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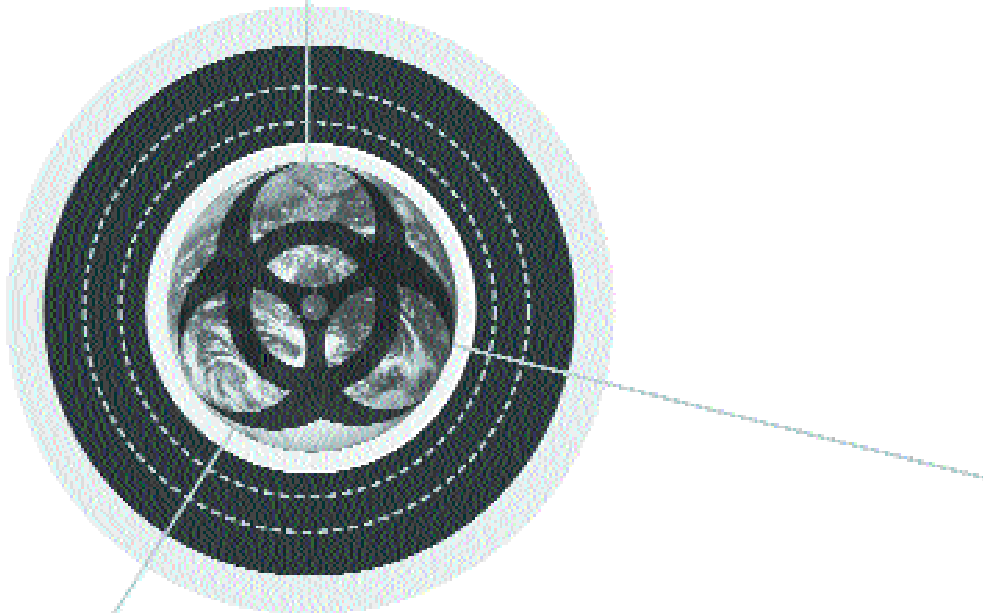

BIOALERT
DISEASE KNOWS NO BORDERS

Prevention is Key

AN INTRODUCTION BY
JAMES M. WILSON

Imagine over twenty points of access to a country. Through these points flow millions of people, animals, and cargo shipments each year. Somewhere, a cryptic pathogen is carried through one of these points undetected. Over the following weeks, the characteristic pattern of an outbreak is recognized only after several people within the same city die of similar symptoms. Public health officials eventually discover that the cryptic pathogen is a virus that attacks the brain and kills 10 percent of the people it infects. They also make the unfortunate discovery that the virus can be carried by native mosquitoes, infect local animals, and thus hide itself in the ecosystem. The epidemic abates but the virus is still there, hiding in the environment until conditions are favorable for it to re-emerge. During the following season more cases are identified. The country now has a new infectious disease with which to contend—one that will cause significant morbidity and mortality and require millions of taxpayer dollars for surveillance and control measures over subsequent years.

Is it possible to have a similar incident here in the United States? With twenty-five major international airports serving as access points, the possibility of exotic pathogens being introduced is a reality. Monitoring these points of entry for disease is a monstrous and nearly impossible task. In fact, the above "hypothetical" scenario actually took place in 1999. Airport-based and national passive surveillance systems in the United States proved ineffective in preventing the introduction of West Nile virus to New York City—where it infected fifty-six people and caused seven deaths—and its subsequent ecological establishment along the eastern seaboard. This was the first documented appearance of West Nile virus in the western hemisphere. Indeed, the United States must repeatedly contend with exotic diseases such as dengue, cholera, and malaria, and there is little question of the impact of HIV, an introduced pathogen, on U.S. society. In some cases these exotic diseases attempt ecological establishment, creating the possibility of additional outbreaks years later. As author David L. Heymann points out, now, more than ever, the United States is not an island. The inability to control and contain an infectious disease abroad can have direct implications for U.S. biosecurity.

Deliberate introduction of a pathogen through a terrorist attack raises additional concerns about the adequacy of U.S. surveillance and response systems. Simulations and response exercises have repeatedly demonstrated the inadequacy of both of these systems. Recognition of these systems' failures can be a positive impetus for change.

In this Forum, leading infectious disease experts offer several articles that challenge the reader to consider the problem of transnational movement of pathogens—either through "natural" or "intentional" mechanisms—and how this can affect U.S. national security. David L. Heymann of the World Health Organization examines the threat that infectious diseases present to global security. He regards the problem as one that all nations must confront—and one that cannot be addressed successfully by any single country.

Duane J. Gubler of the U.S. Centers for Disease Control and Prevention offers two case studies demonstrating why infectious diseases surfacing in a country on the other side of the world are a direct threat to U.S. security. He reminds us that the patterns of global infectious diseases are not static; transnational movement can, does, and will continue to occur, as will the challenge this presents for infectious disease surveillance and response in the United States. Gubler also suggests that while the United States should consider improvements in its own surveillance and response capability, it should also consider assisting with surveillance and response at the source—the origin countries. Control of infectious disease abroad can prevent extension of the problem to the United States.

It was once mainstream to view factors such as war and poverty as the major destabilizing forces on a society and its economy. Yet infectious disease can also be a potent disruptive factor. Maureen Lewis of the World Bank Group discusses the economic impact of AIDS to demonstrate how an infectious disease may place major stress upon a national economy and the individuals struggling to earn an income within it.

Finally, Eric K. Noji of the U.S. Centers for Disease Control and Prevention presents the issue of biological terrorism and its more concrete implications for U.S. national security. The biggest frustration in attempting to identify a solution to the problem is accurately assessing the true threat: Can a mass-casualty event occur through the successful deployment of a biological agent in a U.S. city? How likely is such an event?

As in clinical medicine, prevention is key. For the United States, the first step in contending with infectious diseases is to acquire more knowledge of the situation. Second, the United States must recognize that infectious disease is not just the problem of the rest of the world, but of the United States as well. The point is not to argue whether a successful bioterrorist attack on U.S. soil is likely. Rather, it is to recognize that the problem of infectious diseases requires a common solution, not merely individual action by a single country. It is time to consider the role of the United States in the global solution: Will we seek preventive measures within the international arena or merely wait for the next introduction of an exotic pathogen or release of a bioweapon?

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The Fall and Rise of Infectious Diseases

David L. Heymann

Just twenty years ago, wealthy nations could look on infectious diseases with the kind of smug indifference reserved for vanquished enemies. Smallpox had been eradicated—was so surely gone, in fact, that vaccination stopped—and word was out that polio might become the next candidate for deliberate extinction. Malaria, tuberculosis (TB), and other mass killers from the past had retreated to distant shores. Plagues akin to the Black Death were ancient history—infectious diseases would never again sweep across continents, causing death and instability on such a massive scale. Of the threats that remained, vaccines protected against some of the worst, while potent antibiotics kept most others at bay. Armed with the powerful tools of research, modern science had won the battle against infectious diseases. With these diseases out of the way, research could now concentrate its considerable powers on the fight against cancer, heart disease, and other top priorities for the industrialized world.

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But infectious diseases continued to thrive among the world's neglected and poorest in both industrialized and developing countries, and complacency proved to be an especially good medium for their progressive growth. Those twenty years witnessed the resurgence of malaria and TB, the spread of cholera and yellow fever to new areas, a startling outbreak of plague, foodborne diseases on the billion-dollar scale, and the advent of several lethal new diseases with no vaccines and no cure. Antibiotics began to fail, with replacements either much more costly or not even in sight. Multi-drug resistant strains of TB started appearing in U.S. hospitals, prisons, and homeless populations with a fatality rate of 70 percent and an estimated $1 billion in healthcare and containment costs. Mosquitoes carrying the malaria parasite stowed away on jets, bringing malaria to people working or living near airports in temperate zones where it had long ago disappeared. West Nile fever emerged in New York City and then spread along the coast, costing almost $100 million to control. Altogether, over thirty new infectious diseases appeared in the short span of three decades. Among them, AIDS—the new Black Death—moved swiftly from its spot on the horizon to engulf the globe. What went wrong?

Throughout history, human populations have experienced major epidemics of infectious diseases, often resulting in large numbers of deaths, panic, disruption of trade, and political instability. Before the advent of effective treatments and vaccines, conditions such as poverty, overcrowding, and poor sanitation provided fertile ground for disease transmission. These disease-promoting conditions remain important today, as evidenced by outbreaks in crowded refugee camps, epidemics following the breakdown in sanitation caused by natural disasters, and the persistently high levels of multiple infections seen in developing countries, where poverty and lack of sanitation are so often the norm.

However, an explanation for the current emergence of so many new diseases, and the resurgence of so many others, must look beyond historical causes and consider some striking new trends. These have to do with the way we inhabit the planet—how we produce our food, prescribe and use drugs, travel and trade, and interact with the environment and the infectious agents it hosts. One characteristic of infectious diseases is their potential for change and adaptation, and modern trends have amplified that potential considerably. Not only do infectious diseases travel faster than ever before, but they also have been given novel opportunities to develop resistance to drugs, to jump the species barrier from animals to humans, and to infect our food.

Jet-Set Disease Threats. Of these recent changes, one of the most important is the phenomenal increase in our mobility. Since 1950, the number of international airline passengers has soared from two million a year to over 1.4 billion. In medieval times, deadly plagues were transported from continent to continent by flea-infested rats sailing on ships. Today, infectious agents carried by passengers or insects fly by plane from one corner of the earth to another, all in a matter of hours. In the United Kingdom, nearly 1,000 new cases of malaria are imported every year by passengers arriving from the tropics. In the United States, the numbers are even greater.

Deadly airborne diseases such as the pneumonic plague, influenza, and TB can easily spread in crowded airport lounges, on a jumbo jet, or by passengers after their return home. In 1977, over 70 percent of passengers on board a grounded American airliner were infected with influenza by a fellow traveler. In 1978, the polio virus was imported to Canada by unvaccinated travelers from Western Europe, resulting in an outbreak of eleven cases of the paralytic disease. In the early 1990s, a flight attendant with active TB is believed to have infected up to twenty-three fellow crew members over the course of several flights. Most recently, Ebola-like symptoms in a Congolese woman who arrived in Toronto after stopovers in Addis Ababa, Rome, and Newark created near hysteria in North America.

