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The Surveillance and Control of Emerging Infectious Diseases

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INTRODUCTION

The emergence of new infectious diseases and the resurgence of older infectious diseases that appeared to be close to eradication poses one of the major challenges of contemporary public health. Over thirty new infectious diseases have been identified or recognized for the first time since the 1970's. Many of these have been viral tropical hemorrhagic fevers such as those caused by Ebola and Marburg viruses. Some diseases such as malaria, which was close to worldwide eradication in the 1960's, have experienced a resurgence in previously endemic areas, and diffusion to new areas of endemicity. Other infectious diseases that were responsive to antimicrobial treatment have become resistant to previously effective treatment, and therefore pose a severe threat to public health. The development of Multiple Drug Resistant Tuberculosis (MDRTB) is an important example of this, as is the development of malaria that is not only resistant to choloroquine, but to most other previously effective antimicrobials as well. Geography is an important field in understanding disease emergence, and in developing effective surveillance and control mechanisms to identify and limit the diffusion of new and resurgent infectious agents.

New infectious diseases can emerge for several reasons. These include: (1) cross-species transfer of pathogens, reflecting the *de novo* introduction of a pathogen into the human population. This is usually due to alterations in the stability of human-environment relations, usually by human encroachment of previously isolated environments that are nidi for zoonotic infectious diseases. Frequently, this is the result of deforestation, public works projects in previously stable ecosystems, or other intended or unintended changes in human-environment relations. Thus, human movement into these areas allows species jumps of zoonotic microbes into the human population; (2) the diffusion of microbes from isolated endemic areas to new foci of endemicity, with the concomitant identification of what is thought to be a new agent; (3) microbial mutation through recombination, either increasing the pathogenicity of microbes, or the transformation of microbes into pathogens. This frequently allows the development of resistance to the immune response or to effective antimicrobial treatment. The latter happens periodically with the genetic drift and shift of influenza viruses, resulting in epidemics and pandemics (Shope and Evans 1993); (4) the new recognition or specification of a previously unidentified pathogen..

Disease emergence is portrayed in popular literature (e.g., Preston 1994; Garrett 1994; Close 1995), and hundreds of scholarly articles and books have now been written to what is perceived as the major public health threat of emergence and resistance.
A new scholarly journal, *Emerging Infectious Diseases*, is published by the Centers for Disease Control and Prevention (CDCP), and, in January 1996, dozens of medical and public health journals published special issues that were devoted largely or solely to the topic of infectious disease emergence and resurgence. Scholarly meetings have been

devoted to understanding the dynamics and emergence of new infectious diseases (e.g., Wilson, Levins, and Spielman 1994), and national and international commissions have been formed by both governments and advisory groups to address the public health threats of emerging diseases, and to develop strategies of detection and containment (e.g., Lederberg, Shope, and Oaks 1992).

Resurgent infectious frequently occur because of genetic mutation in pathogens which were previous not threats to human health, or for which adequate chemoprophylaxis or antimicrobial therapy had been available. For example, the development of multiple drug resistant tuberculosis (MDRTB) evolved because of inadequate compliance among patients with the disease or putative exposure TB, to antimicrobial prophylaxis or treatment, resulting in the selective breeding of resistance strains of the mycobacterum.

EMERGENCE AND HUMAN ACTION

Many factors are responsible for the emergence of new infectious agents and the resurgence of old ones. Most of these are social and geographical. Thus, the emergence and resurgence of infectious diseases are anthropogenic. As Roizman and Huges (1995, p. iii) suggest, “The two key factors which affect the spread of infectious diseases in the human community other than the nature of the infectious agent are human ecology and behavior.”

There is great urgency in improving the surveillance for newly or recently emerging diseases, and resurgent diseases. The containment and control of emerging infectious diseases are of paramount importance. Geography can and must play a great role in both the detection and containment of emerging diseases. Accurate predictions of the diffusion of communicable diseases, and prognostic analyses of the impact of disturbing stable ecosystems are both inherently geographical in technique, theory, and methodology. Thus: "Agents evolve in geographical and ecological isolation and then they are transported to human communities when humans enter the habitat of the virus, or by vertebrate or arthropod vectors that move into the human community (Shope and Evans 1993, p. 109)."

The importance of infectious diseases to world health is obvious: they remain the leading causes of death in the world (CDC 1994). Of these infectious diseases, tuberculosis is the leading cause of mortality, killing an estimated 3.1 million people per year. At least 8 million new cases of tuberculosis are contracted annually, mostly in developing countries and among the homeless and poor in developed countries (Hopewell 1996). Malaria is the second major cause of mortality, accounting for an estimated 2.1 million deaths per year. Hepatitis B causes an estimated 1.1 million deaths per year. All diarrheal diseases together account for 3.1 million deaths per year, and all respiratory infections other than tuberculosis result in an estimated 4.4 million deaths per year. One must regard the aggregated diseases, such as diarrheal diseases and respiratory diseases, with circumspection, since these aggregated causes of death are caused by numerous organisms and the resulting diseases are not really comparable. HIV/AIDS currently kills over 1 million deaths per year, and at this point, the number of deaths is approximately equal to that of measles.

Many of these diseases are potentially preventable, through vaccination and adequate medical treatment, but because much of the mortality from infectious diseases occurs in developing countries, the cost of vaccination and treatment is high—prohibitively so—in many cases. There are very effective vaccines against measles and hepatitis B, both of which are required for children to enter public schools in many states of the United

States. Vaccines against cholera and tuberculosis are not effective, and there have been only a few trials that seem to have potential for the development of malarial vaccines.

Antimicrobial treatment is very effective against most bacterial pneumonias, non-resistant tuberculosis, and infectious diarrheas. Like immunization, antimicrobial treatment can be prohibitively expensive burdens for developing countries. Because of this, there have been numerous “appropriate technologies” that have been introduced into developing countries to minimize mortality and morbidity through prevention. These include the development of adequate sanitation systems, potable water supplies, and relatively simple treatments of any diarrhea through the use of oral rehydration solutions. The World Health Organization (WHO) supports the use of these “low-tech” solutions in developing countries.

