deliver services and supplies when epidemics strike. Collaboration is one avenue to success, and there are models that point the way. In the case of tuberculosis, the WHO championed and initiated direct observation therapy (DOTS), for example, wherein a health care provider actually observes patients taking tuberculosis medicines to be sure it is done correctly, thus working to prevent further treatment-resistant disease.<sup>64</sup> In the case of malaria, the WHO developed the *Roll Back Malaria* program, encouraging the use of bednets impregnated with mosquito repellent to protect from mosquito transmission of the disease. At a cost of a few dollars per bed, malaria transmission will be cut by 50%. ExxonMobil contributes to *Roll Back Malaria*, as well as to several other malaria projects investigating antimalarial drugs.<sup>65</sup> Mothers in Ethiopia, trained by a Johns Hopkins School of Hygiene and Public Health project, have reduced malaria in young children by 40% in a program to diagnose the disease, treat it with chloroquine, and detect adverse reactions.<sup>66</sup> This collaboration requires that agencies resolve infighting,<sup>67</sup> corrupt leaders not use national needs to amass personal wealth,<sup>68</sup> and tensions are resolved between the public and private sectors.
- For communities, this will mean financially supporting public health tools so that they are ready when disease disasters strike. The effective methods to address infectious disease are too numerous to list here. But some examples are indicative of the approaches to protecting health. Public funding is one way, private investment is another, and philanthropy is an increasingly important way. In recent years philanthropists have directed their efforts at global health causes. Bill Gates' donation of \$21 billion to The Bill and Melinda Gates Foundation to improve health care in the developing world is the single largest of its type, and since 1998 the foundation has contributed \$845 million<sup>69</sup> to tuberculosis projects. Ted Turner has likewise made notable donations. They are among the richest people in the world, and their philanthropy, as well as the donation of others, is on the rise, particularly among Americans, who are the most generous of all the nations.<sup>70</sup> Their efforts, though criticized by some, are laudable and more should be encouraged, not only here, but

abroad. Our tax-deductibility measures are one way that the social objective of giving is supported by national policy. Other nations, most of whom do not support giving with tax incentives, might well consider doing so. Even Americans, however, can afford to be more generous as a nation. Despite being the most generous—in both real dollar and GDP terms—we still donate a scant one percent of our national GDP. It is estimated that up to half of the health care provided in many developing nations is funded through donations, and so the maintenance and growth of these programs is critical to the future of health.<sup>71</sup>

- For the developed nations, this will mean addressing the underlying causes of disease by assisting with development projects that bring safe water and food and adequate housing and sanitation to those who lack them on the globe. It will also mean addressing other root causes of conflict. The public health community was recently criticized for positioning infectious disease and bioterrorism in the context of the wider social issues of global power shifts, poverty, and injustice. When it advocated that seeking ways to alleviate poverty and negotiate peaceful settlements to disputes was an essential part of prevention, the American Public Health Association leadership was jeered in some quarters. In fact, those healers who ply their skills in the public health arena are calling our attention to a very important fact: that the best way to assure health over the long term is to reach the social roots of disease conditions. They are calling for the interdependence that covenants entail and are warning us that, while depending upon them for assistance at the time of our need is within their covenant of caring, it is also expensive and should be unnecessary. They are inviting us into a covenant of obligation and pointing the way to the social, economic, and cultural issues that must be addressed in order to exercise that obligation. If public health officials can succeed in accomplishing the action steps they intend to take, they may well be able to restore and strengthen confidence of the public in the health care system—and the government—to care for the nation's needs. In return, political leaders and the general public should respond by not only supporting the needed resources, but also with mandates to work toward resolving the political and economic conditions causing intentional and unintentional epidemics.