Not only are infected travelers a threat, but the disease vectors themselves may stow away on flights. Mosquitoes carrying the malaria parasite can enter the passenger cabin before takeoff or during stopovers and survive the trip in the luggage hold. As a result, malaria infections and deaths regularly occur in Europe and North America following one-off bites from imported mosquitos near international airports. London, Paris, Brussels, Geneva, and Oslo have all reported recent cases of such airport malaria, as have cities in the United States and Canada.

Infectious diseases can invade new territories in other ways as well. In 1985, the aggressive tiger mosquito, normally found in Asia, slipped unnoticed into the United States inside a shipment of water-logged used tires. Within two years, the mosquitoes, capable of transmitting yellow fever, dengue, and other diseases, had established themselves in seventeen states. In 1991, a ship carrying contaminated water from Asia in its ballast tanks caused a cholera epidemic in Peru. The disease spread rapidly throughout South and Central America, causing some 11,000 deaths.

Another side of our mobility is our incursion into new or unfamiliar ecological zones, sometimes for economic reasons, sometimes for adventure and fun. When humans penetrate or modify formerly unpopulated regions, they may come into close contact with unfamiliar animal reservoirs or disease vectors against which they have no immunity. Outbreaks of malaria, yellow fever, and leishmaniasis continue to be linked to workers who penetrate rainforests to cut trees. Recent importations of yellow fever into Switzerland, the United States, and Germany have occurred after tourists, unaware of the need for vaccination, returned from excursions deep into the rainforests. In September of last year, the EcoChallenge sports event in the jungles and rivers of Malaysia, which drew over 300 athletes from twenty-nine U.S. states and twenty-six other countries, resulted in the importation of leptospirosis, an acute bacterial disease, to cities in three continents.

Mad Cows and “Chicken Ebola.”

An equally disturbing trend is the frequency with which diseases "previously confined to animals are making the evolutionary leap to humans. Again, exploitation of new ecological zones plays a role. Man-made changes such as deforestation disrupt natural habitats and can force animals into closer contact with humans. Global warming and climate extremes, whether involving excessive rainfall or drought, can likewise displace animal species and bring them into closer contact with human settlements. Over two-thirds of the emerging infections identified during the 1990s are known to have originated in animals, both domesticated and wild. Some are believed to have emerged from animals living in tropical rainforests or elsewhere in close proximity to humans, where microorganisms have succeeded in crossing the species barrier to humans. Though intensive research has failed to disclose the origins of Marburg and Ebola outbreaks, both are thought to have animal sources somewhere in the transmission cycle.

Less exotic but all the more alarming are cases where diseases of domesticated animals have made the leap to humans, with major implications for the food supply and huge costs for agriculture and trade. One dramatic example occurred in 1997 in Hong Kong, where an influenza virus previously found only in geese and chickens caused infections and deaths in humans. Immediately dubbed "chicken Ebola" by the press, the outbreak resulted in the destruction of 1.2 million birds. In 1999 an influenza virus previously confined to swine suddenly appeared in humans, raising the specter of the terrifyingly deadly Spanish Flu of 1918, which some believe was caused by an avian virus that first crossed the species barrier to swine before jumping to humans. In 1999 Malaysia also experienced the transmission of the newly identified Nipah virus from pigs to humans in an outbreak of viral encephalitis that caused panic in the country and among its neighbors.

Today, consumers purchasing foods from the local grocer risk exposure to pathogens native to remote parts of the world.

Most notorious of all is the advent of *bovine spongiform encephalopathy*, or "mad cow disease," first detected in the United Kingdom in 1986. The disease, traced to cattle feed prepared from the carcasses of ruminants, has now been linked to a new and invariably fatal disease in humans, the variant Creutzfeldt-Jakob disease.

Such developments are made particularly ominous by the increase in international trade, which has added food to the list of vehicles facilitating the rapid international spread of disease. Coupled with globalization, advances in food production technology have resulted in a food chain that is longer and more complex than ever before. Today, consumers purchasing foods from the local grocer risk exposure to pathogens native to remote parts of the world. In this remarkable new environment, tracing the origin of all the ingredients in a meal has become virtually impossible, creating an enormous challenge for the control of foodborne diseases.

Blunt Weapons. The food supply is guilty on another count as well: its contribution to the enormous problem of antimicrobial drug resistance. Since the discovery of the growth-promoting and disease-fighting capabilities of antibiotics, farmers, fish farmers, and livestock producers have used antimicrobials in everything from apples to aquaculture. Currently, only half of all antibiotics produced are intended for human consumption. The other half are used to treat sick animals, promote growth in livestock, and rid cultivated foodstuffs of various destructive organisms. Ongoing and often low-level dosing in the latter two uses results in the development of drug-resistant strains of bacteria in livestock. In several disturbing cases, multiresistant bacteria infecting humans have been directly linked to resistant organisms in animals.

A far more important cause of drug resistance is the widespread misuse of drugs prescribed for humans. This phenomenon is the most telling sign that we have failed to take the threat of infectious diseases seriously. It suggests that we have mishandled our potent and precious weapons for disease control, both by overusing them in industrialized nations and, paradoxically, by misusing and underusing them in the developing world.

The dramatic upsurge in the spread of drug-resistant microbes over the past decade is undermining today's efforts to control infectious diseases. As diseases once thought to be under control become increasingly resistant to available drugs, the specter of incurable infectious diseases looms large. In addition to requiring increased length of treatment with more expensive and, in some instances, more toxic antimicrobial drugs or drug combinations, resistant infections have seen a doubling of mortality rates. At the same time, fewer new antimicrobials reach the market, in part due to the high cost of new drug development. In fact, no new class of antibiotic has been marketed for human use since the 1960s.

From the first resistant organisms, the problem of antimicrobial resistance has snowballed into a serious public health concern with economic, social, and political implications that are global in scope, crossing all environmental and ethnic boundaries. Multi-drug resistant TB is no longer confined to any one country or to people co-infected with HIV, but has appeared in locations as diverse as Europe, Africa, Asia, and North America among healthcare workers and in the general population. Penicillin-resistant pneumococci are likewise spreading rapidly, and resistant malaria is on the rise. A study published earlier this year found that in nine U.S. and Canadian cities, 14 percent of those newly infected with HIV have acquired drug-resistant strains of the virus.[1]

Although antimicrobial resistance affects industrialized and developing countries alike, its impact is far greater in developing countries. The switch from normally less expensive first-line drugs to second- or third-line drugs involves a dramatic escalation in the price of treatment. In some of the poorest countries, the cost of lengthy treatment and replacement drugs means that some diseases are too expensive to treat. In the case of TB, the emergence of multi-drug resistant bacteria means that medications that once cost as little as $20 must now be replaced with drugs a hundred times more expensive. In fact, almost all organisms that infect humans are at some stage of developing antimicrobial resistance, thus closing the window of opportunity to effectively treat the infections they cause.

Sensational Costs. The resurgence of infectious diseases imposes other costs as well. The response to an outbreak requires an immediate investigation followed by extensive containment activities, at times placing great financial demands on countries and calling to a halt routine measures for the prevention and control of other important diseases. Such costs can be greatly amplified by sensational media coverage, which can trigger unjustified fear among populations at negligible risk. The collective imagination is fuelled by media stories, such as those that have recently speculated about the origins of the Ebola virus or how West Nile virus entered North America, and by fear of intentional uses of infectious agents, such as smallpox and anthrax, in terrorism or war.

The economic costs of an outbreak with widespread and sensational reporting can be immense. Reports of the 1991 cholera epidemic in Peru resulted in a loss of $770 million in revenue, almost one-fifth of normal export earnings for the trade and tourism sectors.[2] Sensational coverage of the 1994 plague epidemic in Surat, India led to severe economic losses unofficially placed as high as $1.7 billion.[3] Hotel bookings in India fell by 20 to 60 percent immediately after the first media reports, and one airline reported losses of over $1 million in the first week alone. In countries throughout the world, airports were closed to airplanes arriving from India and imports of foodstuffs were blocked. The costs of mad cow disease in Europe will likewise be enormous.[4] Public panic over the safety of beef, which is now banned in school cafeterias in some countries, has recently prompted the European Union to introduce a series of draconian measures that will cost an estimated $2.8 billion in 2001 alone.

Stepped-Up Surveillance. As the world body responsible for leading and coordinating efforts to protect public health, the World Health Organization (WHO) performs a number of functions aimed at curbing the spread of infectious diseases, reducing deaths, and assisting countries in both routine disease control and reactions to outbreaks and epidemics. In this capacity, one of its jobs is to act as a watchdog, alerting health officials of any changes in the infectious disease situation, sounding the alarm when these changes threaten global health security, and ensuring the response necessary for containment.

The WHO has recently stepped up its disease surveillance and reporting activities considerably. In 1997, the WHO facilitated the development of a powerful new Internet-based network that now scans the world for rumors of outbreaks, investigates each case, and verifies genuine outbreaks of international concern. Confirmed outbreaks are immediately announced on the WHO Web site, together with advice on any need to restrict travel or trade and on the containment measures introduced to stop their spread.

This new approach tackles a longstanding problem: the understandable reluctance of some countries to acknowledge outbreaks because of their major negative impact on tourism and trade. Too often, the result of this reluctance has been a call for international assistance at a late stage when the outbreak is much more difficult to control—when it has spread from a localized fire to a conflagration. With the new system in place, countries are now beginning to recognize the considerable advantages of immediate reporting and prompt assistance from the WHO and its partners. These advantages were vividly illustrated by the low fatality rate and quick containment of last year's Ebola outbreak in Uganda, where the outbreak was reported immediately after detection of the first suspected cases. In addition, clear information backed by the WHO's authority about the need for restrictions on travel or trade helps calm panic and gives countries another powerful incentive for prompt reporting. Had this system been in place in the early 1980s, AIDS might never have become a global epidemic on the scale we see today.

