Emerging infectious diseases

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From experience, we know that many different elements can contribute to the emergence of a new infectious disease: these include microbial/virologic determinants (such as mutation, recombination, natural selection, evolutionary progression of the pathogen), natural influences (such as ecologic, environmental, and zoonotic influences on the pathogen), and factors pertaining to human activity (such as personal behavior and societal, commercial, and iatrogenic factors affecting the pathogen). New infectious diseases appear to be emerging with increasing frequency, as suggested by published reports of cases, outbreaks, and epidemics, and by the rate of identification of new pathogenic microorganisms and viruses. The list of newly emergent pathogens of humans and animals is impressive, indeed (Tables 21-1 and 21-2), and is seemingly prophetic of more to come in the future. There are several reasons why emergence of new pathogens seems to be accelerating. The global human population has continued to grow inexorably, bringing increasingly larger numbers of people into close contact. There have been successive revolutions in transportation, making it possible to circumnavigate the globe in less than the incubation period of most infectious diseases. Ecological changes brought about by human activity are occurring at a rapidly accelerating rate. Additionally, now, bioterroristic activities, supported by rogue governments as well as organized amateurs, involving "high-tech" as well as "low-tech" threats, are clearly increasing in scope and scale.

Note an initial tension between national security as usually understood, with its focus on national defense and force projection, and the fundamental nature of infectious disease, which is regional and global in scope, especially given modern international transportation networks. Note also the possibility that, while infectious diseases as a whole may not be a clear national security concern (or, as Allenby (Allenby: Definition) discusses, appropriately researched or managed by the security apparatus), there has always been a concern with infectious disease whenever U.S. military personnel must serve or intervene overseas. Taken together, these two observations suggest that what is required in this area is not a radical departure from past practices, but rather an evolution and strengthening of existing ones (particularly funding practices). What these are, and how they may be addressed and modernized, is discussed in the next two sections.

The "discovery-to-control continuum"

Given the reality of the threat, initial investigation at the first sign of the emergence of a new disease must focus on practical characteristics such as mortality, severity of disease, transmissibility, and remote spread, all of which are important predictors of epidemic potential and societal risk. Clinical and pathologic observations and preliminary agent identification (the new realm of molecular biology) often provide early clues. From this point, various elements of a "discovery-to-control continuum" are usually called for. The continuum starts with (1) discovery, the precise recognition of a disease in a new setting, and continues through (2) epidemiologic field investigation, (3) etiologic investigation, (4)

Table 21-1. Some important new, emerging and re-emerging human virus pathogens.

*Crimean-Congo hemorrhagic fever virus** (tick-borne; severe human disease with 10% mortality; widespread across Africa, the Middle East and Asia)
*Dengue viruses** (mosquito-borne; the cause of millions of cases of febrile disease in the tropics, dengue hemorrhagic fever, a life-threatening disease, especially in children)
Ebola, and Marburg* viruses* (natural reservoirs unknown; Ebola and Marburg viruses are the causes of the most lethal hemorrhagic fevers known)
Group A, B & C rotaviruses (rotavirus enteric disease is the second leading cause of death in infants in the world)
*Guanarito virus** (rodent-borne; the newly discovered cause of Venezuelan hemorrhagic fever)
*Hantaviruses** (rodent-borne; the cause of important rodent-borne hemorrhagic fever in Asia and Europe.
Hepatitis C virus (newly identified; the cause of much severe, chronic liver disease in the United States)
Hepatitis delta virus (an unusual "helper" virus that makes hepatitis B more lethal)
Hepatitis E virus (newly identified; the cause of epidemic hepatitis, especially in Asia; recently recognized as widespread along the U.S. / Mexico border; the infection has a high mortality rate in pregnant women) *Hepatitis G virus* (newly identified; the cause of a small proportion of transfusion-related hepatitis worldwide)
Human herpesviruses 6 & 7 (newly identified; the cause of a substantial proportion of febrile disease in children)
Human herpesviruses 8 (newly identified; associated, possibly causally with Kaposi's sarcoma)
Human immunodeficiency viruses, HIV1 and HIV2 (the causes of AIDS, still emerging in many parts of the world)
Human papillomaviruses (over 70 viruses; some associated with cervical, esophageal, and rectal cancers)
Human parvovirus B19 (the cause of roseola in children; a possible cause of fetal damage when pregnant women become infected)
Human T-lymphotropic viruses (HTLV1 and HTLV2) (the cause of an adult leukemia and neurologic disease, especially in the tropics)
Influenza viruses (the cause of thousands of deaths every winter in the elderly; the cause of the single most deadly epidemic ever recorded—the worldwide epidemic of 1918, in which over 20 million people died)
Japanese encephalitis virus (mosquito-borne; very severe, lethal encephalitis; now spreading across Southeast Asia; great epidemic potential)
*Junin virus** (rodent-borne; the cause of Argentine hemorrhagic fever)
*Lassa virus** (rodent-borne; a very important, severe disease in West Africa; imported into a Chicago hospital in 1990)