There is a simple reason to accomplish these goals: no one is safe. Pathogenic microorganisms do not respect man-made national borders. As people cross borders they bring diseases with them. Whether they know they are carriers or not, whether their intentions are innocent or malevolent, too many of these diseases can kill. We in the U.S. might think we can ignore the actual death toll in other nations, but we cannot. Aside from the human impact, there are the social, economic, and political impacts of disease on those nations, and ultimately on our own. Gro Harlem Brundtland, Director General of the World Health Organization, has said, “With globalization, a single microbial sea washes all of mankind. There are no health sanctuaries.”<sup>72</sup> Not even here, in this most prosperous of lands.

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<sup>1</sup> This appeared originally in 2001 in *Covenants: Inspiring the Soul of Healing*. Readers interested in exploring covenants in greater depth can find background in *The Origins of Healing as Divine Gift* and *History and Modern Applications of Covenant Healing Traditions* which appear in this series.

In summary, healing traditions are based on ancient views that healing skill came from the divine. Healers were aligned with divine forces against the terrible, unknowable and sometimes evil forces of illness. As a result, healer-patient relationships were structured as covenants. Covenants differ from contracts. Contracts have a defined beginning and end and specify the duties of the parties in detail. Covenants do not end and do not detail the duties of the parties.

There are two types of covenants, both are relevant in health care and are expressed in oaths taken by clinicians and others in health care. The first type – a covenant of *grant* – defines what one party does for another, without conditions or expectations. Parents have covenants of this type with their children, providing them food, shelter, clothing and protection. The second type – a covenant of *obligation* – involves mutual promises between the parties. Spouses enter into this type of covenant ‘...for better or for worse.’

The *Oath of Hippocrates*, a classic covenant statement, contains both types. It creates a covenant of *obligation* with other healers, calling for the oath-taker to “...study, learn and teach my fellows...and to treat his sons as my sons.” Then, the oath “...grants health...” to the patient. The *Prayer of Maimonides*, an oath created later, contains the same covenant of *obligation* among healers and calls patients into a covenant of *obligation* as well, asking that patients follow medical advice, take prescriptions and avoid the advice of meddling friends and relatives uninformed about health and disease.

The book suggests that everyone in health care – not just clinical experts but those in any role in research, management, insurance, health reporting and even policy – are the sophisticated extension of ancient tribal healers. Our societies are more complex, as is our knowledge, our data and information, our technology and our systems of providing care. As a result, as healers we have entered healing streams of an ancient origin. Our patients and communities expect us to ascribe to these covenant values.

In my view – and I am not alone in this – health required the integral relationship among healers, patients and communities. I therefore proposed three steps to transform health: first, a covenant of obligation among all healers, as I broadly defined them; second, a covenant of obligation with patients; and third, a covenant of obligation with communities, as well.

This is an application of those ideas to the policy issues addressed here.

<sup>2</sup> Genesis, 9:7.

<sup>3</sup> John Gannon, “The Global Infectious Disease Threat and its Implications for the United States.” Available at <http://www.odcl.gov/CIA/publications/nie/report/nie99-17d.html>. Accessed October 10, 2001.

<sup>4</sup> Several novels have provided glimpses into the impact of infectious disease on a nation and the world: Alistair MacLean, *The Satan Bug* (New York: Fawcett Publications, 1962); Michael Crichton, *The Andromeda Strain* (New York: Knopf, 1969); Stephen King, *The Stand* (New York: Doubleday, 1978); and Frank Herbert, *The White Plague* (New York: Putnam, 1982).

<sup>5</sup> T. McKeown, *The Modern Rise of Population* (New York: Academic Press, 1976). G. Armelagos and N. Cohen, eds., *Paleopathology at the Origins of Agriculture* (New York: Academic Press, 1984). G. Armelagos, K. Barnes, J. Lin, “Disease in Human Evolution: The Re-emergence of Infectious Disease in the Third Epidemiological Transition,” *National Museum of Natural History Bulletin for Teachers*, Vol. 18 No. 3 Fall 1996. Available at <http://www.nmnh.si.edu/anthro/outreach/anthnote/fall99/anthback.htm>. David Satcher, “Emerging Infections: Getting Ahead of the Curve,” *Emerging Infectious Diseases*, Vol.1, No.1, January-March 1995.