DEFINITIONS OF EMERGING INFECTIOUS DISEASES

“Newly emerging diseases” is a label that can be applied to diseases caused by new pathogens or strains of existing pathogens; diseases that have made a species jump from animals to humans; and newly recognized diseases that may have existed for decades or years. Of course, since it is impossible to label a disease as “new” rather than “newly recognized” if the pathogen has not been recognized before, these distinctions may be artificial at times. Nonetheless, recent history demonstrates numerous examples of new or newly recognized diseases, of mutations of existing pathogens, and of diseases which have been present in animals in the enzootic state, and have then been introduced into the human population.

HIV/AIDS is a prototype of a new infectious disease. It was first described in the early 1980's, when physicians in several locations in the United States noted the appearance of a rare skin tumor, Kaposi's sarcoma, with a surprisingly high prevalence that defied conventional explanations. Epidemiologic investigation soon revealed that all of these individuals were male, homosexual or bisexual, and many had traveled to Haiti. Within a few years, the prevalence of the disease increased by a factor of many thousands, a rigorous case definition was developed by the CDC, the syndrome of Kaposi's sarcoma was quickly superceded by a case definition which included severe and progressive immune deficiencies, the "Haiti factor" was discredited as a risk factor, mortality due to AIDS was virtually 100%, and a causal virus was isolated by the CDC and by the Pasteur Institute in Paris, almost simultaneously. Meanwhile, the disease diffused rapidly from metropolis to metropolis in the United States and abroad, and it also diffused into suburban and rural areas.

Though HIV/AIDS was thought to be a new disease, yet serum samples in East Africa that had been saved since the 1950's indicated that at least one individual had antibodies to HIV, indicating that the virus had been present in the human population for nearly a quarter of a century. AIDS began to take its toll in mortality and morbidity, yet, at the time, it was not recognized as a harbinger of what was to come.

A familiar concept in public health and medical geography has come to be known as the "health transition" or the "epidemiologic transition," which argues that as societies develop, that the major causes of mortality and morbidity change from infectious diseases, to non-infectious, or chronic diseases (Omran 1971; Omran 1977). The development of more sophisticated antimicrobials and vaccines augmented earlier public health measures such as better sanitation, potable drinking water, and nutrition, which all served to decrease the impact and the prevalence of infectious diseases. Smallpox was the first disease that was eliminated in the history of public health. Rather than attempting to target the world as a whole, WHO, in cooperation with the involved nations, used a geographical targeting system to immunize people in local areas proximal to smallpox outbreaks. This was a very innovative method that made eradication technically and financially feasible.

In the 1960's, it appeared that malaria and some other tropical diseases were well on the way to eradication. Poliomyelitis virtually disappeared as a major threat in developed countries due to the Salk and Sabin vaccines. It is hardly surprising, then, that the Surgeon General of the United States, William H. Stewart, stated in 1967 that it is "time to close the book on infectious diseases, declare the war on pestilence won, and shift national resources to such chronic problems and heart disease (Stewart 1967)." Of course, the Surgeon General was proven wrong, but he can hardly be blamed, since it appeared that infectious diseases were indeed waning and disappearing as major causes of mortality in the United States and similar countries. Taking a broader view of history, however, William McNeill suggested in 1976 that "infectious disease which antedated the emergence of mankind will last as long as humanity itself, and will surely remain…one of the fundamental parameters of human history (McNeill 1976)." Nonetheless, infectious diseases kill far more people in the world as a whole than do non-infectious diseases, and, within inner city areas such as the South Bronx and Harlem, infectious diseases—particularly AIDS and tuberculosis, account for more deaths than do non-infectious diseases (Sen 1993).

FACTORS IN EMERGENCE

There is widespread agreement that most emerging infectious diseases do not arise *de novo* as a result of major and mysterious introductions of new pathogens. Rather, most emerging diseases occur because of the introduction of new microorganisms into “virgin” populations. Species jumps are certainly important, for diseases as diverse as Lyme Disease, Yellow Fever, and, arguably, HIV/AIDS, have been present in other species (Morse 1995). Species jumps are deeply rooted in human activities. As deforestation, development projects, and urban expansion intensify, the effects on the relationship between humans and their environment become subject to disequilibrium and change, and this change alters the contact patterns between pathogens, their animal reservoirs, and humans. This is the most basic and most prevalent type of change that leads to the emergence of new diseases and the resurgence of old ones.

Another type of emergence is linked to the issue of proliferation. With increasing international travel, and domestic travel, people who previously had contact with one type of environment become exposed to the inhabitants of other nations and environments. This can result in the introduction of new pathogens into populations that lack the immunity to counter the diseases caused by those pathogens, because they have yet to have been exposed to the pathogens. Though this scenario has not been realized to the extent that the popular literature and popular thought would suggest, if a new, airborne disease should become prevalent in one ecosystem, it could diffuse rapidly to new countries and new ecosystems. This is particularly severe if the disease was spread by the respiratory route, which would make transmission very easy, and could result in international disasters should the pathogen not just be easily transmissible, but virulent as well. Consider the theoretical scenarios for viral hemorrhagic fevers such as Ebola. This is transmitted via intimate and close contact with the infected blood of somebody who has this disease, and has a case-fatality rate of 90%. Should this disease become aerosolized and transmitted via the respiratory route, rapid spread could develop. It is not fully understood why some diseases, such as the plague, sometimes have an altered mode of transmission. Similarly, should HIV/AIDS undergo some change that allowed it to be transmitted not just by activities such as sexual contact or sharing of needles among intravenous drug users, this more slowly fatal disease could become a major killer of more than those who engage in well defined risky behaviors.