A Clear and Present Danger. Though surveillance and reporting help contain outbreaks and limit their international spread, the battle is far from won. Infectious diseases continue to rank as the world's biggest killer of children and young adults. They account for more than 13 million deaths a year and one in two deaths in developing countries. The majority of these deaths are caused by just a handful of illnesses: TB, malaria, AIDS, pneumonia, diarrheal diseases, and measles.

Tuberculosis kills 1.5 million people a year. Malaria kills over 1 million, most of them children. Acute respiratory infections claim another 3.5 million lives. Diarrheal diseases kill 2 million. And measles, one of the most contagious diseases known to humans, kills around 900,000 children in the developing world each year.

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But of all these diseases clamoring for attention and help, it is AIDS—and especially AIDS in Africa—that has finally captured world attention and forced recognition of what an epidemic of this scale will mean for the future of our world. Since the beginning of the epidemic HIV has infected 50 million people, of whom 16 million have died. An estimated 1.4 million children have HIV/AIDS. In Africa alone, 5,500 people die from AIDS-related illnesses every day. In Zimbabwe, 20 to 50 percent of pregnant women in some areas are infected with HIV and risk infecting their newborn children. In many countries, life expectancy and child survival rates have plummeted. In Botswana, life expectancy at birth has fallen from 70 to around 50 years.[5]

In January of last year, a special session of the United Nations Security Council took the unprecedented step of declaring that a disease—AIDS—poses a threat to global security. This pronouncement put the official seal on a blatant reality: A continent such as Africa faces a great impediment to survival when up to a quarter of its population is infected with a lethal and rapidly-spreading virus and when hordes of uneducated and untended orphans are roaming the streets, hospitals are losing their doctors and nurses, schools are losing their teachers, and businesses cannot replace sick or dying employees. With the cost of sufficient life-saving drugs exceeding the entire GDP in several countries, world leaders in wealthy countries must address some difficult questions concerning patent protection for antiretroviral drugs and the rights of countries in the grip of the AIDS crisis to produce cheap copies of patented drugs or import them from elsewhere.

AIDS is one ominous problem among many caused by the upsurge of infectious diseases, the outburst of new diseases, and the return of old foes once considered defeated. Now more than ever, no country is an island. No country can fortify itself against an invasion of infectious diseases either from its neighbors or from the remotest corners of the globe. Unlike the situation twenty years ago, we must accept that infectious diseases are not under control and that a massive effort, as well as constant vigilance, will be needed to secure greater safety for the world's populations. The alarm bells sounded by these threats to global health security—a death toll for so many millions—must serve as a wake-up call for us all.

NOTES

1 S. Little, "Is Transmitted Drug Resistance in HIV on the Rise?," *British Medical Journal* 322 (2001): 1074-1075.

2 World Health Organization, *Weekly Epidemiological Record* 66 (1999): 47; World Health Organization, *Bulletin of the World Health Organization* 78.11 (2000): 1362-1363; and E. Harris and N. Kadir, *A Low Cost Approach PCR: Appropriate Transfer of Biomolecular Techniques* (New York: Oxford University Press, 1998).

3 C. Levy and K. Gage, "Plague in the United States, 1995-1997," *Infectious Medicine* January 1999: 54-63, and World Health Organization, *Bulletin of the World Health Organization* 78.11 (2000): 1360-1362.

4 T. Sancton, "Life Without Beef," *Time Magazine* 26 February 2001.

5 World Health Organization, *Removing Obstacles to Healthy Development* , World Health Organization Report on Infectious Diseases 1999, WHO/CDS/99.1 (available upon request from WHO/CDS Information Resource Centre) and Joint United Nations Programme on AIDS (UNAIDS), *AIDS Epidemic Update: December 2000*, UNAIDS/00.44E- WHO/CDS/CSR/EDC/2000.9 (available upon request from WHO/CDS Information Resource Centre).

Silent Threat

Infectious Diseases and U.S. Biosecurity

Duane J. Gubler

In the last thirty years there has been a dramatic global resurgence of infectious diseases. Some important diseases were recognized for the first time, including HIV/AIDS, hantavirus pulmonary syndrome, Ebola, Lyme disease, and ehrlichiosis. Equally important was the rising incidence of many old diseases that had been known for centuries but effectively controlled since the 1960s, such as malaria, dengue fever, yellow fever, plague, West Nile fever, cholera, and tuberculosis. Helping drive this dramatic global increase in infectious disease epidemics is modern transportation, which has not only opened the United States to more trade and travelers, but also to exotic infectious diseases. More integrated with the world than ever before, the United States should pause to consider the implications this has for its biosecurity.

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Biting the Magic Bullet. Looking at the history of infectious diseases over the past fifty years helps to put the present situation into perspective. The twentieth century saw both triumphs and failures. The triumphs came mostly in the first seventy years of the century and resulted from a high level of understanding of the ecology of infectious diseases and a focus on disease prevention. The failures occurred when the medical establishment became complacent. Medicine came to rely too much on the "quick fix" or "magic bullet" approach to disease control while concurrently de-emphasizing disease prevention.[1]

A major casualty of this "age of magic bullets" was preventive medicine. The shift in emphasis to curative medicine has resulted in a whole generation that has no concept of prevention; many primary schools no longer even teach basic hygiene. Add to this the deterioration of public health systems to the point where they are unequipped to deal with infectious diseases in general, and in particular with vector-borne diseases—those that require a blood-sucking arthropod to transmit disease between humans and other hosts—and we have a situation at the beginning of the twenty-first century that is highly permissive for epidemics.

For centuries, vector-borne diseases have been among the most important public health problems. By the 1960s, a focus on breaking the transmission cycle at its weakest link—the arthropod vector—had effectively controlled many of these diseases. The successes were significant. Malaria had been eliminated in North America and Europe and effectively controlled in Asia, the Pacific Rim, and Central and South America, and progress in controlling the disease had also been made in Africa. Urban yellow fever epidemics had been effectively controlled in both Africa and the Americas, as had dengue fever in the Americas and the Pacific. Plague was no longer a major public health problem, while antibiotics, vaccines, and other new wonder drugs effectively controlled most other important infectious diseases. These successes ushered in an era of complacency in the 1970s that continued through the waning years of the twentieth century until today.

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This complacency, and the policy decisions that followed, set the stage for today's resurgence of epidemic infectious diseases. In the 1970s and 1980s, limited resources were redirected to more prominent public health problems such as chronic diseases. At the same time, medical schools and other training institutions emphasized curative rather than preventive medicine. Meanwhile, a revolution was occurring in biomedical research as major advances were made in molecular biology and tropical medicine. Most of the funds available for research were also spent on curative medicine and the development of high-technology solutions to health problems. With decreased funding for field research on disease ecology-epidemiology and prevention, it became more difficult to attract bright young scientists into fields such as vector biology.

In 2001, vector-borne diseases like malaria and dengue hemorrhagic fever are among the most serious public health problems in many countries where there are no properly-trained vector biologists in the ministries of health.[2]

Demographic and Societal Changes. In the past half-century there has also been unprecedented growth in the human population. Projections indicate that the world's population will reach 8.3 billion by 2025 and 10 billion by 2050. This growth has largely occurred in developing countries and is the driving force behind many of the demographic and societal changes that have influenced the resurgence of infectious diseases in the past thirty years. Future prospects are not good. Projections suggest that nearly 95 percent of the world's population growth in the next twenty-five years will occur in developing countries. This growth will primarily take place in urban centers—many of which are in tropical areas where vector- and water-borne diseases occur most frequently.[3]

Population pressure has resulted in unplanned and uncontrolled urbanization. In the past few decades, hundreds of millions of people, mostly in developing countries, have moved to urban centers to seek better lives. Populations in cities have increased dramatically during this time, and it is projected that this trend will continue well throughout this century. Much of the urban poor lives in inadequate housing in areas with unreliable or nonexistent water, sewage, and solid waste management systems. These conditions are conducive to increased transmission of mosquito-borne, rodent-borne, water-borne, food-borne, and sexually transmitted diseases, and lead to increased frequency of all kinds of epidemics.

Changing agricultural practices, driven by population growth, have also contributed to the resurgence of infectious diseases. Many dams and agricultural irrigation systems built in the past fifty years were designed without consideration of their effect on infectious disease transmission. Deforestation has accelerated in developing countries as the need for more agricultural land has increased. Some important emergent and resurgent vector-borne diseases associated with urbanization, deforestation, and changing agricultural practices in the past thirty years are listed in Table 1.[4]

Table 1. Influences on emergent/resurgent vector-borne diseases.

URBANIZATION	DEFORESTATION	AGRICULTURAL PRACTICES
Dengue fever	Loaiasis	Malaria
Malaria	Onchocerciasis	Japanese encephalitis
Yellow fever	Malaria	St. Louis encephalitis
Chickungunya	Leishmaniasis	West Nile fever
Epidemic polyarthritis	Yellow fever	Oropouche
West Nile fever	Kyasanur Forest disease	Western equine encephalitis
St. Louis encephalitis	La Crosse encephalitis	Venezuelan equine encephalitis
Lyme disease	Eastern equine encephalitis	
Ehrlichiosis	Lyme disease	
Plague		

Many societal changes that may be indirectly linked to population growth have also had important influences on infectious disease incidence. For instance, most of our consumer goods are packaged in non-biodegradable plastics and tins, which when discarded into the environment collect rainwater and become ideal breeding sites for mosquitoes. Also, as the number of automobiles in the world increases, so does the number of used tires. These are difficult to dispose of and, along with other discarded items, make ideal larval habitats for mosquitoes and harborages for rodents and other vermin.