<sup>6</sup> Information available at <http://www.doh.gov.uk/cjd>. United Kingdom Department of Health. Accessed September 3, 2001.

<sup>7</sup> A. Kanabus and S. Allen, “The Origin of AIDS and HIV, and the First Cases of AIDS.” Available at

---

<http://www.avert.org/origins.htm>. Accessed December 1, 2001.

<sup>8</sup> E. Crubezy, et al, "Identification of mycobacterium DNA in an Egyptian," *C R Acad Sci III* 1998, Nov:321(11):942-51. Cockburn and Cockburn, eds., *Mummies, Diseases and Ancient Cultures* (New York: Cambridge University Press, 1995). D. Christensen, "Pre-Columbia mummy lays TB debate to rest," *Science News* 143:181 (March 19, 1994).

<sup>9</sup> Hippocrates, *Of the Epidemics*, Book II translated by Francis Adams. Available at <http://classics.mit.edu/Hippocrates/epidemics.html>. Accessed April 6, 2001.

<sup>10</sup> "TB Wars: Man's Ancient Struggle." Available at <http://www.md.huji.ac.il/microbiology/bact330/lecturetb.html>. Accessed April 6, 2001.

<sup>11</sup> K. Fackelmann, "Paleopathological Puzzles: Researchers unearth ancient medical secrets," *Science News Online*, August 30, 1997.

<sup>12</sup> "TB Wars: Man's Ancient Struggle." Available at <http://www.md.huji.ac.il/microbiology/bact330/lecturetb.html>. Accessed May 3, 2001.

<sup>13</sup> T. Dormandy, *The White Death: A History of Tuberculosis* (New York: New York University Press, 2000).

<sup>14</sup> Robert Desowitz, *The Malaria Capers (More Tales of Parasites and People, Research and Reality)* (New York: W. W. Norton & Company, 1991).

<sup>15</sup> *Al-Ruzi (Rhazes) on Smallpox and Measles*. Available at <http://users.erols.com/gnqm/euromed3.html>. Accessed May 3, 2001.

<sup>16</sup> David Satcher, Statement before the Committee on International Relations U.S. House of Representatives, June 29, 2000. Available at [http://www.house.gov/international\\_relations/full/disease/satcher.html](http://www.house.gov/international_relations/full/disease/satcher.html). *Diseases of Entomological Importance*. Available at [http://www.entomology.unl.edu/history\\_bug](http://www.entomology.unl.edu/history_bug). Accessed May 2, 2001.

<sup>17</sup> Suzanne Possehl, "The long reach of bugs without borders," *Hospital & Health Networks*, Vol. 72, 7/5/98.

<sup>18</sup> Leviticus, 14:37-53.

<sup>19</sup> Leviticus, 13:47-59, 14:8-9.

<sup>20</sup> Robert Mackey, "Ten diseases on the way out," *New York Times Magazine*, May 6, 2001, pp34-36.

<sup>21</sup> Information available at <http://www.cartercenter.org>. Accessed November 10, 2001.

<sup>22</sup> A. J. Cann, *History of Smallpox*. Available at <http://www.tulane.edu/~dmsander/Tutorials/pox>. Accessed December 21, 2001.

<sup>23</sup> S. Fretwell and K. Winiarski, "Global warming could devastate human health," *The State*, April 7, 2001. Available at <http://www.thestate.com>. Accessed September 20, 2001.

<sup>24</sup> David Heymann, "The Urgency of a Massive Effort Against Infectious Diseases," June 29, 2000 Statement before the Committee on International Relations U.S. House of Representatives. Available at <http://www.who.org>. Accessed November 10, 2001.

<sup>25</sup> T. Dormandy, *The White Death: A History of Tuberculosis*. New York: New York University Press, 2000.

<sup>26</sup> Abigail Zuger, "Infectious Diseases Rising Again in Russia", *New York Times*, December 5, 2000. Available at <http://www.nytimes.com>. Accessed November 2, 2001.

