"The King of Terrors" Revisited: The Smallpox Vaccination Campaign and Its Lessons for Future Biopreparedness[1]

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"Smallpox was always present, filling the churchyard with corpses, tormenting with constant fear all whom it had not yet stricken, leaving on those whose lives it spared the hideous traces of its power, turning the babe into a changeling at which the mother shuddered, and making the eyes and cheeks of the betrothed maiden objects of horror to the lover."[2] In 1848, British historian T.B. Macaulay first captured the picture of the devastation smallpox wreaked on its victims, but the "King of Terrors," as it was dubbed by future president John Adams,[3] had already decimated populations in the ancient world from Greece to Egypt to China. Smallpox had no respect for authority: the earliest identified victim, Pharaoh Ramses V (d.1157 B.C.) was but the first in a long line of monarchs and rulers who succumbed, including the Hittite king Suppiluliumas I, Aztec Emperor Cuitlahuac, and Queen Mary II of England.[4] Even more catastrophic was the impact of smallpox on ordinary people — up to fifteen million Aztecs out of a total of less then thirty million, huge numbers of Native Americans, and 400,000 people per year in 18th century Europe all fell to smallpox.[5] Those who survived, often through repeated exposures, included Queen Elizabeth I, George Washington, and Abraham Lincoln. Their survival contained the secret of overcoming smallpox: living through one bout meant immunity for a lifetime.

Smallpox as a Weapon

Smallpox has figured in warfare both serendipitously and as a weapon. In the Revolutionary War, for example, the American soldiers were handicapped because of the greater immunity of the British since fewer of the colonists had been previously exposed. On June 26, 1776, John Adams wrote to his wife that "The Small Pox is ten times more terrible than Britons, Canadians and Indians together. This was the cause of our precipitate Retreat from Quebec...."[6] When George Washington heard rumors of a British plot to infect his army with smallpox, he changed from opponent to advocate of inoculation, and assembled one thousand soldiers who had survived smallpox to fight the infiltration of the disease into his ranks.[7] After 1777, Washington's troops, like the U.S. military destined for the Iraq war, were ordered to inoculate themselves, but they endured a much more dangerous vaccination than the one used today.

Smallpox has a long tradition as a stealth weapon. A notorious example of early biological warfare occurred during the wars for control of land in colonial America. Jeffrey Amherst suggested "sending Small Pox among those Disaffected Tribes of Indians."[8] Colonel Henry Bouquet, the top officer in western Pennsylvania, vowed to "try to inoculate the ______ with Some Blankets that may fall in their Hands, and take care not to get the disease myself."[9] Without having ever been inoculated, the Native Americans succumbed completely to the disease, transmitted merely by smallpox fomites (dried scabs and pus) on blankets.

Biological weapons, particularly diseases as communicable as smallpox, are perfectly suited to terrorist acts. Biological weapons are invisible; they spread fear; they move inexorably once initiated so that one infection can lead to the decimation of whole populations. U.S. scientists first alerted the government to the potential danger of biological weapons in 1937, as concern about Germany and Japan was rising. In response to these anxieties, Franklin Roosevelt authorized the production of biological weapons such as anthrax and botulinum toxin, a program that was

Journal of Law, Medicine & Ethics, 31 (2003): 580–589.

terminated in 1969 by President Nixon.[10]

Smallpox's potency only has increased with modern transportation and mobility. D.A. Henderson, who tracked and extinguished smallpox all over the globe, understands its potency as well as anyone: "If smallpox were to appear anywhere in the world today, the way airplane travel is now, about six weeks would be enough time to seed cases around the world. Dropping an atomic bomb would cause casualties in a specific area, but dropping smallpox could engulf the world."[11]

Origins of Smallpox Vaccine

The earliest vaccine attempt *variolation* — infecting the patient with a mild case of smallpox — was introduced in the ancient world, and used through the 18th century. Immunization with live smallpox pustules invariably triggered days of fever and nausea, at the end of which the patient was either immune or dead. Catherine the Great set an example for the citizens of Russia when she had herself inoculated in 1768 by the renowned expert in *variolation*, Dr. Thomas Dimsdale. "My objective was, through my example, to save from death, the multitude of my subjects who, not knowing the value of this technique, frightened of it, were left in danger."[12] As would many subsequent leaders, including President George W. Bush, Catherine the Great sought to inspire her people to endure the risk and pain of inoculation. Catherine's example not only persuaded her citizens to seek *variolation* — clinics were established in Moscow, St. Petersburg, and in the provinces, including even Siberia — but through Voltaire's enthusiastic endorsement of her leadership, word about the benefits of *variolation* traveled throughout western Europe.[13]