Table 21-1. (Continued.)

*Machupo virus** (rodent-borne; the cause of Bolivian hemorrhagic fever, recent outbreaks after many years of quiescence)
Measles virus (re-emerging in several countries because of poor vaccine coverage)
Norwalk and related viruses (major causes of outbreaks of severe diarrhea)
Polioviruses (the cause of poliomyelitis; still an important problem in developing countries of Africa and Asia; targeted by WHO for worldwide eradication by the year 2000)
Rabies virus (transmitted by the bite of rabid animals; raccoon epidemic still spreading across the northeastern United States; new coyote epidemic spreading in south Texas)
*Rift Valley fever virus** (mosquito-borne; the cause of one of the most explosive epidemics ever seen in Africa)
Ross River virus (mosquito-borne; cause of epidemic arthritis; has moved across the Pacific region several times)
Sabiá virus (rodent-borne; virus from Brazil; newly discovered cause of hemorrhagic fever, including two laboratory-acquired cases)
Sin Nombre virus (emerging as the cause of the severe, often fatal acute respiratory distress syndrome in western regions of the United States) *Venezuelan encephalitis virus* (mosquito-borne; cause of recent major epidemics in Central and South America)
*Yellow fever virus** (mosquito-borne; one of the most deadly diseases in history, great potential for urban re-emergence) [** the viruses that cause hemorrhagic fevers in humans*]

diagnostics investigation, (5) focused research, (6) policy and marketplace matters, (7) technology transfer, (8) commercialization, (9) training and clinical outreach, and (10) formalization of disease control organization, nationally and/or internationally. Of course, not all of these elements are appropriate in every emerging disease episode. Decisions must be made and priorities must be set: "We can do this, but not that"; "What is the minimum that must be done to deal with this disease outbreak in this given circumstance?"

This "discovery-to-control continuum" deserves further review, as the basis for planning future interventive strategies pertinent to all potentially emergent diseases. At one time this review would have been rather simple surveillance leading directly to control: identify the new disease, learn its nature, set in place a prevention or control scheme to deal with it. But, along came HIV/AIDS, the ultimate case where surveillance and control have gone separate ways. In the United States, more and more sophistication in AIDS surveillance has not led to satisfactory prevention and control programs: in fact some people say that the exhaustive surveillance system has become a mask hiding failures in prevention and control programs. Globally, where not as much has been spent on HIV/AIDS surveillance, the same separation has occurred, but the failures in prevention and control programs have many other causes, as well. In both settings, the media, politicians, and the concerned public have stepped in and have attacked the citadel: "Your vaccines led to the conquest of smallpox, and to a great reduction in

Table 21-2. Some important new, emerging and re-emerging virus pathogens of animals.