<sup>27</sup> John Gannon, "The Global Infectious Disease Threat and its Implications for the United States". Available at <http://www.odcl.gov/CIA/publications/nie/report/nie99-17d.html>. Accessed November 2, 2001.

<sup>28</sup> G. Armelagos and N. Cohen, *op. cit.*

<sup>29</sup> Gro Harlem Brundtland, "Health and Population," BBC Reith Lectures 2000. Available at



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[http://news.bbc.co.uk/hi/english/static/events/reith\\_200/lecture4.stm](http://news.bbc.co.uk/hi/english/static/events/reith_200/lecture4.stm). Accessed May 18, 2001.

<sup>30</sup> Rebecca Voelker, "Travel Risk of HBV," *Journal of the American Medical Association (JAMA)*, December 13, 2000, 284 (22), pp 2863. This report describes a study of European travelers' knowledge of disease risks. Though nearly 75% were at risk for contracting HBV, only half understood the method of transmission and only 17% were vaccinated.

<sup>31</sup> Marilyn Chase, "New virulent forms of tuberculosis spur concerns world-wide," *Wall Street Journal*, December 17, 1999, p. B1.

<sup>32</sup> Personal Communication, Rick Glover. M.D. Air travel has been investigated as a source of infectious disease. See World Health Organization, *Tuberculosis and air travel: guideline for prevention and control* (Geneva, World Health Organization, 1998).

<sup>33</sup> P. Martens and L. Hall, "Malaria on the Move: Human Population Movement and Malaria Transmission," *Emerging Infectious Diseases*, Vol. 6, No. 2, March-April 2000. "Health: Malaria-Carrying Mosquitoes Hitch Rides on Airplanes," *Inter Press Service English News Wire*, 8/23/00.

<sup>34</sup> John Gannon, "The Global Infectious Disease Threat and its Implications for the United States." Available at <http://www.odcl.gov/CIA/publications/nie/report/nie99-17d.html>. Accessed May 3, 2001.

<sup>35</sup> Pamela Constable, "For Nepali Girls, a Way Station to Dignity," *New York Times*, April 24, 2001, p. A14.

<sup>36</sup> International Federation of Red Cross and Red Crescent Societies, *World Disasters Report 2001*, International Federation of Red Cross and Red Crescent Societies, Geneva, p 198.

<sup>37</sup> "Communicable diseases are main health threat to Kosovo refugees," April 6, 1999. Available at <http://www.who.int/inf-pr-2q999/en/pr-18.html>. Accessed May 6, 2001.

<sup>38</sup> Christopher Wren, "U.N. Council Addresses HIV/AIDS in its Focus," *New York Times*, January 20, 2001, p. A7. Alpha Nuhu, "Refugee Camps Attract Sex Workers and AIDS," *Panafrican News Agency*, January 5, 2001. Available at <http://allafrica.com>. Accessed May 3, 2001.

<sup>39</sup> "Defending National Borders." Available at <http://www.who.org>. Accessed May 3, 2001.

<sup>40</sup> Elizabeth Anne Fenn, *Pox Americana* (New York: Hill and Wang, 2001). See also: Gina Kolata, "New York Was Bioterrorism target, in 1864," *New York Times*, November 13, 2001, F7, col 1; and Gina Kolata, "When Bioterror First Struck U.S. Capital," *New York Times*, November 6, 2001, p F1, col 4; and Mark Derr, "New theories Link Black Death to Emola-like Virus," *New York Times*, October 2, 2001, p F4, col 1.

<sup>41</sup> *1999 Country Reports on Human Rights Practices*, Bureau of Democracy, Human Rights, and Labor, U.S. Department of State, February 25, 2000. Available at <http://www.state.gov>. Accessed May 6, 2001.

<sup>42</sup> Blaine Harden, "For Burmese, Repression, AIDS and Denial," *New York Times*, November 14, 2000. Available at <http://www.nytimes.com>. Accessed May 6, 2001.