At around the same time the earliest settlers in the New World learned of *variolation* through different means. Cotton Mather's slave Onesimus brought knowledge of this method of immunization from Africa. But Mather's attempts to promote it among the colonists failed for two principle reasons: 1) fears of contamination from the *variola*; 2) resistance to tampering with nature by thwarting smallpox.[14] The discomfort of the process also probably played a part; John Adams attributed his toothlessness in old age to the trauma of the smallpox inoculation he endured in 1764.[15]

Today's immunization descends directly from the technique pioneered by Dr. Edward Jenner in 1796.[16] Observing that farmhands (usually milk maids) did not contract smallpox from exposure to a much milder form of ortho pox virus now known as cow pox, Dr. Jenner devised a less toxic alternative to *variolation*. He infected his patients with pustules from cowpox, which protected against smallpox without the risks of using the real thing. He coined the term vaccine–from the Latin *vace*, meaning cow. In 1881, Louis Pasteur took the term one step further, and coined "vaccination" to describe all immunizing injections.[17]

Eradication ... Or So It Appeared

Less than one hundred years later, smallpox had been eradicated, a triumph of global public health. The last naturally generated case occurred in Somalia in 1977, ten years after the World Health Organization launched a worldwide eradication program. But eradication did not mean extinction. After a worldwide debate about whether or not to destroy all traces of the *variola* virus, the decision was made to preserve and confine it to two repositories — the Institute of Virus Preparations in Moscow, Russia, and the Center for Disease Control and Prevention (CDC) in Atlanta.

Containment seemed a viable solution until Soviet defector Vladimir Pasechnik unveiled in 1989 the Soviet strategic biological weapons program. In 1992, defector Kanatjan Alibekov (Ken Alibek), the former first deputy chief of the Soviet biological warfare program *Biopreparat*, sketched a complete and terrifying picture of the comprehensive Soviet program, and of its stores of smallpox and plague. Speculation about the dispersal of biological weapons stores following the dissolution of the Soviet Union haunted the circles in Britain and the U.S. who had learned about the Soviet biological weapons program. By 1998, D.A. Henderson, who had led the successful WHO campaign to extinguish smallpox, realized that he had to prepare to take on his old nemesis, but in a new guise: as Director of the newly founded Johns Hopkins University Center for Civilian Biodefense Strategies.[18]

In 1998, awareness of the potential danger of smallpox was just dawning. Many who did not have D.A. Henderson's knowledge dismissed the danger as improbable. While I served as U.S. Ambassador to the Netherlands (1998–2001), a delegation from Washington visited the Embassy in March 1999 to brief me and others on the threat of anthrax. My question about the potential threat of smallpox was met with a mincing glare, implying that my query was preposterous. But others did not think so. After discussions with Dr. Craig Venter in late December 1998 about the potential threat of biological weapons, specifically smallpox, President Clinton stepped up awareness of the issue through cabinet meetings and speeches.[19] Following a June 2001 "tabletop" exercise of a bioterrorism attack, "Dark Winter," which revealed weaknesses in the U.S. response to a bioterrorism event, steps were taken to augment the CDC's supply of *vaccinia* vaccine.[20] Acambis Plc and Baxter Healthcare won a $428 million contract, pushing the total cost of building up the vaccine supply to more than $860 million, more than triple the original cost of eradicating smallpox in the 1970s.

Dark Winter and Its Lessons

The "Dark Winter" exercise exposed deficiencies at all levels in the response to a simulated smallpox attack. Replenishing the supply of *vaccinia* vaccine to a level sufficient to immunize the U.S. population was an important first step, but the "Dark Winter" scenario revealed other systemic shortfalls which will require more complex and far-reaching solutions. During the exercise even experienced hands such as participants former Georgia Senator Sam Nunn (who played the role of the President) and Former CIA Director James Woolsey found themselves at a loss to evaluate the situation and make critical decisions.[21] Before the House Government Reform Committee, Subcommittee on National Security, Veterans Affairs and International Relations on July 23, 2001, Sam Nunn made the following statement:

> I was honored to play the part of the President in the exercise Dark Winter...You often don't know what you don't know until you've been tested. And it's a lucky thing for the United States that — as the emergency broadcast network used to say: 'this is just a test, this is not a real emergency.' But Mr. Chairman, our lack of preparation is a real emergency.[22]

