A Clearly Present Danger

Confronting the Threat of Bioterrorism

Serious concerns about the possible use of microbes as weapons of terror have heightened markedly over the past five years. This threat, mysterious and little understood, has spawned a spate of docudramas, books, and speculative scenarios, each conjuring up scarcely believable epidemic disasters. Although many such stories are best characterized as flights of science fiction, it has nonetheless become increasingly apparent that the occurrence of a bioterrorist event is

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entirely plausible and could be catastrophic. All countries are at risk. Instruction on how to prepare effective weapons is now available on the Internet, as are offers by laboratories in various parts of the world to provide strains of some of the most deadly microbes. Rapid developments in biotechnology are opening new vistas in medicine, but, at the same time, they are unwittingly providing rogue groups and nations with inexpensive tools to fashion new and more potent bioweapons. Meanwhile, during the past decade, large numbers of Russian scientists have left the extensive biological-weapons complex of the former Soviet Union and have been actively recruited for work in other countries. Thirty years ago, there were only four countries known to be working with biological weapons. Now, however, there are thought to be as many as 12 to 14.

Assessing the Threat

The United States ended its offensive bioweapons program in 1970. Like most countries, the United States has been slow to consider and implement possible defensive policies against "deliberate epidemics." Internationally, primary reliance has rested with the 1972 Biologic and Toxin Weapons Convention. This agreement had been signed by most countries but, as was discovered during the past decade, its terms were flagrantly violated both by Iraq and the former Soviet Union. Although the Convention mandates that no country undertake research on or production of biological weapons, there are no provisions or procedures for verification and enforcement. Countless meetings over a period of many years have so far failed to identify suitable mechanisms that countries could agree upon. Regrettably, the only other international initiative relating to biological weapons is an intention by the World Health Organization to issue a comprehensive booklet dealing with biological and chemical weapons in fall 2001.

A new perspective on the threat is provided by a recent report of the US Commission on National Security in the 21st Century. It singles out bioweapons as perhaps the greatest threat that the United States might face in the next century. Admiral Stansfield Turner, former Director of the US Central Intelligence Agency, believes that, besides nuclear weapons, the only other weapon class with the capacity to bring the nation past the "point of non-recovery" is biological weapons. In 1993, the US Office of Technology Assessment illustrated this threat in their estimate that 100 grams of anthrax released upwind of a large American city—say Washington, DC—could cause between 130,000 and three million

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deaths, depending on weather and other variables. At the high end, this degree of carnage is of a magnitude comparable to that caused by a hydrogen bomb, far exceeding what a chemical weapon could do. There is no doubt that biological weapons can be effective, and their utility has been demonstrated by all possible means short of war.

Heightened interest in bioterrorism by a number of nations can be attributed in significant part to the massive research and development program in this field conducted by the former Soviet Union. In the early 1990s, the West first learned from high-level Soviet defectors that in 1972, when other countries were ending their programs, the Soviet Union opted to expand and modernize its biological-weapons program and to begin to develop genetically engineered pathogens that could serve as weapons. Biopreparat, an ostensibly civilian operation, recruited outstanding scientists from throughout the country; at its peak, it employed over 30,000 people. Another 15,000 scientists were employed in a special military program, and 10,000 more were in an agricultural program intended to devise organisms to attack crops. Besides major research and development efforts, Biopreparat's agenda included the manipulation of microbes so that they could survive delivery on missile warheads, the manufacture of tons of dried anthrax spores and a number of other agents, and the establishment of an industrial capacity for the large-scale production of smallpox virus and antibiotic-resistant strains of plague. Much of the civilian component of this industrial complex is in the process of converting to other areas of research and to commercial production of biologics. However, the biological laboratories under military control remain closed to visitors. Iraq also acknowledges having developed a major program for research and production of biological weapons, primarily anthrax and botulinum toxin. This program remains intact, with its full complement of personnel.

It is generally agreed that overt use of a biological weapon by a nation-state is unlikely if for no other reason than fear of severe retribution were its role to be identified. However, because the production of biological weapons requires only a modest amount of readily procurable equipment, comparatively little space, and few personnel, it is a potential weapon for use by any of a number of extremist groups intent on inflicting large numbers of casualties. Two groups that have used or threatened to use biological weapons are the Osama bin Laden group and the Japanese religious cult, Aum Shinrikyo. The latter released sarin gas in the Tokyo subway in 1995 and had previously sought unsuccessfully to spread anthrax spores and botulinum toxin throughout metropolitan Tokyo.

