The VIGILANCE Defense

Proven systems and

By Stephen S. Morse

Last fall, when physicians diagnosed anthrax in a Florida man named Robert Stevens, they initially suspected that they were seeing a rare, natural case of the disease. The infection of a co-worker of Stevens, however, put the country on alert. Five people eventually died, but the quick recognition that the earliest anthrax infections resulted from a purposeful release of bacteria surely saved many lives: infected people were diagnosed and treated sooner, and officials isolated anthrax-tainted mail.

Federal and local governments have long considered bioterrorism a law enforcement issue. But both the anthrax episode and recent simulations of simultaneous smallpox releases in Atlanta, Philadelphia and Oklahoma City and of a plague attack on Denver highlight what perhaps should be obvious: bioterrorism is first and foremost a public health concern. For now and the foreseeable future, the first indication of a bioterror attack—as in a natural outbreak of a dangerous infectious disease—will be sick people showing up at emergency rooms rather than a high-tech device sounding an alarm that a pathogen has been released in a public place. The smallpox exercise in particular showed that the health care system is unprepared for the large numbers of people who would become sick in a worst-case scenario, not to mention the demands for attention from the "worried well," who would merely fear that they might be ill.

Regardless of whether a disease outbreak results from bioterrorism or natural causes, preparation can make the difference between a quickly contained threat and a widespread health crisis. And those who will make the most difference are the frontline defenders of the public's health: doctors, nurses and others who care for the first patients; laboratory researchers charged with determining the cause of the patients' illnesses; and officials in public health agencies charged with protecting whole populations. Disease control depends on the ability of these caregivers to recognize that something unusual and possibly dangerous is going on and to mobilize the individuals and resources that can best limit the disease's spread. It also requires having action plans in place that clearly define the roles and responsibilities of the nation's public health defense teams.

An effective early-warning system requires three elements, one of which I call "clinical recognition." The system needs physicians or other health workers who can recognize an unusual disease, who will order tests needed for a definitive diagnosis when symptoms seem atypical, and who will report such symptoms and troubling lab results to local or state departments of public health. In the first Florida case, doctors initially suspected meningitis, but thorough testing revealed the cause of the meningitis to be anthrax—half of inhalation anthrax victims also get meningitis—which Stevens's physicians dutifully reported to public health officials.

Hoping that an individual physician will connect one patient's symptoms with an outbreak, however, is unrealistic. A better approach is to train all clinicians to practice "syndromic surveillance": to actively look for and report certain syndromes, such as flu-like illnesses or rashes, that are common with potential bioterror pathogens. In most cases, lab tests will determine the cause to be a natural, familiar disease. Syndromic surveillance for flu-like illnesses should detect—no surprise—the flu, which would be valuable in itself, as pandemic flu strains are a major concern. But potential terror agents, such as pulmonary anthrax and plague acquired through inhalation, also begin with flu-like symptoms.

In addition, municipalities and states can monitor other, more subtle signs of an outbreak. Sudden increases in drug purchases at pharmacies, in workers or students calling in sick and in specific symptoms appearing at hospitals can all be tracked and can warn public health officials of the need for further investigation.

In 1993 my colleagues and I started the Program for Monitoring Emerging Diseases (ProMED), designed to promote global infectious disease surveillance and especially to look for outbreaks of novel diseases. The beginnings of a way to accomplish that goal came the next year when Jack Woodall, then of the New York State Department of Health, and I developed ProMED-mail. This open e-mail system, now administered by the International Society for Infectious Diseases, allows interested parties anywhere in the world to report clinical disease observations. E-mail is edited and evaluated for scientific validity before being sent to the entire subscriber list of 25,000 individuals, including disease experts, who can post comments and take personal action. No formal response system exists, however, although the World Health Organization does monitor ProMED-mail and other sources and has a system for notifying local representatives and recommending further

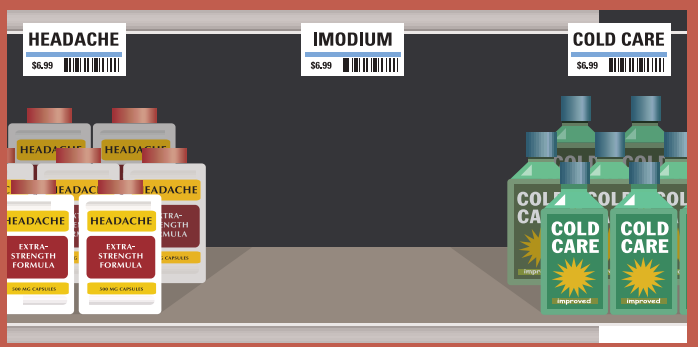
THE AUTHOR

STEPHEN S. MORSE is a virologist who in 1988 coined the term "emerging viruses" and who has led the movement to recognize the threat of emerging infectious diseases. He is director of the Center for Public Health Preparedness at the Mailman School of Public Health of Columbia University and is on the faculty of Columbia's epidemiology department. He was previously at the U.S. Department of Defense's Defense Advanced Research Projects Agency, where he co-directed the pathogen countermeasures program and directed the advanced diagnostics program.

investigation. More comprehensive worldwide surveillance, akin to worldwide weather observation, would only improve our capacity to notice any storms on the horizon and to respond in a timely fashion.