"Dark Winter" highlighted the fact that coping with a bioterrorist attack requires multi-disciplinary knowledge and a complex decision-making ability. In an event of bioterrorism, the enemy must be met not with military aggression but with health and infectious disease facilities, as well as all of the other civil affairs units needed to keep food, electricity and water supplies up to standard and to maintain transportation systems while preventing them from becoming disease vectors. In addition, critical decisions must be made about mobility and containment. Curtailing movement potentially infringes on basic civil liberties and aggravates the secondary economic costs of an epidemic, but isolation and containment may be essential to preventing further infection. Surge capacity proved to be a problem in "Dark Winter." Medical facilities were flooded with people; up to one hundred times the number actually infected demanded care, convinced they had caught the disease.[23] This aspect of the simulation presaged the anthrax scares of October 2001, when 22 people were actually infected but tens of thousands turned up at health facilities asking for treatment and 35,000 were given prescriptions for antibiotics, even when their risk of infection by anthrax was miniscule.

In sum, "Dark Winter" demonstrated the inadequacy of a military/civilian defense response to a bioterrorist attack, and the need to develop new systems and skill sets to cope with such an eventuality. Designating the CDC (Centers for Disease Control) the lead agency in the campaign to build public health capacity to respond to bioterrorism represented recognition of the combination of health and security expertise required to meet this threat. The National SVProgram (smallpox vaccination campaign) would further illuminate the complexity of a bioterrorist challenge and the need for an organic and systemic strategy to prevent and respond to such an event.

The 2002–2003 National Smallpox Vaccination Program and its Lessons

In December of 2002, President Bush launched a multi-phased smallpox vaccination campaign with the ambitious goal of vaccinating 450,000 "first responders," health care workers — the proverbial front line of defense against bioterrorism — in the first phase (by February 24, 2003), to be followed by up to ten million first responder vaccines in the second phase. The administration's strategy planned for containing the disease by the health care workers and 'first responders' vaccinating those infected and potentially exposed during the early incubation period — 7 to 17 days before contagion and disease symptoms set in.[24]

Despite its logic, the smallpox vaccination program has failed to achieve its goals.[25] By June only 36,000 first responders had been vaccinated, a mere 12.5 percent of the original goal of 450,000. Why? A combination of societal, psychological, political, and medical problems contributed to the ultimate demise of the smallpox vaccination campaign. The lessons learned from this first post 9/11 anti-bioterrorist initiative underscore the challenges of an effective response to this new, inscrutable enemy.

When President Bush announced the smallpox vaccination campaign on December 13, 2003, he expressed his concern for the many uncertainties.

> I understand that many first responders will have questions before deciding whether to be vaccinated. We will make sure they have the medical advice they need to make an informed decision. Smallpox is a serious disease and we know that our enemies are trying to inflict serious harm. Yet, there is no evidence that smallpox immediately threatens this country.[26]

For potential vaccination candidates and for health care facilities, weighing the different sets of facts in order to make decisions about whether or not to take or to offer the vaccine was complicated by the many unknowns surrounding smallpox and vaccinia.

Smallpox and other biological acts of terrorism resist a traditional cost/benefit evaluation.[27] The inherent contradiction between the gravity of the threat of smallpox and the lack of evidence of any imminent danger complicates decision-making about the vaccine. Two others factors — a flood of unanalyzed information about potential adverse effects and lack of compensation for those who suffered them — further contributed to the disappointing turnout for the vaccine.

Following in the footsteps of Catherine the Great, the President himself underwent immunization in order to inspire others. Ultimately, however, his leadership and that of the Secretary of Health and Human Services, Tommy Thompson, as well as that shown by local officials such as Dr. Michael Richardson in Washington D.C. was not sufficient to quell fears about adverse effects about the vaccine and the economic uncertainties associated with a personal decision to be vaccinated. Thanks to the transparency of the CDC, information about potential adverse effects was readily available, if somewhat daunting in volume for the layman.[28] But given the uncertainty of the threat as well as the unknowns about adverse effects, how could the average health care worker or "first responder" make his or her choice? Was it worth risking a mild reaction that would absent him or her from three to four days' work, or, even worse, a potentially serious, even deadly reaction? "In 1947, when smallpox was last diagnosed in the U.S., 6.5 million New Yorkers were vaccinated in a matter of days, with only two vaccine related deaths resulting from the campaign. In contrast, however, smallpox had been detected at that time: the threat was tangible, albeit more benign. People still had first or second hand knowledge of the horrors of smallpox, in contrast to the present.