African horsesickness viruses (mosquito-borne; a historic problem in southern Africa; now becoming entrenched in the Iberian peninsula; a major threat to horses worldwide)
African swine fever virus (tick-borne and also spread by contact; an extremely pathogenic virus; recently present in Europe and South America; a major threat to swine in North America)
Avian influenza viruses (spread by wild birds; a major threat to the poultry industry of the United States and Mexico)
Bluetongue viruses (*Culicoides*-borne; the isolation of several strains in Australia has become an important nontariff trade barrier issue)
Bovine spongiform encephalopathy agent (recognized in 1986; the cause of a major epidemic in cattle in the United Kingdom, resulting in major economic loss and trade embargo; recently identified as the cause of human central nervous system disease, variant Creutzfeldt–Jakob disease)
Canine parvovirus (a new virus, having mutated from feline panleukopenia virus; the virus has rapidly swept around the world, causing a pandemic of severe disease in dogs)
Chronic wasting disease of deer and elk agent (a spongiform encephalopathy agent of unknown source, discovered in captive breeding herds in the United States)
Dolphin, porpoise, and phocine (seal) morbilliviruses (epidemic disease first identified in 1988 in European seals was first thought to be derived from a land animal morbillivirus, such as canine distemper or rinderpest, but now it is realized that there are several important, emerging pathogens endangering these species)
Equine morbillivirus (a new virus, the cause of fatal acute respiratory distress syndrome in horses [and humans], in Queensland, Australia, in 1994; recently traced to bats–flying foxes)
Feline immunodeficiency virus and simian immunodeficiency viruses (important new viruses, the one affecting cats in nature and the other serving as an important model in AIDS research)
Foot-and-mouth-disease viruses (still considered the most dangerous exotic viruses of animals in the world because of their capacity for rapid transmission and great economic loss; still entrenched in Africa, the middle East, and Asia)
Lelystad virus (mystery swine disease) (a new virus, causing an important disease, porcine reproductive and respiratory syndrome [PRRS] in swine in Europe and the United States)
Malignant catarrhal fever virus (an exotic, lethal herpesvirus of cattle; an important nontariff trade barrier issue throughout the world)
Myxoma virus (used to control rabbits in Australia, but with diminishing success; now a proposal has been advanced that genetically engineered myxoma virus carrying a gene for a sperm antigen be distributed to sterilize infected surviving rabbits)
Rabbit hemorrhagic disease virus (was being investigated as new way to control rabbits in Australia, but then escaped and is spreading rapidly across the continent)
Rinderpest virus (still considered very dangerous with potential for causing great economic loss; still entrenched in several regions of Africa)

polio, measles, rubella, mumps, and hepatitis B, so why cannot you do the same with HIV/AIDS?" We know the scientific answer to this problem, but we have not successfully explained it to the public.

Today, as more examples are plugged into the model "discovery-to-control continuum," it seems to become more and more complex—nevertheless, there is value in seeking the common lessons from our response to HIV/AIDS, dengue, variant-Creutzfeldt–Jakob disease (v-CJD), Ebola, and other emerging disease episodes. This is particularly critical given recent examples of "species jumping" of viruses and microorganisms (Table 21-3) that pose obvious difficulties. The more examples plugged into the model continuum, the more one is struck by the gap between what is and what might be.

The continuum moves from the perspicacious sphere of discovery, to the scientific area of risk assessment, to the nonscientific, political area of risk management. When one reflects on specific disease emergence episodes over the past few years, one is first struck by the importance of the scientific base upon which public health response depends. This base was established by Pasteur and his colleagues in the founding days

Table 21-3. Recent "species jumping" of viral pathogens.

Year	Virus	Disease	Species transfer	Cause
1978	Canine parvovirus	Pandemic enteritis, myocarditis	Cat to dog	Mutation of feline pan-leukopenia virus
1986	BSE agent	Bovine spongiform encephalopathy	Sheep to cattle to human	Changes in cattle rendering process
1988	Phocid distemper virus 1	Fatal respiratory disease (distemper)	Harp seal to harbor seal	Migration of harp seals due to climatic conditions.
	Phocid distemper virus 2	Fatal respiratory disease (distemper)	Dog to Siberian seal	Contact with terrestrial animals (dogs)
1990	Lelystad virus	Porcine reproductive/ respiratory syndrome (PRRS)	Rodent to swine	?Mutation of rodent virus
1994	Equine morbilli-virus	Acute respiratory distress syndrome (ERDS)	Bat (flying fox) to horse to human	?Mutation of bat virus

of medical microbiology and virology and has been extended ever since. The base has been built by laboratory and field investigation, and by the scientific genius, creativity, determination, organizational skills, and other qualities of the first microbiologists and virologists. The base has been built with great breadth and with a fundamental comparative perspective that reflects the fact that the first microbiologists and virologists were all naturalists at heart. The base has been built from a clear motive of bettering the human condition, globally.