Even one case of a highly unusual disease, such as inhalation anthrax or Ebola, should trigger further epidemiological investigation (including a search for how the disease was acquired), the second key feature of the early-warning system. Unfortunately, despite the commitment and talent of people at the Centers for Disease Control and Prevention (CDC) and local health departments, the current national system is inadequate: public health is still a patchwork, with great variations in capacity from place to place.

Laboratory capacity is the third component. Labs are crucial for identifying specific disease agents in the early stages of an investigation and for determining whether a sample of material from a patient or a place contains that agent. The techniques of molecular epidemiology, which can identify individual strains of a pathogen based on molecular variations, are also invaluable for forensics. Molecular analysis could determine, for example, if a single substrain of anthrax was involved in all the 2001 infections, suggesting that the same person or group was involved.



SOLD-OUT ITEMS in pharmacies can be a sign of widespread illness. After public health officials in Milwaukee in 1993 became aware that the antidiarrheal agent Imodium had disappeared from pharmacy shelves, they discovered that the parasite *Cryptosporidium,* in tainted water, had infected some 400,000 people.

Improved disease surveillance and response capability is a necessary first step. But further improvements are needed: the public health system is increasingly challenged in a variety of emergencies, from hurricanes to heat waves, and would play a major role in the unfortunate event of chemical or radiological terrorism, in addition to bioterrorism. Public health is no less a part of the national infrastructure than are bridges and highways, and a weak link anywhere is cause for concern.

That said, there is some good news to report. Since 1999 the CDC has been developing the Laboratory Response Network for bioterrorism, to complement the regular public health laboratory system. This network includes clinical microbiology labs around the country, which perform basic diagnoses and can culture and identify some pathogens. More specialized labs exist nationally in a system of "upward referral." A low-level lab would send unresolved or suspicious samples up the ladder to those better equipped to examine unusual materials. The ladder's highest rungs include laboratories at the CDC and at the U.S. Army Medical Research Institute of Infectious Diseases.

Ever since September 11 and the ensuing anthrax attacks that rocked the U.S., our government has been addressing the need to improve preparedness for bioterrorism. The establishment of a new Office of Public Health Preparedness in the U.S. Department of Health and Human Services in October 2001 was followed in January by supplemental federal appropriations of $2.9 billion in funding for bioterrorism preparedness—probably the largest single infusion of money into public health, after decades of chronic underfunding. The bulk of this money will help states improve their public health infrastructures. Among the items included is technology to enhance disease surveillance, as well as trained personnel—often the resource in shortest supply—to run that technology, carry out diagnoses and safely handle hazardous material. Another priority is expansion of the number of labs able to make fast, reliable identifications of the most important threats, such as anthrax, smallpox, plague, botulism toxin and tularemia.

In addition, the CDC will receive $116 million, most of which is earmarked for laboratory modernization. The agency will also improve its electronic Health Alert Network, which keeps state and local health departments in touch with one another and clinicians regarding active disease threats. The National Pharmaceutical Stockpile will expand: the number of "Push Packages"—50-ton medical supply kits (syringes, bandages, respiratory masks, antibiotics, etc.) ready to be delivered to disaster sites—will increase from the current eight to 12. And the funding will buy a supply of smallpox vaccine sufficient to protect the entire population if needed. A smallpox outbreak is highly improbable, but the consequences would be so significant that preparation is nonetheless necessary.

Once a disease is identified, the next step is to limit its spread and to treat those exposed. But this, too, is dependent on the quality of surveillance and communications. Where are clusters of clinical cases? What medications are needed where? How can cleanup crews best detoxify a given area, and which areas have priority? What physical evidence can be gathered about the disease agent that might lead to those responsible for perpetrating the attack? What, if any, quarantine measures should be considered? Sharing data is a must, both among local, state and federal health departments and between the public health community and the law enforcement community.

The public health infrastructure is not merely an essential component of biodefense—it may well be the *only* component in the earliest phases of a response to a bioterror attack. Outbreaks of infectious disease occur frequently, and global conditions suggest that the emergence and spread of infectious diseases will increase in the near future. Some, such as a new influenza pandemic, may spread rapidly and with devastating force. A fortunate aspect of the investment in biological defense is that it is sure to pay great dividends: whether a disease emerges naturally or is released purposefully, public health preparedness can save lives either way. SA

FRED RIX