In addition, other factors have changed attitudes towards the vaccine, even in this non-epidemic situation. The overall risk has increased compared to the era when smallpox vaccination was routine, because of the significantly higher vulnerability in the population, for example, persons who are immune compromised (e.g., HIV/AIDS or chemotherapy patients) or have skin conditions (e.g., eczema). Secondly, people have become increasingly risk averse, particularly given the increased knowledge about potential harmful effects. Health care workers are concerned not only about their own risk, but also about the risk to close contacts, including patients and family members. They have also been unwilling to risk illness or fatigue that will force them to miss work. Absences from work affect the financial well-being of health care workers and make it more difficult for overstretched hospitals to function effectively.

After just two months, by March of 2003, the Administration's vaccination program stalled in the face of multiple concerns: uncertainty about the probability of a smallpox attack, adverse effects of the vaccine, economic costs of implementing the program, and lost days of work due to vaccine-induced illness. The numbers told the story: only 29,584 civilian health workers out of the target 450,000 had been vaccinated by the 28th of March, less than 7 percent of the administration's goal. Not only did individual health care workers forego the vaccine, but hospitals and even states suspended smallpox vaccination initiatives because of the occurrence of adverse effects, in particular cardiac events possibly related to vaccination.

Effects from the smallpox vaccine range from the fever, headache, or minor aches and pains that require two to four days to recuperate, to dermatological conditions such as post-vaccine encephalitis, to heart-related problems such as the swelling of the heart known as myocarditis.[29] The military population provides the best gauge of the likelihood of these problems. Out of a population of 350,000 immunized by late March, about one quarter had missed several days work to recuperate from minor side effects, while about ten had suffered heart-related problems, specifically a swelling of the heart known as myocarditis.[30] The greatest concern surrounds the two military and two civilian personnel who died of heart complications following vaccination, but experts are divided about the potential impact of the vaccine as compared to factors in the patients' conditions, such as medical history, smoking history or obesity.[31] There is agreement, however, that more extensive screening for pre-existing heart conditions should become a pre-requisite for candidates for vaccination.

The combination of adverse effects with no compensatory plan for those who suffered them dealt the smallpox campaign a near-death blow in March. Union leaders protested on behalf of their members, and as the numbers of volunteers dropped, the Congress debated introducing compensation plans. An administration-backed package based on a bill introduced by Senator Judd Gregg (R.-N.H.) ultimately passed in April. Although experts on both sides of the political aisle argued in favor of a bill with greater scientific accuracy, specifically one that took as its model the National Vaccine Injury Compensation Program rather than the Public Safety Officers Benefit Program on which the Judd bill was based, all agreed that some form of compensation package was essential.[32] Unfortunately, the late passage of the compensation package after considerable controversy did not significantly augment the numbers of volunteers, and the smallpox vaccination campaign continued to falter. From the perspective of the vaccinees, the seeds of doubt and distrust had been sown too deeply for the compensation program to make a significant difference. Furthermore, by April the attention of the administration and the country was focused on the Iraq war. Ironically, the active conflict seemed to diminish the priority of addressing the smallpox threat.

The question of compensation for adverse effects raises larger issues of trust between a government and its citizens. As it was initially announced, the smallpox vaccination campaign asked citizens to put themselves and potentially their families at risk for the good of their country.[33] In other words individuals were asked to bear the burden of biopreparedness for the larger population. As the administration and legislators recognized, this was f undamentally unfair. While citizens of a democracy are expected to contribute to the public good, and even to make sacrifices for the public good, the fundamental premise of a government responsible to its citizens supposes that the government will support those citizens equitably. In the case of the smallpox vaccination campaign, compensation for adverse effects, whether a couple of days absent from work or hospitalization seemed a" legitimate expectation" on the part of the volunteer.[34]

One of the new challenges posed by bioterroism will be to calibrate the equation of government and citizen responsibility and obligation in addressing this threat. The many unknowns surrounding bioterrorism — who, what, when, where, how, how much — make it even more difficult to arrive at an equitable equation of the rights and sacrifices of the individual for the public good.[35] It was, therefore, all the more important that in this first 'test case', the smallpox vaccination campaign, both citizens and government fulfill their mutual obligations.

In addition to a healthy relationship of trust between a government and its citizens, another essential element for an effective Biopreparedness program is a strong, effective public health system. Although at first it appeared that the smallpox preparedness program would provide a much-needed shot in the arm (as it were), it has instead it has taxed the neglected public health system beyond its limits. In the absence of adequate federal funding, the smallpox vaccination program has impeded other essential public health programs to combat bioterrorism and naturally occurring health threats.[36]

A value of the smallpox program is that it has pointed up shortfalls in the public health system, and has necessitated strengthening in particular areas, such as communication and information. John Agwunobi, Florida's secretary of health, whose state has been among the most successful in implementing the smallpox vaccination program, noted the value of communicating openly and comprehensively the pros and cons of the vaccine to health care workers. Not only have nearly 4,000 health care workers been vaccinated, but also the information network of the public health infrastructure has been strengthened.[37]

Lessons Learned: Where Do We Go From Here?