Modern transportation has played a very important role in the resurgence of infectious diseases. In particular, the jet airplane has had a major influence on global demographics, providing the ideal mechanism for the movement of pathogens between population centers. A person can travel to almost any part of the globe in thirty-six to forty-eight hours, and if he happens to be infected by a pathogen before he leaves, he could potentially introduce that disease to his destination. The same applies to animals. With container shipping, organisms that act as vectors and reservoir hosts for pathogens are transported around the world. For example, in the past twenty years, four exotic mosquito species have been introduced and established in the United States; three of these are potential vectors of local diseases. According to the U.S. Department of Transportation, an estimated 60 million people from the United States traveled to a foreign destination in 2000, compared to an estimated 20 million people in 1983—an increase of 300 percent.[5] As the movement of people, animals, and commodities continues to increase, so will the movement of pathogens of all kinds.

Two Cases. The global epidemic of HIV/AIDS is the best-known example of a newly-emergent disease and its impact on the world. Less well known are epidemics of vector-borne diseases that have been occurring with increasing frequency in recent years. In fact, a significant proportion of the major worldwide infectious disease epidemics in the past twenty years consisted of vector-borne diseases that had been major public health problems in the past. These include malaria, dengue fever, yellow fever, and plague—diseases that were effectively controlled by the 1960s but that have recently resurged.[6] A case study of two diseases will illustrate the impact of infectious diseases on the United States and the world.

The Plague in India. The plague was likely introduced to India in the late 1800s; between 1900 to 1925, it is estimated that 12 million people died as a result.[7] Effective prevention and control programs focused on reducing rat and flea populations. Ultimately, the use of antibiotics resulted in control of the plague by mid-century; the last-reported human case of plague in India prior to 1994 was in 1966. Many public health officials had naively thought that the plague had been eliminated from the subcontinent. By 1994, there were few institutions in India that even had the laboratory capability to reliably diagnose the plague.

In August 1994, an outbreak of plague occurred among rats in Maharashtra in western India. There were no human cases or deaths reported, and this incident was not reported to the World Health Organization. In September 1994, an outbreak of a highly fatal disease of unknown etiology occurred in Surat, Gujarat, about 300 kilometers north of Mumbai (formerly Bombay). The afflicted were primarily adult males who exhibited fever and non-specific signs and symptoms followed by pulmonary hemorrhage and often death.[8] The Indian medical community had not seen a disease like this before. Samples from patients were sent to New Delhi for laboratory diagnosis; the results were equivocal, causing confusion and uncertainty. Although several infectious agents were suspected, based on clinical and pathologic observations, it was concluded that this was an outbreak of pneumonic plague. When the suspected etiology was announced, the human-to-human transmission and the potential for explosive epidemics of pneumonic plague caused panic. In the first two weeks of October an estimated 500,000 people fled the city of Surat, going primarily to other urban centers in India where the principal international airports were located. Within days, secondary cases were reported in cities such as New Delhi, Mumbai, Chennai, and Kolkata, and an international public health emergency was initiated as thousands of people boarded airplanes in India and flew to all corners of the globe.

The lack of a definitive laboratory diagnosis, the uncertainty and confusion, and the subsequent panic that occurred in India created similar confusion and uncertainty in countries around the world. Some countries terminated all transport (sea and air) communications with India. Others drastically curtailed airplane flights in and out of the country as thousands of visitors cancelled their visits to India. Most countries with direct or indirect air connections to India implemented intensified surveillance for plague. The Centers for Disease Control and Prevention (CDC) in the United States provided diagnostic reagents and laboratory test protocols to many countries wanting to develop diagnostic capacity, including India. It also sent two teams of scientists to India to help set up laboratories and investigate the epidemic. Finally, the CDC developed educational materials that were transmitted electronically to public health officials around the globe. In the United States, the CDC established intensified airport surveillance for suspected plague cases at all major ports of entry. International health regulations, which were implemented for the first time in several decades, required airplanes to call ahead to report any suspected illness among passengers on a flight. U.S. Public Health Service quarantine officers met airplanes with such passengers and all such reports were investigated before passengers were allowed to deplane. Passengers with suspected plague were quarantined for observation. In all, the CDC investigated thirteen such patients, none of whom had plague infections.[9]

> **Four exotic mosquito** species have been introduced and established in the United States in the past twenty years; three of these are potential vectors of local diseases.

In the end, plague was confirmed as the etiology of the cases in Surat, but there were relatively few patients. The Indian epidemic was primarily one of panic, not plague. Lack of laboratory diagnostic and epidemiologic capacity led to confusion, lack of confidence, and ultimately panic. The government of India estimates that the incident cost the country $2 billion; other estimates accounting for lost tourism and commerce were as high as $3 billion.[10] Countries around the world, including the United States, experienced economic losses from this epidemic as well; however, no good estimates of their extent exist. It is clear that this epidemic, which should have been a relatively unimportant local public health event, cost the global economy several billion U.S. dollars. Had India possessed adequate laboratory diagnostic and epidemiologic capacity, and had effective international surveillance for infectious diseases been in place to provide governments with accurate and reliable information rather than inflammatory mass media reports, these costs could have been prevented.

The West Nile Virus. In late August 1999 a cluster of eight cases of viral encephalitis were reported in a section of northern Queens, New York City. All patients had signs and symptoms consistent with viral encephalitis. Seven of the eight patients also experienced severe muscle weakness, however, which alerted New York City health officials that these cases might be unusual. Initial laboratory diagnostic tests were positive for flavivirus infection, and the serology, combined with the clinical and epidemiological data, suggested infection by St. Louis encephalitis virus, a flavivirus which is enzootic—epidemic in animals—in the United States. Based on these results, intensified surveillance and mosquito control measures were initiated immediately. By the third week of September, viruses had been isolated from both birds and mosquitoes and were identified not as St. Louis encephalitis but as the closely-related West Nile (WN) virus, an exotic African disease.

WN virus was first isolated in the West Nile Province of Uganda in 1937 in a person with febrile illness. Until recently, its known geographic distribution included Africa, the Middle East, and West Asia; epidemics of WN virus were uncommon and when they did occur were primarily mild.[11] In the past six years, however, increased epidemic activity has been noted in Africa, the Middle East, Europe, and for the first time in history, the United States.

The New York City epidemic was detected by an alert infectious disease physician who reported some unusual cases of neurologic illness in Queens to the city health department.[12] By this time, however, the outbreak had already peaked. Retrospective and prospective surveillance showed that the earliest onset of illness identified was on August 2 and the latest on September 22, 1999. Of sixty-two total cases in the New York City area, fifty-nine were hospitalized with encephalitis, meningitis, or both. There were seven deaths—a case fatality rate of 11 percent. The severe neurologic disease and deaths occurred primarily in elderly persons over the age of fifty.[13]

Concurrent with the human epidemic, but unknown to public health authorities, an epizootic was also occurring in birds and horses. It was determined retrospectively that bird die-offs, primarily among American crows, had been occurring in New York City since early July, and that an outbreak in horses occurred in the Riverhead area of Long Island in August and September. Investigation revealed that both epizootics were caused by WN virus.[14] The natural life cycle of WN virus involves transmission to birds by mosquitoes. This virus was not normally known to kill birds, so it was not until the virus was isolated from the brain of sick birds that the connection was made to the human epidemic.[15] Epizootic WN virus activity in birds was ultimately detected in New York, New Jersey, Connecticut, and Maryland in 1999.[16]

Although this was a relatively small outbreak in terms of human cases and deaths, it became a major media event primarily because it involved an exotic virus and occurred in New York City. The New York City Health Department responded appropriately and initiated mosquito surveillance and control as soon as WN was identified as a mosquito-borne virus. Very quickly the city established an effective outreach program to educate the public about the disease and how to protect oneself from mosquito bites to reduce the risk of infection.[17] It purchased and distributed insect repellent and advised people on how to control mosquitoes that might be breeding on their property. The Department also contracted with a private mosquito control company to spray insecticides for adult mosquito control.

In November, after transmission had stopped, the CDC and the U.S. Department of Agriculture brought together both national and international experts to review the data from the epidemic and draft guidelines for surveillance, prevention, and control. Recommendations from that meeting included monitoring for possible overwintering in mosquitoes (a process by which the virus lies dormant in the species, only to potentially emerge later on), implementing early spring surveillance in the bird populations, executing early spring control of *Culex* species mosquitoes that might carry the virus through the winter and amplify it in the spring, and developing a more effective national surveillance plan for WN and other related arboviruses (viruses transmitted chiefly by arthropods).[18]

These recommendations were implemented and WN virus was isolated from overwintering *Culex pipiens* mosquitoes collected in New York City in January and February 2000. New York City treated over 130,000 storm drains with insecticide to kill larval mosquitoes in the spring of 2000. Additionally, dead bird surveillance was initiated in twenty-two local and state health departments along the east and Gulf coasts of the United States—areas where the potential for WN virus activity was projected based on known bird migration patterns.

The surveillance, prevention, and control plan was successful. Spring transmission to birds was detected in May 2000, although retrospectively laboratory investigation identified a WN-positive bird as early as April 1st. Widespread epizootic WN virus activity was detected before the first human cases occurred. That year, the virus was detected in birds in twelve states and the District of Colombia.[19]

In 2000, only twenty-one laboratory-positive human cases were documented despite the intensified surveillance and widespread epizootic activity in the northeastern parts of the country. It is likely that the early spring larval mosquito control, the continued adult mosquito control, and the public outreach programs to reduce risk of human infection played a major role in preventing illness.

It is not known how WN virus was introduced into the United States. Possibilities include infected persons, birds, or mosquitoes traveling from an area where recent epizootic activity has been documented, such as the Middle East. Another possibility is purposeful introduction by terrorists.[14] While it is not known for sure which of these was the mechanism, all available evidence suggests that this was a natural introduction —

most likely by a person who was infected in the Middle East, got on an airplane, and traveled to Queens, New York, where he was bitten by local mosquitoes that became infected in turn and triggered a local transmission cycle in birds.

There is no good estimate of the economic impact of WN virus on the United States. New York State estimated that the 1999 epidemic cost it in excess of $30 million. The CDC provided several million dollars through cooperative agreements to state and local health departments in 2000, but this was only a very small proportion of the total amount of money spent by local jurisdictions. Congress has provided an additional $20 million ($25 million total) for 2001. The bulk of this money was passed on to state and local health departments in order to improve surveillance, prevention, and control in the spring and summer of 2001.