These scenarios have not been realized, and probably will not, with the diseases mentioned above. World history, however, has seen the aerosolization of some diseases, wherein the transmission cycle changes. The bubonic plague has frequently undergone transformation in the mechanism of transmission. The “Black Plague” represents such a transition, and a recent outbreak of the plague in India provides a more contemporary example of this. The bubonic form of the plague became more easily transmissible as it became aerosolized into the pneumonic form and the route of contagion was through respiratory droplets. The exact pathological mechanism by which this change occurs is yet to be explained fully, but probably is a result of a heavy bacterial load resulting in sepsis, and diffusion through the respiratory system.

Another type of threat to the human population is the emergence of antimicrobial resistant strains of older diseases, largely due to mutations in the DNA or RNA of microorganisms. Minor changes in the DNA or RNA structures of bacteria and other pathogens can select for new strains that are not affected by existing antimicrobials, or at least, by the antimicrobials that are in common use. Some examples include the development of penicillin-resistant respiratory infections, multiple drug-resistant tuberculosis (MDRTB), resistant forms of malaria, and resistant forms of sexually transmitted diseases such as gonorrhea. The latter has been traced geographically, using molecular amplification techniques, and even relatively new antibiotics are increasingly ineffective in the treatment of some forms of the disease.

The most dangerous types of antimicrobial resistance occurs in two instances. First is multiple drug-resistant tuberculosis, and second are hospital acquired ("nosocomial") infections. Those most subject to multiple drug resistant tuberculosis (MDRTB) are the homeless populations, and especially homeless populations who are immunosuppressed due to HIV/AIDS. There are five medications that are important in the treatment of tuberculosis, a bacterial disease that is spread by the respiratory route, particularly in crowded places. Infection with tuberculosis was very common in the last century and in the earlier parts of this century, but the availability of antibiotics, beginning after World War II, made tuberculosis treatable. However, it required vigilance on the parts of physicians, public health authorities, and patients to adhere to a regimen of at least two medications for a minimum of six months. What has happened with the homeless population is a very complex story, but as with all antibiotic treatment, failure to complete the treatment exactly as prescribed resulted in the genetic breeding of drug-resistant bacteria—not all the bacteria died, in a sense, as a result of incomplete treatment, and those which survived in large populations became genetically resistant to the antibiotics. Thus, newer and more complex regiments were begun, sometimes with as many as four or five antibiotics, and the same social conditions that produced pathogens that were resistant to two antibiotics soon became resistant to four antibiotics. The existence of MDRTB is a result of human behavior and microbial behavior. The reason that the homeless, in particular, frequently do not and have not complied with the prescribed treatment include issues of cost, reliability of knowledge of the fact that failure to complete treatment could render existing treatments totally impotent, and the inherently itinerant life of the homeless, where adhering to medication regimens is difficult. Monitoring homeless patients in urban areas is very difficult, and compliance with recommended treatment protocols, which can be very complex, is also difficult. There has been some demonstrated success with directly observed therapy, where a health worker observes the dosing of an outpatient several times per day, but this can be quite costly.

Nosocomial infections are major problems in large teaching hospitals in the United States and elsewhere. The nature of hospitals, with dense quarters, particularly in intensive care units, has resulted in two types of infections that are particularly serious. The first, and less serious, is methicillin-resistant *Staphylococcus aureus*, or MRSA. This first appeared in the 1960's. The bacterium is responsible for a number of different types of infections, yet the standard treatments, with medications similar to a penicillin-related antibiotic—methicillin—has resulted in a fairly common situation which began in large urban hospitals and has diffused to other hospitals, where only a few costly medications showed any promise for eradicating the infections, which are usually life-threatening. MRSA has followed a diffusion pattern that is a blend of contagious and hierarchical diffusion.

A more serious threat is that of vancomycin-resistant enterococcus, or VRE. It is also a disease that has undergone diffusion, but it is even more serious than MRSA for two reasons. First is that vancomycin is an agent of last resort for some infections, including MRSA. If an organism becomes resistant to vancomycin, there may be no effective antibiotic to use, and this resistance results in a very high case-fatality rate. In the case of VRE, there is no agent to use. Supportive care is all that can be done for patients with VRE. VRE is very easily transmissible—even more transmissible than is MRSA. Both sets of infections must result in the isolation of the patient and in detailed sanitary precautions by the health care giver, but with VRE, it has been shown that a patient's room can be positively cultured for VRE many feet away from the patient. Both pathogens require meticulous vigilance, yet with a pathogen as easily spread as VRE, there is sometimes no way of controlling it, beyond the strictest measures of isolation and sanitation. Alas, while this may help other patients and hospital personnel, little can be done to reverse the course of VRE for patients who have it. Whole wings of hospitals that are contaminated by VRE or MRSA have been closed and decontaminated as a last resort.

Thus, changes in the modes of transmission could be very important and could signal a very serious challenge to societies should diseases that are virulent, easily transmissible, and rapidly fatal, undergo such a transition. There is nothing to prevent this from happening. Our only protection against such a scenario is the rapid detection, surveillance, and control of new or transformed pathogens.

FOODBORNE AND WATERBORNE INFECTIONS

Food and water are also important routes of contagion. The globalization of the food supply is a well-established fact, yet most people in the non-scientific community do not realize the extent to which feed is imported to developed countries from developing countries. (Hedberg, MacDonald, and Osterholm 1994). The main source of contamination in foodborne disease is fecal, either from natural fertilizer or from the hands of agricultural workers. The formation of the North American Free Trade Agreement (NAFTA) may encourage the northward trade of produce from Mexico, a country from which many travelers return with diarrheal diseases, most of which are self-limiting, but some of which can become life threatening. Infection from food produced outside the United States is quite common, but statistical estimates are difficult since existing surveillance systems are inadequate.