What do the initial phases in the "discovery-to-control continuum" look like? The important early role in the continuum of people outside the citadel (the citadel defined as the international community of exotic disease investigators and public health officials) must be recognized—the key players are local clinicians, pathologists (including medical examiners and forensic pathologists), and public health officials, many of whom have not been enamored by their experiences in dealing with those inside the citadel. The important early role of primary diagnostic laboratories and the reference laboratory networks that support them must also be recognized. Additionally, the importance of focused research, aimed at determining the nature of the etiologic agent, the pathogenesis and pathophysiology of the infection it causes, and related immunologic, ecologic (including vector biology, zoonotic host biology, etc.), epidemiologic, and behavioral sciences must be recognized.

In this era of the primacy of molecular biology (and molecular microbiology and virology), it bears reminding that many of the early investigative activities surrounding the identification of a possibly emergent disease must be carried out in the field, not in the laboratory. This is the world of "shoe-leather epidemiology." It is no accident that the logo of the epidemiology program at the CDC is the outline of the sole of a shoe, with a prominent hole worn in it. In the same way, it bears reminding that there is a distinction between the search for an etiologic agent, whether bacterium, virus, protozoan or fungus, and development of diagnostic tests. Recent experiences have illustrated our continuing need for experts who can take a new isolate and turn it into practical tests for the presence of microbial/viral antigen(s), antibodies, and nucleic acids. Here, we need controlled sensitivity, specificity, reproducibility, rapidity, simplicity, and economy, and then we need proof-testing of the whole diagnostics system in the field in the setting of the disease episode at hand.

What do the intermediate phases in the "discovery-to-control continuum" look like? The continuum progresses to the general area of risk management, the area represented not by the question, "What's going on here?," but by the question, "What are we going to do about it?" This phase may include expansion of many elements: (1) policy and marketplace decisions and actions that involve the interface between government and the pharmaceutical industry; (2) technology transfer involving diagnostics development and proof testing, vaccine and drug development and proof testing, sanitation and vector control, and medical/veterinary care activities, and their adaptation to the circumstances of the locale where the disease is occurring; (3) commercialization, where appropriate, of diagnostics, vaccines, therapeutic agents, or provision of alternate sources in quantities needed through "nongovernmental organizations" (NGOs) or developed-country government sources; (4) training, outreach, continuing education, and public education, each requiring professional expertise and adaptation to the special circumstances of the disease locale; (5) communications, at appropriate scope and

scale, employing the technologies of the day, such as the Internet, and employing professional expertise that is so often lacking.

It is one of the worst of life lessons that risk assessment does not naturally lead to risk management. It has always been confounding that some diseases touch a public and professional nerve so that efforts to move through the phases of the continuum are well supported, while others equally important in terms of morbidity/mortality stall out. For example, investigation of the 1995 Ebola epidemic in Zaire (now the Democratic Republic of Congo) was well supported internationally (although overwhelmed by patient care needs), but many diseases, usually endemic diseases and those stemming from problems in the food and water supply, are underfunded in developed countries and not funded at all in most developing countries. For example, in the United States, with overwhelming data at hand, it was decided not to spend any money to eradicate the recently imported Asian tiger mosquito, *Aedes albopictus*, even though it is a proven vector of dengue, California encephalitis and yellow fever. Recently, we have seen all vector-borne disease control budgets in crisis.

There is also a life lesson in seeing the arbitrariness in public expectations for success in dealing with emerging disease outbreaks. There is often what I call the "One Riot, One Ranger" level of public expectation. [In the early days of Texas, law enforcement was in the hands of a few Texas Rangers—no matter what the problem, whether it be a bank robbery involving one outlaw or a riot involving hundreds of people, one Ranger was sent in to resolve it.] No matter what the disease outbreak looks like at first, one state or federal epidemiologist is sent in to resolve it. The public expectation is that this person will succeed, because the public has been led to believe that disease outbreaks are fundamentally simple events—the "food poisoning at the picnic" metaphor. It is also the public expectation that if the "first responder" does not succeed, there will always be opportunity to expand the response later. The idea that some diseases move faster than this does not enter the public's mind. Beyond this, all too often there has followed a public sense that if the expanded response does not work, then, "well, we'll just have an epidemic." For example, in 1991, the Pan American Health Organization (PAHO) sent some resources to Peru to deal with the first cholera introduction into the western hemisphere in 75 years. One million cases later, 9000 deaths later, one might wish that the initial response had been more vigorous. Alas, there never is a chance to reconsider, to start over, and the public has rising expectations that disease control officials should get it right the first time.