Thanks to the smallpox vaccination program administered by HHS through the lead of the CDC, the nation now is much better prepared to meet a potential smallpox attack. Sufficient supplies of the vaccine exist for the population, and significant progress has been made in vaccinating the 'first responders' so that they can meet the needs of the population as a whole. The failure of the Program to meet its goals reveals both specific problems with the vaccination campaign as well as much broader issues. These problems can be summarized as follows: 1)communication of information — praiseworthy openness, but too much, too fast, often conflicting; 2) underestimation of the financial and systemic cost of vaccine; 3) erosion of trust due to lack of compensation; 4) uneven distribution of vaccines, so some states and localities were better prepared than others.

The critical question raised by the smallpox vaccination campaign is whether the number of vaccines is the most effective or valuable measure of biopreparedness. The most important lesson learned from the smallpox campaign is the necessity of addressing biopreparedness systemically, through strengthening the public health infrastructure and through improved communication and information networks.

In addition, scientific research plays a critical role. Work on an improved vaccine with fewer adverse effects, Modified Vaccinia Ankara, should be accelerated. For now, more research into the current vaccine and its effects is needed in order to eliminate people with predispositions that will endanger them. Eczema and heart conditions are known factors that precipitate adverse effects, but are there more? More research into the new science of genetic risk identification would enable those with elevated risks to choose to quarantine themselves when necessary in lieu of dangerous exposure to the vaccine.

The experience of the smallpox vaccination campaign points the way to a comprehensive national biopreparedness program. The key features of such a system are outlined below.

Biopreparedness and Communities

The shortcomings of the National Smallpox Vaccination Program demonstrated the immediate and compelling need to understand and address biopreparedness and homeland security risks at all levels of government, throughout American society, and the world. A robust preparedness infrastructure at the Federal level with holes in preparedness infrastructures at the local level will only provide convenient targets for would-be terrorists. It can also be argued with substantial evidence from the 2003 smallpox vaccination program, the 2002 DC sniper shooting, the 2001 anthrax attacks, and September 11, 2001 that the decisions made by citizens and their communities have a vital role to play in the preparedness continuum.

Understanding the various dimensions of preparedness and responses needed for different types of biological threats in the broader context of homeland security and emerging diseases will yield dividends not only in terms of biosecurity and short-term reductions in morbidity and mortality, but also in strengthening communities and public health to face new types of challenges in our rapidly changing global environment. Communities that take seriously the development of new assessment and communication capabilities will improve their abilities to respond, and govern effectively in the heated moments of unforeseen challenges.

Another critical element of preparedness is investment in new public health infrastructure. Yet, this investment should not be made at the expense of the commitment to the wide variety of everyday public health services (e.g., material and child health programs, vaccinations, health education, epidemiology, sanitation, food safety, water systems, environmental health, health policy, behavioral health, prevention, community medicine). Rather a strong public health system that meets its communities' needs every day is the best defense against a terrorist attack.

Thoroughly understanding our present and emerging vulnerabilities can be achieved through validated assessments of our state of readiness. Comprehensive analysis of community-level preparedness at the state and national level is the first step to building an effective response to both anticipated and unanticipated threats. In other words, "you cannot know where you are going until you know where you are."

Risk Assessment and Communication

Whether preparedness is perceived as a function of government alone or is perceived in the broader light of emerging participatory governance (e.g., as a part of citizen-centric democracy within the eGov movement), the ability to assess risk, communicate, and take responsive action to reduce threats and vulnerabilities is essential to biodefense and homeland security. Elements of a potential solution are described below in the form of a National Biopreparedness Program, as a natural extension of the lessons learned from the identified shortcomings of the National Smallpox Vaccination Program. The proposed National Biopreparedness Program will require both the creation of a human infrastructure and an information infrastructure to ensure verifiable preparedness in every community throughout the country. Immediate creation of high priority and representative test sites (e.g., National Capital Region, combination of urban and rural counties in the East, suburban and urban counties in western regions, a Midwestern state) is needed to scope the necessary human infrastructure, validate the essential biodefense information infrastructure components, and to evaluate the synergistic impacts a robust biopreparedness program and infrastructure may have on participating communities, their citizens, and all levels of government. The components should be developed as self-replicating, interoperable toolset elements that enable rapid national distribution of standardized, yet locally customizable, community infrastructures.