<sup>43</sup> John Pomfret, "The High Cost of Selling Blood," *Washington Post*, January 11, 2001, p. A01.

<sup>44</sup> Denise Grady, "Drug Resistant Bacteria Still on the Rise," *New York Times*, December 28, 2000. Available at <http://www.nytimes.com>. Madeline Nash, "The Antibiotics Crisis," *Time.com*, January 10, 2001. Available at <http://www.time.com>.

<sup>45</sup> An unimmunized American child contracted measles and died after being exposed to the disease while standing in line next to a measles-infected Brazilian child at an amusement park in the U.S. Personal communication Robert Howard, Centers for Disease Control, 2002.

<sup>46</sup> F. Cox, Z. M. Khan, J. E. Schweinle, L. Okamoto, and T. McLaughlin, "Cost associated with the treatment of Influenza in a managed care setting," October 3, 2000. Available at <http://www.medscape.com/medscape/GeneralMedicine/journal/2000/v02.n05/mgm1003.cox/pnt-mgm1003.cox.html>. Accessed February 24, 2001. Centers for Disease Control and Prevention, "Prevention and control of influenza. Recommendations for the

---

Advisory Committee on Immunization Practice (ACIP),” *MMWR* [SPELL OUT FIRST TIME]1999; 48:1-28. K. L. Nichol, A. Lind, K. L. Margolis, M. Murdoch, R. McFadden, M. Hauge, S. Magnan, M. Drake, “The effectiveness of vaccination against influenza in healthy, working adults,” *New England Journal of Medicine (NEJM)* 1995; 333:889-893.

<sup>47</sup> *Guidelines for Prevention and Control of Pandemic Influenza in Healthcare Institutions* Draft 03/23/2000. Available at [http://www.ahcpub.com/ahc\\_root\\_html/hot/breakingnews/flue03232000.html](http://www.ahcpub.com/ahc_root_html/hot/breakingnews/flue03232000.html). Accessed February 4, 2001.

<sup>48</sup> *WHO Information Fact Sheet on Influenza*. Posted February 1999. Available at <http://www.who.int/inf-fs/en/fact211.html>. Accessed February 4, 2001.

<sup>49</sup> *WHO Information Fact Sheet on Influenza*. Posted February 1999. Available at <http://www.who.int/inf-fs/en/fact211.html>. Accessed February 4, 2001.

<sup>50</sup> P. A. Patriarca and N. J. Cox, “Influenza pandemic preparedness plan for the United States” *Journal of Infectious Diseases (J Infect Dis)* 1997; 176 Suppl 1:S4-7.

<sup>51</sup> S. Jones, “The Flu Hunters,” *Time Magazine*, February 23, 1998, 151(7), p56.

<sup>52</sup> Centers for Disease Control and Prevention, *Pandemic Influenza: A Planning Guide for State and Local Officials* (Draft 2.1). Available at <http://www.cdc.gov/nypa/pandemicflu.htm>. Accessed February 24, 2001. M. I. Meltzer, N. J. Cox, K. Fukuda, “The economic impact of pandemic influenza in the United States: priorities for intervention” *Emerging Infectious Disease* 1999; 5(5): 659-71.

<sup>53</sup> R. Snacken, A. P. Kendal, L. R. Haaheim, and J. M. Wood, “The Next Influenza Pandemic: Lessons from Hong Kong, 1997,” *Emerg Infect Dis* 1999; 5(2): 195-203.

<sup>54</sup> FluNet: Global Influenza Surveillance Network. Available at <http://oms2.b3e.jussieu.fr/fluenet>. Accessed on March 2, 2001.

<sup>55</sup> D. Stambouliau, P. E. Bonvehi, F. M. Nacinovich, and N. Cox, “Influenza,” *Infect Dis Clin North Am* 2000; 14(1): 141-66. A. Flahault, V. Dias-Ferrao, P. Chaberty, K. Esteves, A. Valleron, and D. Lavanchy, “FluNet as a Tool for Global Monitoring of Influenza on the Web,” *JAMA* 1998; 280(15): 1330-2.