The United States's experience with WN virus during 1999 and 2000 suggests that the virus has become established in this country and will continue to expand its geographic range in the years to come.[20] This epidemic that resulted first from an epizootic demonstrates once again the ease with which exotic pathogens can spread to new geographic locations in today's era of modern transportation and the increased movement of humans, animals, and commodities. It also underscores the inadequacy of state and local public health infrastructures in dealing with epidemic vector-borne diseases.[21]

What Could Happen to the United States? The global resurgence of infectious diseases clearly has a greater impact on areas in the developing world where public health infrastructure is lacking. These are the areas where pathogens are maintained and in which major epidemics, whether local or global, usually begin. In today's era of modern transportation, pathogens move freely between cities, countries, and regions. The result has been the globalization of infectious diseases. The organisms that cause disease know no national boundaries, and if one of these agents is introduced into an area that is conducive to transmission, an epidemic or epizootic can occur. The WN virus is a classic example of this phenomenon; the virus was introduced into an area where the bird (and human) populations were susceptible to infection and where there were competent mosquito vectors that could effectively transmit the virus locally. With the increased movement of people, animals, and commodities between countries and regions of the world, this scenario will occur more and more frequently.

The United States, like all other countries, is at risk of suffering epidemics caused by the introduction of exotic pathogens. The hundreds of dengue fever and malaria cases that are imported each year are evidence of the regularity with which this occurs.[22] The plague and WN virus epidemics illustrate that the United States is at increased risk as the global economy and modern transportation continually shrink the world to a global village. Although the economic impact of globalization can be great, the public health impact can be devastating.

There are important lessons to be learned from the experience of the past thirty years. First, it is unlikely that we will eradicate many infectious diseases from this planet; they are here to stay and we must develop effective, sustainable prevention and control programs to reduce human morbidity and mortality. Second, we should not become complacent after a few successes. We must learn from the experience of the 1970s that infectious diseases will return in epidemic form when resources are redirected and prevention programs terminated. Third, we should not place all of our research emphasis on high-technology, "quick fix" solutions. There are some diseases that will not be effectively controlled in this manner; thus the emphasis should be placed on sustainable surveillance, prevention, and control programs. Lastly, because infectious diseases know no national boundaries, we must develop and implement effective international cooperation and collaboration in these programs. Only by knowing what is happening to our neighbors can we predict what will happen to us. Fortunately, effective prevention and control of epidemic infectious diseases can be achieved by building global public health infrastructure, and by developing international surveillance and information exchange programs.

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The Economics of Epidemics

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Infectious and parasitic diseases have always been part of man's existence. Only occasionally, however, does a single infectious agent transform societies and their economies with devastating results. Where infectious disease has swept through communities, countries, or continents and caused sharp increases in disease incidence and high mortality, it has been due to a set of unique circumstances that enhanced the risks of infection. Such epidemics have only rarely had significant national and international economic impacts, although disease has played an important role in destabilizing rulers and tipping the balance in combat.[1] Nevertheless, the influence of disease on economic growth and well-being is an issue of increasing importance as new and virulent diseases emerge and spread quickly across the globe, exposing the world to a whole new class of illnesses.

Increasingly, infectious diseases are taking on the characteristics of "public goods"—affecting society at large and therefore requiring broad public intervention. Such pervasive effects have implications for economic and political stability. Profound epidemics hinder economic growth, which in turn determines government revenues and expenditures. At the same time, losses at the household and community levels reduce income earning capacity and lead to greater reliance on the government for support just when government capacity is waning. This is what is occurring with AIDS in Africa and elsewhere.

Epidemics and Economics: Measurement. Measuring the economic impact of epidemics poses problems since health and economic development are intertwined. Lower levels of growth (or income as measured by GDP) are associated with worse health, and vice-versa. Moreover, economic agents—individuals, households, firms, and governments—react to adverse health circumstances, making the impact hard to capture since adaptations occur constantly at all levels. To surmount these measurement problems, Ainsworth and Over have divided the impact of illness into three stages: initial shock in the face of ill health or death; initiation of coping strategies by economic actors as a response; and, finally, net outcomes on well-being that are adjusted according to the success of coping strategies and represent the impact of an epidemic on the national economy.[2] Their approach highlights a key point: Assessing the economic impact of diseases requires measuring the effects of ill health and death at the microeconomic level—households and firms—as well as their aggregation to the macroeconomic level—the national economy.

Knowledge of the microeconomic impact of an infectious disease assists economists in understanding the disease's incidence and distributional impact within the economy. Epidemics can lead to rising mortality of the heads of households. The most important consequence of this is a reduction in labor productivity. Illness of household heads leads to direct losses of income and output—for example, in agriculture—that also hamper the productivity of other household labor, as time and energy are redirected to care for the primary breadwinner. The second-round response to disease-related shocks is reductions in savings due to loss of income and the costs of treatment. In time, reductions in savings lead to "disinvestments" in human capital, notably the education of children, and to the loss of productive assets, including land or housing.

Macroeconomic analysis captures the implications for both the sectors most commonly affected—such as health, education, agriculture, and social welfare—and the overall economy. Such analysis presents difficulties, however. Since the macroeconomic level represents a complex interaction of individuals, households, firms, and sectors, it becomes difficult to ferret out individual effects. Indeed, poorly designed macroeconomic analysis can generate distorted, inaccurate results. For example, in cases where disease prevalence leads to dramatic decreases in population while GDP remains constant (possibly from lags in reporting), there will seem to be a rise in GDP per capita. Hence, selecting and applying appropriate measurement tools becomes critical to capturing the true economic impacts of disease.

In the aggregate, macroeconomic indicators measure growth in the factors of production: land, labor, and technology. Slower growth in any of these will retard overall economic output as measured by GDP. Common economic models used to predict impacts of disease on national production include demographic projections that extrapolate from past trends to predict the course of the epidemic, and behavioral models that predict the economic growth implications of diseases and their intermediate effects on the economy.

AIDS, the Ultimate Epidemic. AIDS poses a distinct set of challenges. At the end of 2000, 36 million people were living with AIDS, of which 5.3 million had been newly infected that year. Since the onset of the epidemic, almost 22 million people have died, four-fifths of them adults, reversing the gains in life expectancy in some developing countries back to the level of the 1950s.[3] From an economic perspective, the concentration of victims within the economically-active population (ages fifteen to forty-five) leads to dissolution of families, impoverishment of households, and low returns to investments in education.

AIDS is ravaging Africa—in both human and economic terms.

The sharp rise in AIDS incidence is a worldwide phenomenon. Africa is the region most seriously affected, suffering the most rapid growth in AIDS over the past decade. Indeed, the ten countries with the highest prevalence of AIDS in the world are all African, with Botswana topping the list. By the end of 1999, they exhibited an adult prevalence rate of over a third of the economically-active population. Some developing countries, notably Brazil and Thailand, have aggressively addressed AIDS through effective prevention strategies, the only certain and affordable means of stemming the epidemic.[4] Yet throughout Africa as a whole there are few prospects for widespread treatment to prolong life given the prohibitively high costs. AIDS is ravaging Africa—in both human and economic terms.

Can AIDS Infect the Economy?

Conclusions on the economic impact of AIDS are mixed, being highly dependent on the assumptions, level of analysis, and data quality of each study. Implications at the household level differ from those at the macroeconomic level.

Considerable controversy surrounds the macroeconomic impact of the AIDS epidemic, partly because the evidence on the extent of effects varies and partly because data are uneven. Alternative assumptions concerning the pathways of effect, the timing and availability of data for empirical analyses, and alternative measures of impact lead to different conclusions.

For example, using a sample of fifty-one countries, Bloom and Mahal find no association between AIDS prevalence and levels of economic growth. They likewise suggest that the bubonic plague had little effect on European economies in the fourteenth century, using real changes in wage levels as a proxy for income shifts.[5]

On the other hand, Over predicts a reduction in per capita income of between 0 and 10 percent for thirty sub-Saharan African countries.[6] This larger impact derives from the assumption that the infection is concentrated in higher-income individuals, whose illness would therefore disproportionately affect the level of per-capita income, and that a significant proportion of healthcare treatment is financed through reduced individual savings.

Country-level statistical analyses for Malawi, Tanzania, and South Africa suggest a loss in GDP per capita between 0 and 10 percent depending on assumptions made regarding the direction of the epidemic, the public costs of AIDS treatment, and the effects of the epidemic on labor productivity.[7] But because developing countries hit hardest by AIDS often face already high levels of unemployment, the effects of AIDS on employment levels and productivity—when taken in the aggregate—can be hard to discern. Excess labor already exists; replacements are readily available. Macroeconomic analysis, then, discounts shifts in labor productivity, which have a larger effect on households than they do on economies as a whole.

Data gaps in behavioral responses of households and sectors, both public and private, complicate the economic modeling of responses to the AIDS epidemic. Aggregate economic projections suffer from uneven information and measurement, but those from the studies above represent the best estimates for a handful of countries. The more specific and detailed the modeling, the greater the projected losses in GDP per capita. As the epidemic ages, the quality and breadth of data make measurements more accurate.

Sectoral effects are more directly measurable. Take healthcare systems: Evidence from a sample of African countries suggests that the average total cost of AIDS treatment ranges from a low of $290 in Tanzania to a high of $938 in Kenya, and projections estimate that this will continue to climb. Within households, such expenditures claim multiples of average per capita income, which for the poor implies a significant mortgaging of future earnings.[8] In African countries, where hospitalization is typically free, AIDS patients often represent over half of all bed occupancy and consume close to 75 percent of public budgets.

In African countries… AIDS patients often represent over half of all bed occupancy and consume close to 75 percent of public budgets.