The threat of foodborne infectious diseases, however, is certainly not limited to internationally exported food. For example, there have been major pockets of a serious diarrhea that sometimes progresses in children to a fatal involvement of the kidneys that is caused by a coliform bacterium, closely related to the coliforms found in human digestive systems. *E. coli* 0157:H7, which has been responsible for several large outbreaks of diarrheal illness and is occasionally fatal in children due to renal complications. One outbreak in the State of Washington was traced to meat contaminated in the butchering process by fecal contamination from the bowels of the cow and then transformed into hamburger. The outbreak was exclusively linked to one fast food chain and one meat producer, and resulted in several deaths in children. Hundreds of adults and children alike suffered from severe diarrhea due to this pathogen (CDC 1993; CDC 1992-1993). The reason that this was not detected before it entered the human link in the food chain is evidence for the fact that the United States has an inadequate system of food quality control and surveillance. An outbreak of *E. coli* 0157:H7 in Japan in 1996 affected thousands of people, though the link to specific foods remains controversial.

Other foodborne diseases are also important in the United States. Most common is hepatitis A, which is transmitted via the fecal-oral route, and can cause months of infirmity from the resulting liver infection. Again, this is particularly significant in places where large quantities of food are handled, and most state and county health departments mandate serologic tests of food handlers in an effort to minimize the prevalence of this disease. A reliable vaccine is also now available, and gamma globulin injections are advised for all who may have eaten in a specific place once an epidemic becomes evident. By that time, however, secondary transmission to others within a family or social group may have been infected.

Waterborne diseases are also important in the United States and other countries. Certainly in developing countries, diseases such as schistosomiasis, amoebiasis ("amoebic dysentery"), cholera, and coliform diarrhea takes its toll both in terms of morbidity and mortality. A new strain of cholera was introduced to the Americas off the coast of Peru in the early 1990's by a ship that apparently dumped its bilgewater close to shore. Thus, the new strain, which had hitherto been restricted to Asia, made its way to the Americas. The conditions of poor sanitation and water supplies, and dense population, are ideal conditions for the transmission of this potentially fatal disease. A few cases have been reported contracted within the United States.

Another example of a waterborne diarrheal disease affected most of the population of Milwaukee in 1993. The disease, cryptosporidiosis, was traced putatively to contamination from the excreta of bovines within the watershed of one of the rivers that feeds Lake Michigan and which is instrumental in supplying Milwaukee with potable water. Over 400,000 people developed severe and untreatable diarrhea; of these, 4400 needed to be hospitalized, and the disease proved fatal to several dozen individuals, most of who were immunocompromised from HIV/AIDS or other sources (Bryan, Pinner, and Berkelman 1994).

AIRBORNE DISEASES: INFLUENZA

There are numerous diseases that are experienced in epidemic form throughout the world, on a seasonal basis. These are frequently not regarded as serious threats to health, but they are. The most common of these is influenza, which is spread via the airborne route, is highly virulent due to the fact that the influenza virus replicates on the outer lining (epithelial cells) of the respiratory system, and then the virus is easily transmitted. Influenza viruses mutate regularly. Relatively minor mutations result in epidemics that are often localized, and major mutations result in major pandemics, with high case-fatality rates. The 1918-1919 pandemic killed at least 20 million people worldwide. This pandemic resulted in the greatest mortality of any infectious disease. Mortality could have been as high as 50 million. The mortality rate from the Black Plague was higher, but since the world's population was smaller and the plague was geographically more limited, the total mortality was less than that of the 1918-1919 influenza pandemic, which lowered life expectancy by 10 years in the United States. Newly mutated forms of influenza, and its related complications, including meningitis, encephalitis, and, most commonly, viral pneumonia, make influenza one of the diseases most likely to pose a threat to life in the future. The

1918-1919 pandemic was recently identified using molecular “fingerprinting” techniques, using autopsy organs preserved at the Armed Forces Institute of Pathology, and it was proven that the virus was the most was a small variant one type of periodically recurring influenza, the H1N1 subtype (Taubenberger, Reed, Craft, et al. 1997).

Influenza will continue to present major challenges to public health throughout the world. Though a vaccine is available each year, targeted at the three most likely strains of influenza to emerge in the coming year, predictions are not always completely accurate, and are the result of an annual consensus meeting of public health officials and infectious disease specialists each February. Obviously, if the predictions fail, the vaccine that is produced will not protect people from the unexpected strain of influenza, and, with little cross-protection from the vaccine for other strains, mortality and morbidity can be potentially quite high.

This is what was responsible for the “Swine Flu” scare in the United States in 1976. The 1918-1919 pandemic had its highest mortality rates in the 20-40 year old age groups, for reasons that are not understood. In 1976, when a serious outbreak of influenza occurred at Fort Dix, New Jersey, some public health officials became concerned that this might be the same strain as in 1918-1919. The resulting national campaign for immunizations in the United States and other countries was therefore understandable, yet there was no epidemic or pandemic that occurred, and the immunization program was terminated when several apparently iatrogenic cases of a potentially fatal neurological disease-- Guillain-Barre Syndrome-- was associated epidemiologically with the immunization.

SOCIAL RESPONSE

One area for study that has been neglected has been to examine and analyze the human response to infectious disease in the same terms as has been done with natural hazards (Lewis and Mayer 1988). Though the study of natural hazards and the individual, social, and governmental responses to natural hazards has resulted in much fascinating science and social science, the concentration of natural hazards research since its inception has been on physical and climatic hazards, to the virtual exclusion of biological hazards. However, Lewis and Mayer (1988) argue that diseases, and particularly infectious diseases, can be examined in the same framework as tornadoes, floods, and volcanic eruptions, and that it is important to consider the social responses to infectious disease. As many epidemics have demonstrated, people have a need to feel in control of events that surround their lives, and that includes issues of health and death. Thus, there seems to be an imperative to take control, to exert tangible influences, on the progression of epidemics, even when there is no evidence that these measures of control will be effective. It is within this framework that the critical issues of infectious disease surveillance and disease control can be analyzed.