In some cases, public expectation for disease control is absolute. As an example, consider what a foot-and-mouth disease (FMD) introduction into the United States might be like. A model of an introduction was constructed by M. W. Miller, based on the 1967–68 FMD epidemic in the United Kingdom. The model showed that decisions about appropriate resource allocation and actions would have to be made very quickly, within days—if everything were not done right, within four weeks the epidemic would be uncontrollable. Other studies have indicated that the smallest FMD episode in the United States, say one represented by the discovery of virus on one farm, would cost more than $1 billion. With FMD, the concerned public (livestock farmers and rural people whose employment depends upon livestock industries) has a very high level of expectation that everything would be done right—this public believes that its tax money has paid for standby resources to deal with an episode, no matter what. This public would expect that if necessary the National Guard and the Army would be called

out, that all government resources would be used to deal with the problem. There are several human viruses that have the same transmissibility characteristics (reproductive rate, Ro) as FMD virus. Most happen to be those controlled by childhood vaccination programs, but other human viruses could emerge with transmissibility characteristics like FMD viruses, so the need for systems for flexible allocation and delivery of disease control resources is an important issue. In this regard, the public will have to understand better that resources to deal with any eventuality will cost much more than present allocations to national response agencies, and that additional funds will also have to be lodged in international agencies like the World Health Organization (WHO) if we are ever to be able to deliver appropriate global response.

As one goes further and further along the "discovery-to-control continuum," intervention gets tougher and tougher. Frustration often occurs at intermediate points along the continuum as administrators and politicians drag their feet in regard to resource allocation ("No one ever says 'no'—it's just that nothing happens."). This frustration, in turn, drives scientists back to their laboratories, to the world of research, to the front end of the continuum. Younger scientists, particularly, develop an abhorrence for the harsh political world of risk management, even though this is the arena wherein their discoveries must prove themselves.

More and more expensive, specialized expertise and resources come into play in the final phases of the continuum:

1. Public health systems (including rapid case reporting systems, ongoing surveillance systems, vital records and disease registers, additional staffing and staff support, logistical support such as facilities, equipment, supplies and transport, legislation and regulation development, and senior management, administration, and leadership)
2. Special clinical systems (including isolation of cases by quarantine [usually requiring legal authorization and enforcement] and/or strict barrier nursing, patient care and management, and improvement in the general health of the population at risk)
3. Specialist and public infrastructure systems (including sanitation and sewerage, safe food and water supplies, environmental control, and reservoir host and vector control)

One last comment on the continuum: in recent years, it has seemed inevitable that research has been stopped when the goal of control of a given disease has come into sight. For example, measles research, globally, virtually stopped after the attenuated live-virus vaccine came into use 40 years ago, and arbovirus research, globally, is today minuscule relative to its scope and scale 20 years ago. The over-riding issue here is global funding—it has dried up in regard to the need to continue research to deal with the new tricks of microorganisms and viruses.

Applying the "discovery-to-control continuum" to bioterrorism and national and international security

The "discovery-to-control continuum," as described, has been meant to pertain to natural threats, threats stemming from natural changes in microbial or viral agents, *per*

se, or from innocent ecologic, environmental, behavioral, societal, or commercial perturbations leading to disease emergence. Nevertheless, since a framework is needed to discuss "unnatural threats," and since it is a practical necessity to integrate all elements of our national capacity to identify, characterize, quantify, and respond to microbial and viral threats, it may be of interest to test the appropriateness of the continuum in regard to the threat of bioterrorism.

First, the elements of the continuum would likely be the same as in a natural threat episode regarding discovery, the recognition of a disease in a setting suspicious of bioterroristic activity. Initially, responders and local clinicians, pathologists and public health officials would most likely be the first to recognize an unusual disease episode. At first, it is unlikely that bioterrorism would be suspected—a terrorist-caused infectious disease episode would not present the unique time/place characteristics as other kinds of terroristic actions. It seems likely that the usual civilian field-based epidemiologic investigation and laboratory-based etiologic investigation would follow, again because it is unlikely that bioterrorism would be suspected. Then, as the nature of the microorganism or virus was discovered, either because of unique clinical characteristics or more likely because of work in the primary laboratory or the state or national reference laboratory system, the agencies concerned with national and international security would take over. At this point, quite a different continuum would be set into motion, but with the same purpose, that is disease control and prevention (response against the terrorist agency, once identified, is not part of the continuum in this model).