Analysis of the economic impact of AIDS at the firm level has received scant attention, though it is extremely relevant. One study analyzed the impact of AIDS on Thailand's long haul trucking industry, showing the risks faced by individuals and the implications for the industry.[9] Thai enterprises in the formal sector finance medical care, sick leave, and death-related costs for employees, and bear the costs of both reduced output during disability and of replacement and training when employees terminate employment. The more skilled the worker, the more costly the replacement. Recent studies in Africa indicate that prevalence among workers ranged between one-quarter and one-third. Costs to employers come from low productivity, worker attrition, and training new workers. As a result, private companies must expend resources on launching prevention efforts to inform employees of what constitutes risky behavior and of means to avoid infection.

On the household level, the epidemic's economic impact emerges more clearly. Across countries the epidemic has led to greater inequality, because infection rates vary within countries and across families. Those families whose breadwinners become infected will grow more impoverished not just from loss of income through reduced employment, declining remittances, and lower labor productivity, but also from the cost of treatment and the diversion of time among household members to nursing the sick and mourning the victim.[10] Sex workers bear a disproportionate brunt of the AIDS epidemic in all countries, reinforcing the concentration of infection in lower income groups. As information has emerged regarding prevention, the better educated, who also tend to be the better off, have altered their behavior, leading to a more concentrated impact among lower income groups.

The economic impacts on survivors in these households can be extensive. The most important effects include shifting consumption toward lower-cost foods—for example, cassava rather than maize—raising the risk of malnutrition for both children and adults; allowing land to lay fallow due to lack of labor to manage its productive use; moving from cash to subsistence crops; selling productive assets to finance both consumption and healthcare; and reducing investments in human capital such as schooling. For example, in the Kagera region of Tanzania, where AIDS accounts for over half of all deaths, farm incomes declined by over 25 percent during the 1990s due to the disease, leading to reduced food security. In poor households, spending on food declined by almost one-third and food consumption by 25 percent in the six months following the death of a parent. Similar findings emerge from various research programs in Zambia.[11]

Compounding these effects, the poor face fewer and more costly coping options due to a combination of limited access to resources, greater discrimination, decreased ability to cushion disaster, and inaccessibility to formal institutions like disability or health insurance.[12] Extended families appear to substitute for formal safety nets, although evidence from Tanzania's Kagera Region indicates that the poorest families are more likely to take out formal loans requiring collateral and interest, while better-off families rely on private, generally costless transfers from friends and relatives.[13]

Widows face limited economic options. Often, land ownership laws prevent women from inheriting land. In some African countries, women must resort to prostitution and bootlegging to survive, instigating a vicious cycle of infection.[14] A particularly tragic consequence of the epidemic, particularly in Africa, is the increasing number of orphans. By the end of 1999, 121 million African children were orphaned due to AIDS, as were over 200 million children elsewhere in the world. While a humanitarian disaster, the lack of parental income and care has alarming consequences for the next generation, which will lack education and parental guidance. This will pose serious economic challenges for the future.

Economic Anti-Virus. The evidence on the economic impact of AIDS is mixed. At the household level, labor shortages jeopardize the well-being of the family, but at the sectoral and national levels, the excess labor in the overall economy leads to projections of uncertain impacts. Over time, where the epidemic is not stemmed, the devastation is likely to reverberate throughout the economy. The sheer number of orphans in countries already struggling to maintain positive economic growth will create a drag on the economy. State welfare investments to ensure the survival of orphans and the elderly become essential where the economically-active population that supports and cares for both groups is lost to AIDS. Nonetheless, these demands divert government expenditures away from investments in education, roads, water supply, and other factors that foster economic activity toward consumption, thereby undermining the foundations of economic growth. Economic models capture these phenomena imperfectly, but the consequences are real.

Stemming the AIDS epidemic and others like it confounds public health experts and governments alike. The "invisible," behavioral-based nature of AIDS, its easy transmission through international migration, the lag between infection and the onset of symptoms, the enormous cost of treatment, and the social costs that linger after death make AIDS a global hazard. Because it affects not only health, but also overall economic well-being, AIDS is no longer the purview of health experts alone, but is a national challenge that requires multiple levels of decision-making to ensure national consensus on an appropriate response. Only national policies addressing prevention, disability, healthcare access, tradeoffs between investment and consumption, and interventions to control the epidemic can constrain this affliction.

Potential models already exist. Thailand successfully reduced AIDS incidence through aggressive efforts among commercial sex workers. In Brazil, transgression of international property rights of drug patents—whatever its legal flaws—has allowed affordable treatment, and public service messages inform the public of sensible means of prevention, such as condom use. In all cases, policies have had to go beyond traditional efforts to convince government and non-government bodies alike of the need to take aggressive action. Those countries that have been successful have faced the challenge and altered their approach to the disease and its control.

The role of the government in identifying, measuring, and addressing the problems of rising infectious disease incidence is key. Though the public health system represents the front line of intervention, diseases like AIDS cannot be effectively addressed through it alone. Moreover, because the impacts of disease are felt increasingly beyond the health sector, the responsibility for repelling and responding to epidemics now extends beyond the public health system to include the private sector, the judiciary, and welfare agencies. Indeed, private companies in Africa are investing heavily in AIDS information and counseling. The need for comprehensive strategies and a strong political stance requires central governments, along with parliaments and local governments, to be active in the effort to squash diseases like AIDS. Without such commitment, society worldwide is at risk.

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Hazardous World

The Real Risk of Bioterrorism

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Despite their current notoriety, biological weapons are not new. Two of the earliest reported uses occurred in the sixth century B.C. when the Assyrians poisoned enemy wells with rye ergot and Solon used the purgative herb hellebore during the siege of Krissa. In 1346, plague broke out in the Tartar army as it sieged Kaffa in the Crimea. The attackers hurled the corpses of those who died over the city walls, and the plague epidemic that followed forced the defenders of the city to surrender. Some infected people who left Kaffa may have started the Black Death pandemic that spread throughout Europe and killed one-third of the population. Indeed, the destructive power of biological weapons has long been known.

Yet biological weapons have not always been understood. Biological weapons differ fundamentally from other weapons of mass destruction and therefore require a unique response. Whereas nuclear and chemical weapons cause immediate casualties, biological agents require hours, days, or even weeks of incubation before they cause fatalities. This delay gives such agents special advantages as terrorist weapons.[1] Barring an announcement by the perpetrators of the attack or a fortuitous discovery, a biological attack could only become known hours, days, or even weeks after its execution, when victims begin to appear in doctors' offices and hospital emergency rooms.[2] Sufficiently subtle biological terrorist attacks might even go unrecognized for longer periods.

Many of the pathogens potentially used as agents of bioterrorism initially cause symptoms that are very similar to common illnesses such as the flu, making the detection of biological attack extremely difficult. Early in an epidemic, it is difficult even for seasoned clinicians to distinguish between patients with the common cold or allergic sinusitis and those in the early phases of pneumonic plague.[3] Once news of the epidemic reaches the public, the resulting rush to hospitals and medical facilities by thousands of the "worried well" is likely to be a major patient management disaster in itself.

Moreover, although conventional military users of bioweapons do not desire high contagiousness because it could produce an epidemic that might boomerang on the attacking forces, terrorists may consider contagiousness an asset. Contagious agents can spread disease far beyond the population initially exposed in the attack, amplifying destruction with minimal effort. For example, the two- to three-day incubation period for plague [*Yersinia pestis*] is long enough to allow victims of an attack to travel by air between virtually any two cities in the world before seriously becoming ill—especially if the organisms were released in the departure area of a major international airport or train station.

The unique qualities of biological weapons underscore a key point: Preparing for bioterrorism requires improving the recognition and information-sharing mechanisms of existing public health surveillance systems within the United States and overseas. Domestically, physicians and other healthcare workers must be given the training needed to recognize or at least suspect unusual diseases. The ability to check these suspicions rapidly at the local, state, regional, and national levels must be available. Within the U.S. government, coordination among public health, law enforcement, and intelligence agencies should be strengthened.[4] Internationally, the United States should work with foreign governmental, multilateral, and non-governmental organizations to improve global surveillance for suspicious outbreaks. In this context, responsibility for national security extends throughout society—from primary care physicians and pathologists at local hospitals and clinics, to state and national health laboratories and officials, to overseas public health surveillance networks.[5]

More Technology, More Players. Before examining the problems of responding to bioterrorism and the importance of improving public health surveillance systems, a discussion of the spread of biological weapons is helpful.

The human and technical resources needed to develop biological weapons programs are proliferating throughout the world. While it may still be true that most developing countries lack the microbiological capacity to develop biological warfare agents, eight or more developing nations have been implicated in developing offensive biological warfare capabilities.[6] A prominent Russian defector has alleged that Russian scientists have used genetic engineering to produce antibiotic-resistant strains of a number of disease organisms.[7] Some of this research has been published in open literature and therefore is available to other nations seeking to develop biological weapons capacities. In January 1998, Iraq reportedly sent approximately one dozen scientists to Libya to help develop a biological warfare complex near Tripoli that was disguised as a medical facility.[8] In a report issued in November 1997, then-Secretary of Defense William Cohen singled out Libya, Iraq, Iran, and Syria as countries "aggressively seeking" nuclear, biological, and chemical weapons.[9]

Take Iraq's program, for example. Fermenters found in the Al Hakan plant in Iraq had volume capacities of 1,500 liters. Organic solutions produced in these fermenters can achieve concentrations of 100,000 lethal doses per milliliter with approximately one billion spores of anthrax per milliliter—a weapon of mass lethality. Iraq has subsequently admitted to the United Nations Security Council Observer Mission (UNSCOM) that it was able to produce about 8,000 liters of concentrated anthrax solution; UNSCOM suspects that Iraq actually made ten times this amount.

That is to say nothing of the non-state-based threat. Biological and chemical agents are now demonstrably within the technical expertise of non-state groups, and even primitive and inefficient versions of these weapons could wreak economic or psychological devastation. The Aum Shinrikyo cult, for example, was a multinational terrorist group intent on the development and deployment of an array of weapons of mass destruction. Aum Shinrikyo's release of sarin nerve agent in the Tokyo subway system in 1995, not to mention the group's attempts to attack Tokyo using anthrax and botulism, indicates that large-scale terrorist attacks on civilian populations using weapons of mass destruction are no longer in the realm of fantasy. At least, the Tokyo attacks represent the crossing of a grim threshold—resulting in the weakening of long-standing taboos on attacking civilians and positing an increased likelihood of analogous attacks in the future.