NEED FOR SURVEILLANCE AND CONTROL

The first step in disease control is that of surveillance: detecting that a new disease is potentially threatening to the population of a defined region and people. Some diseases may have the potential for threatening much of the world's population, such as the influenza pandemic of 1918-1919, and sometimes the threat may be more limited to certain subgroups of the population, such as hepatitis B. The threat may also be perceived as being more limited geographically. Malaria and its vectors, anopheline species of mosquitoes, cannot survive freezing temperatures in temperate or Arctic areas, and so one would not expect to find malaria in those regions, depending on the season.

Effective disease surveillance requires the knowledge of how widespread and dispersed cases of a specific disease are, and the geographical and temporal dynamics of changes in the pattern of that disease. Geographical models such as diffusion models, and extrapolations using Geographical Information Systems and interfaces with spatial analytic techniques are crucial in this endeavor. Of course, the use of any predictive analysis is only as good as the data that are used, and the accuracy of reporting specific diseases is highly variable. In a country that has ready access to health care personnel and quick and accurate reporting of new diseases, predicting and describing spread is much more accurate than in a country where there is a paucity of people who can recognize the symptoms of what might me an emerging disease. Indeed, when mortality is high for most infectious diseases, such as in parts of developing countries that are spatially isolated, a few cases of a new disease may go unrecognized simply because morbidity and mortality from other causes is quite high. On the other hand, in a country with well trained medical personnel and a good infrastructure of laboratories and diagnostics, the "index of suspicion" for a particular illness or death can lead to more rapid identification of the cause of death or disease. In a hierarchically structured government, there must be territorial cooperation and multisectoral collaboration in reporting and surveillance.

This is exactly what happened with Hantavirus Pulmonary Syndrome in the Four Corners area of New Mexico, Colorado, Utah, and Arizona that struck swiftly in 1993 and had a high case-fatality rate. This syndrome was completely unknown until its emergence. The coordinated efforts of the Centers for Disease Control, the University of New Mexico

Medical Center, the Indian Health Service, and the New Mexico Department of Health allowed for the quick identification of the virus that caused this epidemic. It was very similar to a virus—hantavirus--which has a high prevalence rate in Korea and neighboring countries, yet DNA techniques demonstrated that the virus was not identical. The virus was finally called the *Sin nombre* (Spanish for "without a name") type of hantavirus. Moreover, within a few weeks, much of the pathobiology of this virus became understood, and though the prognosis of a patient with this virus remains grave, some antimicrobials may be effective in treating bacterial complications of this viral syndrome. Nonetheless, the mainstay of treatment, which remains severely limited, consists only of supportive measure for Respiratory Distress Syndrome in an intensive care unit.

The ecology of this disease was also well described within months of its initial manifestations. As with other Hantaviruses, the *Sin nombre* virus has its reservoir in a rodent—in this case, a mouse called *Peromyscus maniculatus*, which transmits the virus to humans via the aerosols of the mouse excreta and the subsequent inhalation by people who move in close proximity to the excreta. Though the outbreaks of Hantavirus Pulmonary Syndrome have been in rural areas, there is nothing that would prevent its spread to more densely settled urban areas, and should this happen, the effects on large populations could be quite severe, therefore indicating the need for close surveillance of this disease and its animal reservoirs.

The need for surveillance is great. Emerging diseases, resurgent diseases, and newly introduced diseases should be thought of as matters of national security. As Lederberg, Shope, and Oaks remind us in the Institute of Medicine's study of emerging infectious diseases:

> in the context of infectious diseases, there is nowhere in the world from which we are remote and no one from whom we are disconnected. Consequently, some infectious diseases that now affect people in other parts of the world represent potential threats to the United States because of global interdependence, modern transportation, trade, and changing social and cultural patterns (p. v.)

As one high ranking scientist with the World Health Organization has echoed, and what the geographical community realizes, is that national boundaries are meaningless in disease diffusion (LeDuc 1996). Containment using quarantine, or, in the case of a disease with a very short incubation period, health screening at a point of disembarkation, could be effective in specific circumstances.

The very transportation links that allow and promote economic development and trade themselves have the potential of becoming conduits of disease, potentially of epidemic and pandemic proportions. This can be particularly severe when an infected traveler's travel time exceeds that latency period of the disease, since that passenger may be lost to official surveillance and epidemic control under those conditions (Plotkin and Kimball 1997).

SURVEILLANCE

Because of the potential seriousness of newly arising diseases, and pathogenic mutation of existing diseases, the threat of rapid emerging disease diffusion, and cross-species jumps which are largely due to human alterations in a pre-existing ecosystem, it is incumbent on governmental organizations at all levels, and supranational organizations such as the World Health Organization, to focus much attention and devote resources to strategies that will contain and minimize the effects of emerging diseases.

However, control strategies presuppose the existence of adequate disease detection networks, since responses to disease are contingent upon recognition that the disease is present and that it constitutes a potential threat. Thus, governmental units, ideally in cooperation with one another and with local hospitals, universities, and other institutions, should institute measures to allow the rapid identification and isolation of new diseases and the populations who might be affected. Geographically meaningful “sentinel sites” at the locations of greatest probability of being an entrance point for diseases—major international airports and other points of disembarkation—can and have been specified. This is certainly the case with WHO Collaborating Centers for the surveillance of influenza and other infectious diseases.

The purpose of surveillance is to allow the detection of new disease patterns in terms of time, place, and individuals. A surveillance system should facilitate the detection of new organisms, identify epidemics at an early stage, indicate how the epidemic may be contained; evaluate the existing prevention and response systems; and plan and coordinate future responses (Bryan, Prinner, and Berkelman 1994.) It should identify the prevalence of existing diseases, and should detect the geographical patterns of disease, the diffusion patterns, and identify the magnitude of the threat to humans in affected and potentially affected areas (Lederberg, Shope, and Oaks 1992). Moreover, surveillance programs can and should exist at all scales from the local to the global.