Given the character of infectious agents, including all those that have ever been considered as bioterrorism threats, a major focus of national security and law enforcement agencies would have to be microbial or viral source elimination, perimeter isolation, confinement and quarantine of exposed people and animals, area decontamination, and other area-based activities (although with human movement, with fomite transport and with vector-borne agents area confinement would not be simple). Seemingly, many of the professional activities called for are quite specialized and not readily available in any appropriate scale in the public health agencies. The question is whether they are available from the military or other national security agencies. This question must be begged in regard to, for example, supplies, equipment, on site facilities, transport and other logistics, staffing and staffing support, management and administration systems, trusted knowledgeable leadership, legislative and regulatory authority and law enforcement, special surveillance resources, case reporting, vital records, disease register resources, training and professional clinical outreach resources, public education resources, specialized patient care resources, and technology transfer.

The metaphor for envisioning a national or even international bioterrorism response system is the national response system for dealing with a terrorist bomb or an earthquake or hurricane. Yet, responding to a bioterrorism episode is different enough, especially in regard to the need for specialized microbiological and virological expertise, equipment, supplies and logistics, that it would seem necessary to play out separate "war games" to help understand the question of preparedness. Since the answer to the question of preparedness may in part be classified, it is not clear how much further this matter may be pursued in the open literature, or through the usual civilian channels discussed above. How can the concerned public be assured that national security and

law enforcement agencies are "up-to-speed"? How can the concerned public be assured that there is appropriate interagency cooperation, communication, and collaboration in regard to dealing with bioterrorism threats as there is in dealing with natural emerging disease threats? How can the concerned public be assured that there is an appropriate interagency administrative and management system in place, with appropriate leadership identified, to deal with bioterrorism threats? Three examples point to present difficulties in answering these questions:

1. Unclassified descriptions of "war games" involving exotic pathogens have not been encouraging in regard to any sense of preparedness. In 1989, Col. Llewellyn Letgers, U.S. Army, organized an exotic disease response exercise at the annual meeting of the American Society of Tropical Medicine and Hygiene. Knowledgeable "actors" representing the leadership of all involved federal agencies dealt with a mysterious hemorrhagic fever outbreak, following a realistic script and timeline. In the end, it seemed quite clear that the United States has no interagency "team" or ready-to-go framework for dealing with a large exotic disease outbreak. (Garrett 1990)

2. Interagency planning to deal with natural emerging disease episodes has not been followed by appropriate federal funding. In 1995, the report of the NSTC Committee on International Science, Engineering, and Technology (CISET), entitled "Global Microbial threats in the 1990s" was published. It represented the cooperative input of 17 federal agencies and called for improved global surveillance, improved global alert/response capability, increased targeted research and training, and an enhanced national collaboration and communication system. The report of the committee included the statement: ". . . an effective global disease surveillance and response network will enable the United States to respond quickly and effectively in the event of terrorist incidents involving biological or chemical agents. The experience gained in controlling naturally occurring microbes will enhance our ability to cope with a biological warfare agent, should the need arise. The release of nerve gas in the Tokyo subway system in March 1995 has underscored our need to be well prepared to counteract deliberate attempts to undermine human health."(NSTC/CISET 1995) At the time of this writing, late in 1996, there was little evidence that the CISET proposal would be appropriately funded.

3. Attempts to provide centralized national leadership to deal with bioterrorism and aspects of chemical, biological and nuclear threats have been stymied by turf and primacy issues among federal national security agencies. In 1996, the Nunn, Lugar, et al., act "Defense Against Weapons of Mass Destruction" (U.S. Senate Bill 1745, title XIII), outlined in excellent fashion the nature of the non-military target risks faced by the United States from rogue governments and terrorist movements. The bill noted post–Cold War changes that accentuate the risks (small, difficult to detect weapons; simple transport systems including commercial cargo and FedEx) and noted the inadequacy of our present state of preparation, training, coordination (local, state, federal, interagency) and

sharing of expertise and capabilities. The bill passed, with funding authorized but not appropriated, but only after the role of a national coordinator was minimized. Public discussion suggested that it was national security and law enforcement agencies that preferred a less integrated organization.