Lax oversight of former Soviet technologies has exacerbated the problem of proliferation. As the United States and its allies learned from high-level Soviet and Russian defectors in the early 1990s, the USSR took advantage of loopholes in the 1972 Biological Weapons Treaty and scientific advances in genetic research to modernize its existing offensive biological weapons program.[10] This included the development of genetically-engineered pathogens and other bacteria and viruses useful as strategic bioweapons. In 1973, Soviet leader Leonid Brezhnev signed a decree creating Biopreparat. This was an ostensibly civilian operation that recruited the best and brightest physicians and scientists of a generation and became the heart of a burgeoning Soviet bioweapons program.

At its peak, Biopreparat employed over 30,000 people. There was also a military program of at least 15,000 people and an agricultural program employing 10,000 people that concentrated on producing pathogens that targeted crops and animals. The production capacity of Biopreparat facilities was measured in the hundreds and thousands of tons of pathogens annually. Since the collapse of the Soviet Union, security and accounting oversight of materials produced under Biopreparat programs have degenerated. Moreover, many Biopreparat employees lost their jobs, and Biopreparat material and expertise from former employees are now reportedly for sale to the highest bidder.

Biological terrorism is not new, yet since the end of the Cold War concern about this threat has escalated.[11] During the Cold War, the Soviet Union posed the greatest biological threat to the United States; that threat seemed most likely to be manifested in overt war, however, than in acts of terrorism. Additionally, rogue states had less freedom to launch bioterrorist attacks in a bipolar world because of alliance restrictions. With the collapse of the Soviet Union, the threat of overt war no longer seems likely. Yet the accompanying collapse of the Cold War alliance network also means that there are fewer restraints on rogue states that wish to engage in bioterrorism. The current overwhelming conventional military superiority of the United States means that biological weapons, used in unconventional warfare, might now be seen by conventionally weaker nations as a way to bridge the power gap.

Problems of Response. There is a substantial extant level of naturally-occurring infectious disease in the United States that can mask sufficiently subtle and dispersed bioterrorism. From the point of view of improving bioterrorism surveillance, it is important to recognize the practical difficulty of discerning the difference between spontaneous outbreaks of infectious disease and deliberate acts of terrorism. Given this fact, effective surveillance for biological terrorism requires effective surveillance for general infectious diseases.

Incubation delay endows biological agents with advantages as terrorist weapons that nuclear or chemical weapons lack. The possibility of uncontrollable contagion (in the case of agents such as smallpox, for example), and the fear that this sparks, provides perpetrators with a distinct terror advantage. These characteristics of biological agents highlight the importance of public health surveillance strategies for incidents of bioterrorism—an approach that is inapplicable to cases of chemical or nuclear attacks. Therefore, it is crucial to understand the threats posed by biological weapons and to address them in a very different way.

Barring a terrorist announcement or the interruption of an attack already underway, traditional "first responders" (fire, rescue, police, and paramedics) or quick-response teams with specialized equipment and training will not initially recognize a biological attack. No announcements accompanied the biological terrorist attacks conducted by followers of Baghwan Shree Rajneesh, who poisoned several salad bars in Oregon with salmonella bacteria in 1984, and those attempted by members of Aum Shinrikyo in the early 1990s.[12] These attacks also remained unrecognized while in progress.

Recognition of and response to a biological attack, whether domestic or abroad, will depend on the sensitivity and connectivity of the existing public health system. "Sensitivity" refers to the likelihood that a physician or healthcare worker will recognize a given manifestation of a disease as being out of the ordinary. "Connectivity" refers to how quickly and accurately information about a case passes vertically from the clinical level up to state, national, and international authorities, as well as horizontally within these levels.

A survey of the possible scale of terrorist attacks and the extent to which these have proven or may prove difficult to distinguish from outbreaks of infectious diseases makes it clear that improvements to surveillance systems for biological terrorism must build directly upon existing public health surveillance systems.[13]

The most dramatic biological threat is a major terrorist attack against an urban center that employs an efficient mechanism for the dispersal of the biological agent. The destructive effects of this form of biological attack could be similar to a chemical or nuclear one. In 1993, the Congressional Office of Technology Assessment estimated that 100 kilograms of aerosolized (confined to respirable particles in the one to five micron size range) anthrax spores dispensed by an airplane upwind of a major city could kill hundreds of thousands to millions of people.[14] In another scenario, the dispersion of an anthrax aerosol from a boat sailing upwind from New York City could result in over 400,000 deaths.[15]

Although no such major biological attack has succeeded yet, the last decade has seen the release of sarin nerve agent in the Tokyo metro system by the Aum Shinrikyo religious cult in 1995. This act killed eleven people and injured over 5,000, more than 700 of whom required hospitalization. Moreover, Aum Shinrikyo attempted biological attacks on Tokyo as well as nearby U.S. naval installations at least nine times. Although the failure of Aum Shinrikyo's attacks suggests that acquiring and weaponizing an effective biological agent remains challenging, the attempts themselves indicate that large-scale attacks on large urban populations are distinct possibilities.

Preparing for biological terrorism actually has more in common with confronting emerging diseases than with preparing for chemical or nuclear attacks. Most incidents of biological terrorism will bypass the quick-response hazardous material teams that are critical in coping with attacks using explosive, chemical, or radioactive materials. The disease agents likely to be used as terrorist weapons may incubate for hours, days, or even weeks before victims feel any symptoms. Sufficiently hidden or dispersed terrorist attacks may initially be indistinguishable from naturally occurring infections or outbreaks. This emphasizes the importance of training physicians and other healthcare workers to determine rapidly that an unusual infection is involved.

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In the event of a biological attack, public health surveillance is critical to minimizing deaths and casualties as well as economic costs. A recent study examined the expected deaths and economic impact for scenarios involving three different biological agents [*Bacillus anthracis*, *Brucella melitensis*, and *Francisella tularensis*] released as aerosols in a terrorist attack on a major city.[16] According to the study, the time required for effective intervention varies with each agent.

First, consider the case of anthrax. The study found that intervention (defined as 90 percent effective administration of antibiotics and vaccinations) within one day after the attack could keep deaths below 10,000; in contrast, if intervention occurred five or more days later, the toll could rise to over 30,000. Moreover, early intervention could save $15 billion to $20 billion. At the other extreme in incubation timescales is the case of brucellosis, where intervention within the first two weeks after the attack would only reduce deaths by about 100 as compared with over 500 if intervention takes place two months later.

Effective intervention would be possible only if family physicians and emergency department personnel recognized the nature of the disease outbreak as early as possible and if these concerns were effectively passed to state and national authorities for rapid diagnosis and response.[17] These same public health capabilities are required to detect more subtle attacks as well. One can envision terrorists introducing a disease into the United States in such a way that no easily recognizable outbreak occurs or that the outbreak is not noticed until the epidemic is well underway. Such a masked attack, followed by a credible terrorist announcement, could spark a reaction far out of proportion to the deaths that actually result.

Current Responses to Bioterrorism. In the United States, surveillance for infectious diseases is largely a passive process, focusing on reporting of actual cases rather than prevention.[18] Each state has its own requirements for physicians, hospitals, and other healthcare providers to report specific diseases. Physicians or laboratories are supposed to notify local or state health departments if a patient is diagnosed with a disease defined as reportable by the state government. At the national level, the Centers for Disease Control and Prevention (CDC) collaborates with professional organizations such as the Council of State and Territorial Epidemiologists (CSTE) to develop and maintain a list of national reportable diseases. Individual state requirements for reportable diseases typically parallel this list.

Through the National Notifiable Diseases Surveillance System (NNDSS), states voluntarily report weekly to the CDC on the incidence of some fifty diseases. These diseases include several of potential interest to bioterrorists, such as anthrax, botulism, brucellosis, and the plague. Reporting is mandatory for a small number of diseases requiring quarantine, such as smallpox, infectious tuberculosis, and viral hemorrhagic fevers. The CDC regularly analyzes the data it receives from the states and reports summary statistics in its *Morbidity and Mortality Weekly Report*. Unfortunately, one result of this system is that outbreaks of diseases not on the national reportable disease list may remain undetected until an outbreak is well underway.

A second type of national disease surveillance by the CDC involves the use of "sentinel" hospitals.[19] In this case, there is no attempt to gather comprehensive national data. Rather, the National Nosocomial Infection Surveillance (NNIS) system gathers data voluntarily provided by 163 hospitals. (Nosocomial infections are infections acquired while a patient is hospitalized.) Incidence of infections in the participating hospitals may be used to estimate the national incidence of nosocomial infections. In addition to the NNDSS and the NNIS system, the CDC also engages in pilot projects with certain states, key U.S. cities, and individual "sentinel" physicians to gather data on the incidence and characteristics of other diseases or disease outbreaks.[20]

Improving Surveillance. Surveillance efforts are complicated because of the complexity of the task. As pathogens may have long incubation periods, no nation can protect itself by simply screening travelers at its borders. Nor can a country such as the United States hope to inspect more than a small fraction of the food it imports daily. Yet the United States can strengthen its chances of catching biological terrorism by improving surveillance before such an incident occurs.

As agricultural markets become increasingly global, the potential vulnerability of nations to foodborne natural or intentional disease will continue to increase. Nevertheless, screening and quarantine efforts at ports of entry and inspection of food imports are an important component of public health surveillance. In 1995, the Committee on International Science, Engineering, and Technology of the Clinton administration's National Science and Technology Council called for the strengthening of screening and quarantine efforts at ports of entry into the United States. With respect to food safety, the Clinton administration issued the National Food Safety Initiative, which included improved surveillance coverage for imported foods as well as for domestic produce, seafood, and livestock. These initiatives should improve surveillance for both natural and deliberate epidemic outbreaks in food sources.