For the human infrastructure and biodefense information system described below, legal issues and public policy concerns also come into play. For example, considerations of privacy must be balanced with assurances of broad participation while providing protections against malevolent use of sensitive systems. Critical decisions must be made regarding the definitions of authority. In times of crisis, tradeoffs may be made regarding resource allocation, priority of response. How will issues of malfeasance be managed regarding key decision-makers and responders when things do not go well in high risk, low trust environments? Substantial participation by interdisciplinary medical/legal and policy experts is essential to help ensure the viability of biopreparedness and response.

Human Infrastructure

An effective National Biopreparedness Program stemming from and encompassing the National Smallpox Vaccination Program would focus on rapidly building out verifiable systems of biodefense at the community level, linked to state and federal decision and supply nexuses. The National Biopreparedness Program requires a broad coalition of players throughout the nation, and, in fact, throughout the world, given the increasingly global nature of markets, transportation, networks, communication, and the rapid global movement of individuals, resources and ideas. True biopreparedness will require states, local communities, businesses, universities, professional groups, nonprofits and average citizens to play their part along with the Federal government. Legal and public policy professionals will be required to define key parameters regarding these emerging systems.

The first task is to develop and approve taxonomy (i.e., elements and interrelationships between elements) of the biopreparedness infrastructure. In association with the taxonomy, criteria, benchmarks, and thresholds enabling validation and verification of biopreparedness assessments, plans, and monitoring systems must be elucidated. Organizations with demonstrated core competencies in specific areas of the infrastructure would be encouraged to cooperate in planning efforts and compete for funds targeted at rapid development of the most critical elements of the infrastructure.

The National Biopreparedness Program (NBP) should be jointly mandated and evaluated by the Secretaries of the Department of Homeland Security (DHS) and the Department of Health and Human Services (DHHS). Congress should authorize legislation supporting the ongoing efforts of the NBP. Sufficient funds must be appropriated to enable its swift and effective establishment and ongoing operation. Where appropriate, dual use infrastructure functionality must be defined and encouraged in order to shift a portion of the financial responsibilities for maintaining the infrastructure to the private sector.

As the level of national biopreparedness reaches an acceptable level of standardization and validated effectiveness, the tools and methodologies for global biopreparedness should be shared with overseas communities and nation states, in conjunction with international organizations worldwide. Ultimately, biopreparedness requires the development of new organizational structures throughout diverse societies and sub-societal elements within and beyond the borders of the United States. It will require the training of traditional health care workers, emergency management personnel and other first responders at home and abroad. In addition, new work processes, roles and responsibilities will emerge and be codified as biopreparedness becomes an essential part of systems for sustainable security in the United States and globally.

These new systems must acknowledge and address the fact that a virus (e.g., West Nile Virus, the SARS coronavirus, smallpox), in a human host or in a vector like a goose, a mosquito, or a genetically modified plant protein, can easily travel or be transported across national boundaries and be propagated internationally within a few week's or a few year's time — depending upon the nature of the agent, vector, or weapon delivery system. This relatively new social realization speaks to the need for a global biodefense information system to protect America's own interests at home and abroad, while contributing to global health as well. Our efforts to protect ourselves can be developed into international product components (e.g., software, hardware, devices) similar to those listed under the Biodefense Information System below. The export of approved system elements will help provide sustainable security infrastructure to other parts of the world that are even in more disparate need of these traditional public health and security systems.

Biodefense Information Systems

As critical as the human infrastructure is to biodefense, it cannot address the growing threat without sufficient information infrastructure to help the decision-makers and responders to understand clearly the vulnerabilities, the nature of the threats, and appropriate responses to them. A biodefense information system is inherently interoperable component of the larger homeland security infrastructure. It must be designed with its subcomponents standardized to interoperate with the other components of the homeland security infrastructure and global health monitoring systems.

Given a robust National Biopreparedness Program, the biodefense information system (BIS) components would provide early examples of how other homeland security components can be constructed to be interoperable. In this spirit, the BIS would be designed to support a multi-leveled component-based architecture, which enables rapid prototyping and supports web services, distributed databases, and collaboration modules. The architecture will be compatible with and extend the recently released Federal Enterprise Architecture (FEA) Technical Reference Model Version 1.0[38] and the National Health Information Infrastructure standards.[39]

A rapid prototyping-enabled BIS toolset of self-replicating web services-based components would allow the United States to rapidly develop interoperable preparedness and response capability across all levels of government and American society. The initial interoperable components of the BIS would include (but not be limited to): 1) Risk modeling; 2) Biopreparedness assessment and automated planning; 3) Disease surveillance; 4) Detection technologies; 5) Alert systems; 6) Risk assessments; 7) Triage; 8) Referrals; 9) Risk communication; 10) Knowledge management systems; and 11) Community networks.