Notwithstanding these difficulties in developing and funding a federal interagency action arm to deal with emerging disease risks and similar risks posed by bioterrorism, there has been much recent progress in advancing surveillance and investigative programs: the National Center for Infectious Diseases (NCID) at the CDC has received funding for the first elements of a national emerging infectious disease network. Some progress is also being made in advancing an international network under the auspices of the WHO. The final element, the keystone of the whole edifice, is the research base for all of these programs—much research expertise in emerging infectious diseases is lodged at the CDC and much expertise in biological warfare defense is lodged at the U.S. Army's Research Institute for Infectious Diseases (USAMRIID). However, the largest part of the pertinent research base is lodged in academic institutions and biomedical research institutes throughout the country. The same is the case in other developed countries. The National Institutes of Health, through its extramural programs, has a long tradition in tying together the many disparate parts of the biomedical research community of the country, and recently much progress has been made in tying together academia and the NCID/CDC. Where is the basic research base to support bioterrorism risk management activities in the national security and law enforcement agencies other than the U.S. Army? Should these agencies rely on interagency cooperation or ad hoc consultants? How is the concerned public to know whether the overall system to deal with bioterrorism is working? Surely, recognizing the value of the flow of information and expertise between surveillance, diagnostics, related biomedical research, and other phases of the "discovery-to-control continuum" requires a tightly integrated national system, with clear authority and leadership, and with financial resources so as to be able to deal very quickly with any bioterrorism threat.

Conclusions

In an editorial on May 12, 1995, the *New York Times* asked, "So, who will be the world's public health doctor?" It seems that many institutions, including the CDC, the NSTC/CISET and the WHO, now have the answer to this question. The answer is in the form of proposals and funding requests to expand (1) a global disease surveillance system, (2) a global diagnostics system, (3) a global integral research base, (4) a global communications system, (5) a global technology transfer system, (6) a global emergency response system, (7) a global training program, and (8) a global stable-funding base. In some cases, these proposals have been condensed into a mantra—"surveillance, diagnostics, infrastructure"—but this over-simplification does not seem helpful. In any case, little new funding has been committed to date and, in my view, more, much more, public explanation of the importance of the "global emerging infectious disease network" is needed if this is to change. In some cases, it seems that senior political staff officers are saying, "Those fellows in the citadel just want more money to do their thing, to support their personal adventures," or "If things are so bad, then how did those

fellows crack the hantavirus pulmonary syndrome episode in the United States in a week and how did they resolve the Ebola hemorrhagic fever episode in Kikwit in a month?"

It seems clear that the bottom line issue is funding and our failure to communicate the need for funding. Today, many activities involving disease control are at risk because of inadequate funding—this is leading to failed infrastructure, failed intellectual base, failed training of the next generation of specialists, etc. In the case of the emerging infectious diseases, *per se*, failure occurs quickly when research is stopped. For example, tropical infectious disease research, nationally and globally, is today minuscule relative to its scope and scale 20 years ago. In some cases, it is not even clear who might do the focused, applied research that must underpin advances in tropical disease prevention and control. In present circumstances, where the survival of institutions is at stake, turf battles are exacerbated and competition rather than cooperation between academic institutions and government agencies ensues. This happens in contradiction to public expectations: There are clear data that the concerned public wants more disease control and intervention actions and the medical research needed to drive such actions, and there are clear data that the concerned public is willing to pay for this. Our most senior political leaders, however, have not understood or responded to this rising public expectation. How can this kind of indifference be overcome? I am not sure, but here are three ideas:

1. Develop a greatly expanded communications system, reaching up, down and across, bridging with comprehensive information the gap between (a) the rising public expectations for more disease prevention and control action and the biomedical research that must underpin it, and (b) the seeming satisfaction of political leaders with the present state of affairs.
2. Integrate the "global emerging infectious disease network" with networks focused on threats posed by livestock animal diseases, crop plant diseases, and bioterrorism and diseases pertaining to national and international security. The public should see such an overall network as having a high "benefit: cost" ratio, solving several high-priority problems in a most efficient way.
3. Integrate the national emerging infectious disease "needs list" more clearly with a comprehensive set of public health control strategies—including proven interventive approaches such as safe food and water systems, sewerage systems, vector control systems, vaccine usage systems, and primary medical care systems. The public would then see this "holistically," as an overarching national need, not just another rationale for gaining more funding for those in the citadel.

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