Further improving domestic surveillance requires improving sensitivity and connectivity in the flow of information from physicians to national health authorities. An announced biological attack, or one discovered while underway, will require first responders who have appropriate training. Unannounced biological attacks must first be recognized by pathologists, physicians, nurses, infection control staff, and other healthcare personnel in family practices, clinics, and hospitals. It is important, therefore, that these medical professionals have knowledge of the clinical presentations of likely bioterrorist agents. The best way to ensure that busy physicians improve their expertise in this area is to require relevant training as part of medical school curricula and certification examinations, as well as to offer appropriate training to practicing physicians. The first step in improving sensitivity for incidents of biological terrorism is for the federal government to make a long-term, sustained commitment to training the nation's physicians, nurses, infectious disease specialists, pathologists, and other first responders.

Next, regional centers of public health laboratory sciences must be able to perform rapid diagnoses of clinical samples from within their geographic areas. These regional centers must have the trained personnel and diagnostic tools necessary to accomplish this mission, and connections to both local and national institutions must be assured. This high-volume rapid diagnostics capability differs from the traditional expertise of national reference laboratories. New regional centers of laboratory excellence should build directly on the best state public health laboratories in order to minimize additional expense. The president's budget requests to Congress from fiscal years 1999 to 2001 also ask for additional funding to improve the ability of public health centers to recognize and share information on outbreaks of suspicious diseases. These policies, if successfully implemented at local and state health department levels, should improve both sensitivity to detect epidemics and connectivity between all major levels of the U.S. public healthcare system.

Emergency planners also need to devote more attention to developing rapid diagnostics appropriate to this sort of laboratory setting. For example, state or regional laboratories will need diagnostics and appropriate reagents that are capable of thousands of sequential assays. Such diagnostics would not have to be hand-held or necessarily employ cutting-edge technologies, but they would need to be robust and reliable. A related requirement, also with resource implications, is to maintain cadres of individuals at laboratories throughout the United States with expertise in the diseases and biological agents likely to be employed by terrorists. Presently the CDC has the only laboratory in the world that serves as a WHO reference laboratory for plague.

International Cooperation. Surveillance for disease outbreaks overseas also needs improvement. The surest way to prevent virulent non-endemic diseases from reaching America's shores, not to mention to alleviate human suffering, is to detect and stop outbreaks quickly while they are still abroad. Trained healthcare workers and epidemiologists, regional laboratories with reliable diagnostic equipment, good communications, and the ability to rapidly send in teams of experts to investigate reports of outbreaks will help spot both emerging diseases as well as outbreaks resulting from the use, testing, or accidental release of biological warfare agents.

There are two broad and interrelated categories into which international surveillance for bioterrorism may be divided. The first is enhanced collection of information regarding general, naturally-recurring diseases with the intention of recognizing outbreaks as they occur. The second involves a directed expert field and laboratory response to the outbreak of a specific, new epidemic. The latter category falls under surveillance provided that the response includes an investigation whose goal is to identify the nature, extent, and origin of a disease outbreak. Investigation of new outbreaks, especially those deemed suspicious, and the identification of the responsible organism or strain are critical, but these capabilities are dependent upon a general epidemiological surveillance system operating in the background that is able to detect outbreaks as soon as they occur.

While egregious attacks or accidents in biological warfare programs may be difficult to miss, the ability to deter potential violators of the 1972 United Nations Biological and Toxin Weapons Convention (BWC) would be enhanced by having the most sensitive public health surveillance network possible. This means having the ability to detect subtle outbreaks or to identify more obvious outbreaks in their earliest stages. From a national security perspective, such a network provides the best opportunity to stop an outbreak of infectious disease before it reaches the United States.

Establishing an international bioterrorism surveillance system means improving the existing international network for the detection of infectious diseases. Currently there are too many geographic holes in the international disease surveillance system. Yet there is cause for growing optimism. The WHO has established a program whose mission and mandate is to strengthen national and international capacities in the surveillance and control of communicable diseases, primarily in the developing world.[21] The WHO now publishes in both print and electronic format the bilingual English/French *Weekly Epidemiological Record* and the electronic *Disease Outbreak News*. The WHO is also compiling a searchable database of WHO collaborating centers worldwide. Along with the World Bank and the Joint UN Programme on HIV/AIDS (UNAIDS), the WHO is also connecting the collaborating centers electronically.[22] Simultaneously, the Program to Monitor Emerging Diseases (ProMED), an international non-governmental group of infectious disease experts, has established an electronic reporting system open to unconfirmed reports of disease outbreaks.[23] This system parallels the more strongly filtered WHO *Outbreak Verification List*.

The United States has also been crafting an individual response to the global problem. In 1996, then-Vice President Gore announced the Clinton administration's new policy for responding to emerging global infectious diseases. Under that policy, President Clinton directed the U.S. government to "work with other nations and international organizations to establish a global infectious disease surveillance and response system, based on regional hubs and linked by modern communications technologies."

One such global system is comprised of WHO Collaborating Centers, which form a network of over two hundred laboratories and institutions around the world. WHO Collaborating Centers carry out specific activities on behalf of the WHO such as providing information on disease distribution as well as conducting laboratory diagnoses and training in the host nation or region. Host governments agree to allow the centers to report directly to the WHO without first going through the government. Unfortunately, there are large regions of the world where these centers are absent or rare, including Eastern Europe, much of Saharan and sub-Saharan Africa, Central America, and Southeast Asia. These areas need new regional networks to help fill these gaps.

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Another element of the global biosecurity monitoring system being strengthened by the WHO provides a model for public health reporting that does not require explicit bioterrorism surveillance. The International Health Regulations (IHR) are the only components of international public health legislation that require mandatory reporting of infectious diseases. Yet reporting is currently limited to cholera, the plague, and yellow fever. To transform the IHR into a global alert system, the WHO is broadening their scope to include many diseases and syndromes for which they currently make no provision.

The IHR require initial notification of the appearance of certain syndromes, which will then be followed by reporting of specific diseases once clinics and laboratories establish the diagnosis. Reporting suspicious syndromes, however, allows medical interventions and studies to commence even before a laboratory diagnosis is made. From the point of view of those concerned with incidents of biological terrorism, reports of syndromes may help to identify incidents of bioterrorism at an early stage. This method of reporting could provide regional networks with a way to participate *de facto* in surveillance relevant to biological agents without having to do so explicitly.

Another form of international cooperation provides a powerful deterrent for would-be developers and users of biological weapons. The same molecular biological technologies that facilitate the engineering of improved biological agents provide international surveillance experts with a way to track biological weapons. Genetic fingerprinting provides scientists with a way to identify the biological "signatures" of particular strains of organisms through biochemical or molecular biological analyses of those strains. This technology may enable scientists to track the source of even a secret biological release. Greater transparency, including the exchange of strains of organisms held in the national laboratories of individual nations, could facilitate tracking. Moreover, development of a DNA-sequence database for different strains of organisms, especially those associated with bioweapons programs, would aid in investigation of domestic or international outbreaks. Biological signature tracking and attribution could become a powerful tool for identifying when an outbreak is intentional and who its perpetrator might be.

The threat of biological terrorism, and potential early ambiguities between natural outbreaks and intentional or accidental releases of biological agents, demands that closer ties between law enforcement, intelligence, and public health officials be established. For example, public health officials would benefit from domestic and international intelligence reports of a probable biological threat and concern over the potential use of a particular biological agent. Conversely, law enforcement and intelligence agencies could benefit from being informed regularly about what outbreaks are being seen in public health surveillance (domestic and overseas) and how these events are being resolved.

Despite its potential benefits, international cooperation is currently hampered by conflicting demands on public health organizations. On the one hand exists international public health organizations' desire for transparency and scientific analysis; on the other are restrictions imposed by law enforcement or intelligence gathering requirements. Consider, for example, an institution such as a hospital or university that experiences a disease outbreak. Personnel and administrators may talk freely to scientists pursuing a public health investigation, but may be much less forthcoming if they perceive investigators as surrogates for law enforcement agencies, who could pursue possible prosecutions or litigation.

Internationally, the situation is even more delicate. After the 1995 plague outbreak in Surat, for example, the Indian news weekly *The Week* explicitly accused the United States of being responsible for the outbreak and identified by name four members of the CDC field team who had arrived in India to study it. The CDC's desire to send epidemiologists was described as suspicious. U.S. agencies conducting epidemiological or other public health activities, be they civilian or military, will understandably be reluctant to risk compromising their credibility and their ability to detect and respond to diseases overseas by appearing to have ties with intelligence gathering or covert activities.

The Realm of Possibility. Terrorist attacks using biological weapons have been carried out or attempted at virtually every scale, from individual assassinations to indiscriminate attacks meant to harm thousands. While apocalyptic urban attacks have fortunately not succeeded, they have been attempted by at least one terrorist group. This puts biological attacks well within the realm of possibility.

Prudent national security policy requires that the United States prepare for biological terrorist attacks. On one hand, this means stepping up prevention efforts in order to pre-empt a possible bioterrorist attack. Such action calls for increased intelligence, counter-terrorist, and deterrence activities as well as international efforts to check the development, spread, and use of biological weapons. Unfortunately, pre-emption must be accompanied by the understanding that no preventive measures are absolutely foolproof.

On the other hand, the United States must prepare itself to respond effectively to biological attacks should they occur. This necessitates improving existing domestic disease surveillance systems that focus on natural epidemics as well as global cooperation in surveillance and information-sharing to allow for the timely detection of, and response to, biological attacks. Enhancing the ability to respond successfully to bioterrorism also means giving emergency services and laboratories the training and equipment necessary to contend with a biological attack.

Even if a major biological terrorist attack never occurs, the investment in strengthening the U.S. public health infrastructure will work, on a daily basis, to benefit the health and welfare of all citizens. An appropriate national security response to the threat of biological terrorism is similar to that necessary to combat the threat of emerging infectious diseases. By preparing for acts of bioterrorism, the United States will be ready to face the looming danger of epidemic outbreaks. Public health and national security merge in the realm of emerging diseases and biological terrorism.

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