Risk Modeling

A risk modeling toolset for countering asymmetric warfare would describe and analyze the most critical threats from the molecular level to the economic and political dimensions of any threat. A multi-level risk modeling environment will provide all relevant data and analysis to the homeland security decision-maker in a single secure networked environment. An effective risk modeling system will address not only the physical and biological dimensions of the threat, but also the amplification of an asymmetric attack through the psychosocial dimensions of propagating terror. Special attention would be focused not only on the primary targeted victims affected by the physical attack, but also on secondary victims of terrorism, who adversely change their behavior, because of perceived risk, even when not exposed or at risk from an actual threat (e.g., anthrax). It is the changes in behavior and culture associated with the far larger population of secondary victims that often more accurately predicts the cascading social and economic effects of an asymmetric attack. Unfortunately, these critical concerns are often not considered in the traditional economic models of preparedness and response.

Biopreparedness assessment and automated planning

Biopreparedness assessments would be available to the states and local governments over the web. For example, when the DHS and HHS Secretaries need to make decisions regarding the allocation of personnel and resources in simulated (e.g., TOPOFF) or actual crises (e.g., a simultaneous Flu/SARS outbreak or anthrax attack), they would be able to identify specifically where key assets (e.g., personnel, equipment) are missing. With precise information of this kind, appropriate resources can be rapidly directed to the affected jurisdictions.

With this knowledge, federal and state employees and elected officials can act quickly to address critical issues. In some cases, this quick response may mean saving the lives of sentinel cases (e.g., first anthrax cases discovered). In the case of a community spread of SARS or smallpox, quick response with this kind of system may mean saving enormous numbers of lives and the protection of the economy and critical infrastructure.

Disease surveillance

Disease and syndromic surveillance systems (e.g., LEADERS, RODS) will provide key information early on regarding endemic disease and newly emerging suspicious symptomology and disease patterns. These systems will incorporate traditional infectious disease reports from hospitals, clinics, and doctor's office. They will also use unconventional data feeds [e.g., data from pharmacies on consumer purchases (e.g., a rapid increase in over-the-counter cough medicine sales) as well as mimetic data derived from the backend of internet portals (e.g., number of hits with reports of symptoms of high fever and respiratory symptoms, informational requests on SARS)]. In a crisis, the ability to correlate the current situation with preparedness assets and liabilities would not only help decision-makers with the crisis at hand, but also would enable them to anticipate future conditions.

Detection technologies

In addition to knowing when people are already affected, we would like to be able to look even further upstream to know when environmental conditions would favor a disease outbreak. Ideally, we would want to be able to identify pathogens in the environment before they show up as clinical symptoms. There is a need for global remote sensing systems that show when enviroclimatic conditions favor the emergence of disease vectors (e.g., West African black fly) leading to disease epidemics (e.g., river blindness from onchocerciasis). Technologies that enable the identification of a pathogen (e.g., anthrax) at choke points, such as in airliner air filtration systems or in cargo containers, are a priority. In the not too distant future, one can imagine the global tracking of disease epidemics in real time connected to a system component that is responsible for tracking movements of genetic material that may pose a natural or manmade threat.

Alert Systems

All of the data collected from the different system components must be tied to alert systems that identify any signal that exceeds normal thresholds. Alert systems would convert any high risk information (e.g., biological and chemical optrode data) to an electronic signal. These alert systems would then send a message to the decision makers and responders, such as, 'anthrax bacillus identified with 98% certainty,' in a mailroom PCR/DNA probe detector.

The data feeds from the other components of the BIS would provide highly specific enhanced alerts in contrast to the present DHS alert system. The alert systems would avoid general warnings with no geographic relevance or useful information to assist state of preparedness.

Risk Assessments

The anthrax attack of 2001 caused 22 cases of anthrax with 5 deaths and 35,000 prescriptions of antibiotics. This demonstrates how quickly communication of the presence of primary victims leads to secondary cases that have psychosomatic symptoms. The behavioral patterns associated with this condition, called MIPS (Multiple Idiopathic Physical Symptoms), can overwhelm health and response infrastructures. The public needs to be able to rapidly assess their risks of disease and exposure to pathogens on an ongoing basis. This empowers them to make better decisions regarding their risks in crises, which in turn reduces anxiety, and the economic drains of community bereavement, and infrastructure overload.