The establishment of good surveillance networks was one of the major recommendations which was made by the Institute of Medicine (Lederberg, Shope, and Oaks 1992), and this recommendation was made in a more detailed policy document published by the Centers for Disease Control and Prevention (1994), and an interagency working group of the U.S. government, which is named the Committee on International Science, Engineering, and Technology Policy (CISET). The recommendations of the latter group constitute a major policy document for the United States, and the recommendations were far-reaching, representing a very major effort of every affected agency of government in the United States, ranging from the Department of Defense to the Peace Corps, and obviously including many of the departments of the CDCP, the National Institutes of Health, and other agencies (CISET 1995)

One possible impediment to reporting of emerging diseases is that there is no legal basis for the mandatory reporting of emerging diseases. This is particularly important since the diffusion of new infectious diseases is necessarily a type of diffusion that may not remain within one country's boundaries. There are some existing and evolving international legal provisions. The World Health Organization (WHO) could serve as a conduit for surveillance and control, yet its role has been much more effective in surveillance than control. WHO's International Health Regulations only include plague, yellow fever, and cholera (Fidler 1996). In addition to the International Health Regulations, there are a variety of other regulations and mechanisms, such as the International Civil Aviation Organization's (ICAO) Article 9, as well as other regulations such as the U.N.'s Food and Agricultural Organization's Codex Alimentarius, which applies to food and water. None of the Regulations have been effective (Plotkin and Kimball 1997). Though the problem of emerging diseases is global, any actions taken at the local level must necessarily involve the member states of WHO. As Fidler suggests (1996), it is a problem in international law generally when international law is seen as usurping state sovereignty. Furthermore, even when there is compliance with the International Health Regulations, in many of the tropical countries where emerging diseases are problematic, the basic laboratory and personnel are often lacking, making surveillance and containment that much more difficult. Fidler (1996) proposes a variety of alternate legal strategies that are outside the scope of this analysis.

In a recent article, Plotkin and Kimball (1997) have suggested a series of innovative steps to institute programs for controlling and detecting emerging infectious diseases. Some of their proposals include expanding the International Health Regulations to include diseases other than plague, cholera, and yellow fever; expansion of the reporting mechanisms to WHO other than officially reported statistics at the national level, and reporting of syndromes to allow the timely reporting not just of identified diseases, but also of unusual signs and symptoms that may herald the emergence of a new disease. They also suggest using agencies that are not just related to health. They propose using the World Trade Organization that has regulations pertaining to sanctions for action targeting health, but these regulations include only transmission of agents in contaminated water, animals, plants, and commodities. Plotkin and Kimble (1997) therefore propose that the World Trade Organization cooperate more actively in the detection and control of emerging diseases. Other sectors of international trade and regulations also pertain directly to various aspects of health, and Plotkin and Kimball suggest that “Truly intersectoral, interagency, and interorganizational collaboration in addressing the broad factor of emergence and expanded reporting of disease are major steps in this process (Plotkin and Kimball 1997, p. 7)

The World Health Organization (LeDuc 1996) has also developed a global response network for the surveillance of emerging diseases, and non-governmental groups have taken leadership in considering surveillance and what it ought to be (Wilson, Evans, and Spielman 1994). It is certainly no surprise that scholars, private agencies, and public agencies, including the World Health Organization, agree upon the need for surveillance strategies. The specific recommendations of these groups are similar, but also differ in subtle ways, based upon the politics and constituency of the agencies.

The most international of these groups is, of course, the World Health Organization, which, as an agency of the United Nations, is singularly equipped to develop policies and concepts for surveillance. WHO interacts constantly with more local agencies and groups, and has the mandate to collect needed data on disease outbreaks. The World Health Organization adopted four principal goals for addressing the threat of emerging diseases: 1) strengthen the ability of agencies to conduct disease surveillance worldwide; 2) rebuild a somewhat decimated structure for responding to diseases once they have been detected; 3) promote applied research in academia and at all layers of government, not the least of which is the WHO itself; and 4) enhance rapid response and control abilities within the international community. Considering LeDuc's (1996) excellent and concise summary of these initiatives, it is easy to understand the goals of the efforts of WHO.

The World Health Organization has a structure of "collaborating centers" where diseases are identified, and which have advanced laboratory capabilities and the scientific expertise, in depth and in breadth, to detect outbreaks. These centers are in Atlanta, GA (U.S.A.), London, and Melbourne, Australia. Because influenza surveillance is well established and has been remarkably accurate at detecting new strains of the virus and responding to them through specifying the next year's vaccine, the idea of collaborating centers has already proven itself. There are over 200 collaborating centers in the surveillance network for influenza. WHO has been targeting several areas of particular concern, and early response. These are influenza, “exotic” viral diseases, such as tropical hemorrhagic fevers, antimicrobial resistant bacteria and other pathogens, and foodborne diseases. There are, however, tremendous variations in the laboratories’ technical abilities to carry out the mandate, and some of the laboratories that have been designated to monitor and detect the viral diseases lack the capability to do this adequately. Out of the 36 laboratories that are included in this network, WHO discovered that the local laboratories lacked the necessary reagents to detect common viral diseases, particularly those which are in other parts of the world. However, since spatial diffusion of diseases into new regions is a major concern in responding to emerging diseases, this is disconcerting.

Internal studies by WHO conclude that the laboratories within the network are well equipped to detect diseases that are fairly common in the regions that they serve as their primary targets, but that many of the laboratories could not identify viruses that might diffuse from other parts of the world. Should this persist, it could compromise the whole international surveillance effort specifically because a major concern is the rapidity with which diffusion can occur, with the availability of jet aircraft and rapid travel. This example reflects the fact that until recently—and some would even question the course of recent surveillance efforts—the public health infrastructure for the surveillance and detection of new diseases has eroded as a result of fragmentation of authority, diminishing budgets, and poor coordination and communication. Yet, there are many problems with current surveillance systems, including tracking diseases in the homeless populations and impoverished communities; poor capabilities, in the United States, for microbiologically sound techniques of pathogenic identification, and the rapidity of transportation itself.