<sup>56</sup> Norman E. Cantor, *In the Wake of the Plague: The Black Death and the World It Made* (New York: The Free Press, 2001).

<sup>57</sup> Laurie Garrett, *Betrayal of Trust: The Collapse of Global Public Health* (New York: Hyperion, 2000).

<sup>58</sup> Elizabeth Anne Fenn, *Pox Americana*. See also: Gina Kolata, “New York Was Bioterrorism Target, in 1864,” *New York Times*, November 13, 2001, F7, col 1, and Gina Kolata, “When Bioterror First Struck U.S. Capital,” *New York Times*, November 6, 2001, F1, col 4.

<sup>59</sup> Jonathan Tucker, “Historical trends related to bioterrorism: An empirical analysis,” *Emerging Infectious Diseases*, Vol 5 (4). Available at [www.cdc.gov/ncidod/eid/vol5no4/tucker.htm](http://www.cdc.gov/ncidod/eid/vol5no4/tucker.htm). Accessed May 6, 2001.

<sup>60</sup> Natalie Angier, “Together in sickness and in health,” *New York Times Magazine*, May 6, 2001, pp 67-69.

<sup>61</sup> James Hughes, Statement before the Subcommittee on National Security, Veterans Affairs, and International relations, Committee on Government Reform, U.S. House of Representatives, July 23, 2001. Available at [http://www.bt.cdc/press/Hughes\\_072320001.asp](http://www.bt.cdc/press/Hughes_072320001.asp). Accessed October 10, 2001. See also: Annie Fine and Marcelle Layton, “Lessons for the West Nile Viral Encephalitis Outbreak In New York City.1999: Implications for bioterrorism preparedness,” *Clinical Infectious Diseases*, 2001;32:277-282.

<sup>62</sup> Joseph Barbera, et al., “Large-scale quarantine following bioterrorism in the United States: Scientific examination, logistic and legal limits, and possible consequences,” *JAMA*, 2001;286: 2711-2717.

<sup>63</sup> Marilyn Werber Sheafini, “When quarantines are needed,” *National Journal*, November 17, 2001, pp 3612-3613.

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<sup>64</sup> David Heymann, "The Urgency of a Massive Effort Against Infectious Diseases," Statement before the Committee on International Relations U.S. House of Representatives, June 29, 2000. Available at <http://www.who.org>. Accessed November 2001.

<sup>65</sup> "Resurgence of a killer," *National Journal*, April 28, 2001, p. 1241. Available at <http://www2.exxonmobil.com/corporate/files/corporate/260401.pdf>. Accessed January 16, 2002.

<sup>66</sup> Rebecca Voelker, "Mothers fight malaria," *JAMA*, September 13, 2000, Vol. 284 (10) p 1235.

<sup>67</sup> Daren DeYoung, "Global AIDS Strategy May Prove Elusive," *Washington Post*, April 23, 2001, A01.

<sup>68</sup> Eric Schmitt, "Helms Urges Foreign Aids be Handled by Charities," *New York Times*, January 12, 2001. *Transparency International 2000 Report on County Corruption*. Available at <http://www.transparency.org>. Accessed May 3, 2001.

<sup>69</sup> Catherine Arnst and Kerry Capell, "Tuberculosis roars back," *Business Week*, October 2, 2000, p 153.

<sup>70</sup> "Giving Something Back, A Survey of the New Rich," *The Economist*, June 18, 2001, pp 15-17.

<sup>71</sup> Personal Communication with Jim Russo based on report of the World Bank pending publication.

<sup>72</sup> Gro Harlem Brundtland, "Health and Population." Available at [http://news.bbc.co.uk/hi/english/static/events/reith\\_200/lecture4.stm](http://news.bbc.co.uk/hi/english/static/events/reith_200/lecture4.stm). Accessed May 18, 2000.