Triage

Once the individual has an assessment of high, medium, or low risk, he/she could use a validated triage system to assist the decision making in uncertain or urgent conditions. Independent of personal identifiers, the triage system would match the individual's information (e.g., current symptoms, limited medical history information, current location, travel history) to known information of known exposure data, current cases, and pathogen propagation. This pattern match would then provide triage recommendations. In the case of high risk individuals, the most general aspect of the message might be "Seek immediate medical attention." Low risk patients with psychosomatic concerns might receive a message like, "You are at low risk for anthrax exposure at the present time. Consider seeking help from your doctor or community mental health services, if you do not feel better within 48 hours." Low risk individuals with no psychogenic concerns might be provided information on prevention and self care information or with a message of no specific action is needed at the present time. Special attention would directed to time sequencing of behaviors to reduce the risk of infrastructure overload, and to avoid sending non-infected individuals into environmentally contaminated areas or potential high concentrations of infectious individuals, such as in hospital emergency rooms.

Risk Communication

The risk communication system component would contain messages that could be found through the web and other media. The messages would favor evidence-based messages over persuasion-oriented ones. Individuals would be encouraged to seek multiple-points of view, when uncertainty warrants multiple perspectives being a part of the decision-making process. Individuals would always have the ability to seek multiple perspectives and multiple sources of information with data transparency.

Community networks

Robust community networks that allow citizens and community decision makers to understand and improve the socio-ecological factors underlying health, biopreparedness and community response would greatly enhance homeland security. This fundamental local infrastructure is essential for community knowledge bases, communication, and collaborative decision-making directly serving biodefense. The community network component, primarily focused on biodefense yet allowing more generalized utility, can establish mechanisms for improving the health of the community beyond its initial homeland security focus. A metaphor for how a tool of this kind can start with a focus on defense and security — yet seeds generalized economic growth and social evolution — can be found in DARPA's work on the initial stages of the internet. This initial work on the ARPAnet, which led to the development of the internet, still provides key technical underpinnings for today's worldwide web.

If community networks with embedded biodefense information systems were developed as semi-autonomous nodes designed to survive failure of larger systems, they would also provide a resilience that centralized networks could not provide. When community networks are designed to be used for everyday functions as well as emergency functions, they have a higher probability of being used effectively in times of crisis. The dual use functionalities of community networks could have a role to play not only in protecting our democratic process from natural and man-made assaults, but could become the foundation of enabling more participatory governance at the local level to evolve our living democracy.

Conclusion

Ultimately, our greatest vulnerabilities to weapons of mass destruction and natural pathogens lie in our lack of preparedness and response capabilities at the local level. These systems must have robust local links to state, federal, and international resources and decision-makers that have a high probability of being available and used effectively during crises. At present, both expertise and information infrastructures are inadequate and unevenly distributed at both the state and the local levels. Self-replicating, web-services-based, interoperable, homeland security components would allow for rapid development of local infrastructures with fully functional biodefense information systems.

The combination of human infrastructure and biodefense information systems as established by a National Biopreparedness Program would create a complex, self adaptive system for confronting the emerging challenges of asymmetric attacks, emerging diseases, and other social crises. Biopreparedness infrastructure, if properly designed, has the potential for being used for other dual use functions that can help pay for maintaining the infrastructure with reduced government expenditures over time. This dual use functionality would enhance the resilience of local infrastructures and inspire greater participation in local governance.

The National Biodefense Program would break new ground in both human organizational processes and in the development of homeland security infrastructure. As a result, numerous legal and policy questions arise such as:

1) How should a National Biodefense Program (NBP) be governed?
2) If the NBP is to be a multi-sectoral program, who shall be the key decision makers in times of establishing preparedness, and who shall make the decisions in times of crisis?
3) Who should have access to which elements of the biodefense information system?
4) How can malevolent interests be kept from misusing the system?
5) If the system is used for forensic tracking, as well as for epidemiologic case surveillance and other broader uses, under what legal and policy frameworks can privacy and civil liberties be protected?

A challenge in building a National Biodefense Program is calibrating the balance between individual rights and the common good, and, more importantly, maintaining trust between citizens and government (local, state, and federal). Even the most technologically advanced web-based preparedness systems will require human intervention and analysis. And ultimately, it is upon that human response that our safety depends, as we construct the foundations of biodefense as a critical component of homeland security.

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