One of the major impediments to global surveillance is the limited telecommunications capabilities in many developing countries. Whatever laboratory information that develops must be communicated to other areas within the country, continent, and the world. This requires assistance in the funding of telecommunications systems, and experimental satellite communications efforts are being developed.

Part of the World Health Organization's efforts has been aimed at enhancing the rapid detection of resistant organisms through a standardized computer and communications system called WHONET. Over 100 laboratories participate in this effort (LeDuc and Tikhomirov 1994). A more ambitious plan of expanding the Collaborating Centers network and enhancing guidance for intervention is a major priority of the World Health Organization, and is already in effect through the WHO's Antimicrobial Resistance Monitoring (WHO ARM). Laboratory programs in developing countries are particular needy for technical assistance, and the WHO has made major inroads into providing this technical assistance.

One very innovative program in international communications regarding the instantaneous transmission of information relevant to new outbreaks has been the establishment of ProMED, which uses the Internet in an interactive format. Anybody with access to the Internet can subscribe to this exciting experiment for free, and can participate interactively in reporting disease outbreaks and discussing more conceptual issues. Representatives of nearly 150 countries generate between 10 and 50 messages in a given day, and all subscribers see the postings. ProMED was established by the Federation of American Scientists. It is a vibrant medium for communication, and also demonstrates the utility of the Internet and new technologies for disseminating vital information to the public health community without first dealing with the sometimes burdensome bureaucracies of many countries and states. It depends only upon access to the Internet: an obsolete computer with a slow modem is quite adequate for participation in ProMED. Readers of this article can subscribe to ProMED in the following manner:

1) send a message to: *majordomo@usa.healthnet.org*
2) in the body of the message (not in the "subject" area) send the following message: *subscribe promed.*

Participants will then receive computer confirmation of their subscription, along with simple instructions for using ProMED.

The goals of surveillance in the United States are similar to the goals of the World Health Organization. The U.S. has much more advanced mechanisms of communications, and more advanced laboratories than do developing countries. The Centers for Disease Control and Prevention work closely with state and local health departments to investigate outbreaks at a variety of scales. Of course, there is still a major bureaucracy that sometimes impedes the rapidity of coordination, and before the CDC becomes involved in an outbreak, they must receive a specific request for assistance from local authorities. Occasionally, there are political "turf" disputes, yet the surveillance system seems to be working well. Epidemiology Intelligence Officers from the CDC are attached to all state and many county health departments, and they are on-site for immediate technical assistance and participation when the need arises. In more complex outbreaks, the CDC can dispatch a much larger taskforce of epidemiologists, behavioral scientists, microbiologists, and other, in a matter of a few hours.

Partly as a result of the Institute of Medicine's report (Lederberg, Shope, and Oaks 1992), the CDC issued a report and strategy for responding to the threat of emerging and resurgent infectious diseases (CDC 1994). The CDC proposed a four-pronged strategy aimed at responding to the challenges posed by infectious disease emergence and resurgence.

Largely in response to the fragmentation of governmental units, the CDC has developed a series of goals for funding and programmatic development. These include *surveillance*, and fostering the development of structures to detect and monitor emerging diseases; *applied research*, to integrate laboratories with epidemiologic investigation; *prevention and control*, to improve communications links to governmental units and hospital laboratories; and *infrastructure development*, to improve communications, surveillance, and investigation among the various layers of government and the CDC (Bryan, Pinner, and Berkelman, 1994).

Improving the surveillance capabilities in the United States also includes improving international surveillance because of the rapidity with which a disease may appear in one part of the world and then be transmitted in the United States. Thus, the CDC emphasized further strengthening of links with surveillance efforts abroad. Also included in this category is the funding of the Emerging Infections Programs, which will be discussed shortly; the National Nosocomial Infection Surveillance System (NNIS), which consists of several hundred hospital laboratories which voluntarily report the occurrence of hospital acquired infections, and the Sentinel Surveillance Networks which will ultimately unite laboratories, primary care physicians, infectious disease physicians, emergency departments, and other foci in a system that will allow the rapid identification of emerging and resurgent diseases, and the communication of this information to emphasize containment, eradication, and prevention.

TYPES OF CONTROL

Though the United States has a very advanced medical care system, and its capacity for isolating and containing infectious diseases at the CDC and by CDC personnel, the basic structure for detecting new infections is suffering because there has been a failure of "the infrastructure to maintain vigilance and to respond to most emergent or reemergent infectious diseases has generally continued to deteriorate (Berkelman, Pinner, and Hughes 1996, 315)." This is largely due to the lack of funding and to the complex structure and jurisdictions of cities, counties, states, and the federal government. Indeed, each state has its own criteria for reportable diseases that must be reported to the respective state's Department of Health, and the communication of this information to CDC is voluntary and is frequently incomplete (Bryan, Pinner, and Berkelman 1994).

As part of its Emerging Infections Program, the CDC initiated funding of ten sites for collaborative research and to serve as sentinel states for diseases that are of particular concern or interest for the states that are involved. In addition, the U.S. Department of Agriculture and the Food and Drug Administration are participating in the identification of food-borne pathogens. The foodborne route of contagion is obviously important, as previously stated, and indeed, as this draft of the paper is being concluded, there is a multi-state outbreak of Hepatitis A that is being traced to the shipment of contaminated strawberries from Mexico to the United States. The strawberries were "supposed to" have been grown in the United States for distribution in school lunch programs in Michigan, but the fact that they were grown in Mexico, and were contaminated, illustrates the point that surveillance is inadequate for foodborne pathogens, both for domestically produced food and for foreign produced food. Other common activities will be to conduct laboratory and epidemiological studies on unexplained deaths due to apparent infectious causes; molecular biologic studies of antimicrobial-resistant isolates, and other specific ongoing surveillance, such as the incidence of three major pathogens which are proving resistant to many antimicrobials and are tremendously important in community-acquired infections. These are *Streptococcus pneumonia, Haemophilus influenzae,* and *Neisseria meningitidis (*Berkelman, Pinner, and Hughes, 1991)..

The California program is being conducted jointly between the State Department of Health and the School of Public Health at the University of California—Berkeley, and will concentrate specifically on coccidiomycosis, or “Valley Fever,” which has emerged as a major infectious disease in the San Jouaquin Valley and other locations in California. Coccidiodomycosis is a potentially fatal fungal infection. Its spores have been shown to exist in the topsoil of semi-arid areas throughout much of the Americas, and a recent study has shown that the spores can emerge from the topsoil into dustclouds following an earthquake (Schneider, Hajieh, Spiegel et. Al 1997). There has been a tenfold increase in the incidence of coccidiodomycosis over the past decade.

The Connecticut program consists of a collaborative effort of that state’s Department of Health and the Yale University School of Medicine. Tick-borne infections have had a tremendous increase in their reported incidence, and this is of specific concern to Connecticut because of the increase in reported cases of several subtypes of ehrlichiosis (Fishbein and Dennis 1995). Connecticut is one of the states that is most affected by ehrlichioses. Moreover, some of the tick vectors are the same vectors as for other tick-borne diseases such as Lyme Disease, which has much spatial overlap with the distribution of the ehrlichioses. Another syndrome that serves as a focus for the Connecticut program are cases of community-acquired pneumonias in which no causal organism can be isolated or identified, even with the most advanced molecular techniques.

In Minnesota, the University of Minnesota School of Public Health, the Association for Practitioners in Infection Control, and the Minnesota Department of Health will conduct the general studies described previously, and will also provide surveillance for a number of gastro-intestinal outbreaks that are caused by enteric (intestinal) pathogens. The State of Minnesota has one of the finest foodborne-surveillance systems in the United States, uniting both classical epidemiology and molecular epidemiology and surveillance.

Finally, the Oregon program is investigating the nature of meningitis, in addition to pursuing the generalized studies. There has been an increasing number of isolates of a particular sub-type of meningococcal disease, and there is no definitive hypothesis of why this is occurring.

There are a number of other mechanisms by which the CDC will promote projects that are aimed at improving the surveillance of infectious diseases, including funding extramural research in universities and hospitals, and providing specific awards to various governmental units to improve surveillance.

SPECIFIC ROLES FOR THE GEOGRAPHICAL COMMUNITY

Many of the causes for the emergence and resurgence of infectious diseases are of direct geographical importance. Transportation and spatial interaction allow the spread of new or resurgent diseases; changes in the human-environment relationship may have the unanticipated consequence of introducing enzootic diseases into the human population. (Mayer 1996). Geography, however, can and should play an equally vital role in the surveillance and control of emerging diseases.

Geographical Information Systems, frequently used in conjunction with remote sensing and global positioning systems (GPS) has gained great currency in various public health endeavors, including the surveillance of disease. This should be done in conjunction with spatial modeling and the "geographical imagination," and not just as a tool to be "visually and analytically linked to images of the environment (Bryan, Pinner, and Berkelman 1994, p. 359)." GIS is growing in importance and at all levels of government in the detection and surveillance of infectious and noninfectious diseases.

The role of remote sensing has been articulated in the context of malaria control (Roberts and Rodriguez 1994) The use of these technologies, in concert with the underlying geographical theories and models, may assist in the detection of foci which possess the correct conditions for infectious disease vectors, which in the context of malaria, are anopheline *spp*. The same holds true for all vectored diseases.

GPS and GIS can also play a crucial role in the detection of areas that may be particularly prone to the transmission of existing and new waterborne diseases; the documentation of disease diffusion; and the relationships between environmental characteristics and concentrations of human settlements. The role of GIS in infectious disease epidemiology is discussed by Clarke, McLafferty, and Tempalski (1996). Adequate description of new and emerging foci is the crucial step in predicting where the disease will next appear. For slowly diffusing diseases, such as cholera, time is not of the essence, and specific responses need not be momentary. In the case of rapidly diffusing and virulent diseases, such as those which are transmitted via the airborne route, information that is accurate up to the moment may assist in the implementation of containment strategies.

Drawing upon Environmental Impact Statements, McSweegan (1996) suggests that there should also be systems of Disease Impact Statements, particularly when water projects, deforestation, and environmental change are concerned. This is no less important than environmental impact statements, and it has long been ironic that most Environmental Impact Statements have not included an assessment of the health effects of proposed projects. One example comes from the fact that nearly half of the approximately 4 billion people in the world live in places that subject them to vectored diseases, and McSweegan (1996) suggests that a Health Impact Statement would assist more conventional surveillance methods of noting the location other characteristics of cases of vectored diseases, determining vector distribution, monitoring animal reservoirs, and assessing changing climatic and weather patterns to predict areas that are prone to vector redistribution.

What makes the idea of Health Impact Statements particularly alluring is that they would allow and require the assessment of an environmental modification project, ranging from the construction of a dam to the construction of new housing. While surveillance is itself important, it is also necessary to anticipate the unintended health consequences of environmental modification.

CONCLUSION

Emerging infectious diseases are mostly unintended consequences of human behavior and environmental modification. The diffusion of emerging diseases is even a more direct consequence of human invention: transportation. Just as transportation allows international commerce and passenger movement to occur, so it allows emerging disease agents to move. In the case of airborne diseases, this is particularly significant, but, as the experience with the latest pandemic of cholera illustrates, it is also the case with waterborne diseases. Human activities, however well intentioned they are, can and often do pose threats to human health. A geographical framework of analysis is crucial to understanding the emergence of infectious diseases, and the diffusion patterns of those diseases.

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