Concern about the possible con-

US marines carry a simulated casualty to a decontamination site during biological/chemical-weapons training.

Photo courtesy US Department of Defense

sequences of the prodigious advances now occurring in the biosciences was recently expressed by Harvard University Professor Matthew Meselson: "Every major technology—metallurgy, explosives, internal combustion, aviation, electronics, nuclear energy—has been extensively exploited, not only for peaceful purposes, but also for hostile ones. Any major turn to the use of biotechnology for hostile purposes could have consequences qualitatively very different from those that have followed from the hostile exploitation of earlier technologies. Unlike. . .conventional or even nuclear weapons, biotechnology has the potential to place mass destructive capability in a multitude of hands."

The Effects of an Attack

The consequence of a biological weapons attack would be an epidemic, the nature of which would depend on the organism used. In theory, virtually any infectious microbe could be considered a candidate for use as a weapon, but some diseases have more serious consequences than others. For example, cities have continued to function essentially normally even in the face of community-wide epidemics of influenza. Conversely, in 1994, nearly half of the population of a large Indian city fled when only tens of cases of plague were reported. In 1999, an expert committee convened at Johns Hopkins University analyzed the various attributes of different diseases in terms of their capacity to cause a public-health emergency sufficiently serious as to compromise the functioning of government. Diseases considered to pose, by far, the most serious problems were smallpox, anthrax, plague, botulinum toxin, tularemia, and a group of agents such as Ebola virus that result in hemorrhagic disease. Any one of these organisms dispersed as a fine particle aerosol could result, under the right conditions, in thousands of casualties. Several of these organisms, as well as others, could also be dispersed in water or food to cause substantial numbers of infections.

The most serious bioterrorism scenarios would result from a covert, unannounced attack. There would be no explosion or other evidence of release—just the silent dispersion of an invisible, fine-particle aerosol without odor or taste. In all probability, the first knowledge that something had happened would occur when patients started appearing in the emergency rooms and in doctors' offices with strange illnesses, some severe and rapidly fatal. This could be days to weeks after the release. Some infected persons, by then, may have traveled to other countries and continents.

Even worse, physicians are not trained to diagnose the pathogens thought most likely to be used as bioweapons. Few have ever seen anthrax or smallpox or pneumonic plague, and ordinary hospital laboratories do not have the necessary reagents or experience to rapidly diagnose these infections.

Few persons have witnessed or endeavored to cope with a fast-moving lethal epidemic. Epidemics tend to be terrorizing. In 1994, cases of plague occurred in Surat, India, as a result of an ecological disruption caused by earthquakes. Within 12 hours of media reports of a deadly, mysterious fever, people began streaming out of the city. Among the first to leave were many from the medical community. Eventually half a million people fled, leaving the city a ghost town. It is estimated that India lost US$2 billion dollars in trade, embargoes, and industrial output. Some 6,500 illnesses and 56 deaths were reported to have occurred, although later studies indicate that few were actually plague cases—a disease, incidentally, that is treatable with antibiotics.

A second characteristic of epidemics is that they have the potential to cause large numbers of casualties. The best known example of a pandemic (global epidemic) is the so-called swine influenza of 1918-1919. It circled the world in about four months in an era of cargo ships and railroads and trolley cars. In all, 20 to 40 million people died. The mortality rate, however, was "only" two percent. If it had had a mortality rate similar to that of a new influenza strain such as that dis-

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covered in Hong Kong three years ago, more than 15 times as many deaths would have occurred. Fortunately, the Hong Kong outbreak was contained before spreading abroad.

A third special problem posed by epidemics relates to difficulties associated with control of a contagious disease. In 1972, there was a smallpox outbreak in Yugoslavia when a returning pilgrim became ill shortly after returning home. He was met and honored by family and friends. Eleven of his contacts became ill two weeks later. The doctors who treated them did not suspect smallpox—no cases had occurred in Yugoslavia in 45 years, and compulsory vaccination against smallpox was still in practice. Another two weeks elapsed before the disease was correctly diagnosed. By that time, cases were occurring in many different towns and cities in different regions; 150 people were already sick or dying. To prevent spread of the disease, the surrounding countries closed their borders to trade and transport. Yugoslav authorities decided that their only option was to vaccinate the entire population and this they did—all 20 million people. Ten thousand patient contacts were isolated in hotels and apartment buildings until after the incubation period had passed. As a result of such heroic efforts, the epidemic was contained. It is worth bearing in mind that, compared to other outbreaks, this was not a large epidemic—it only led to 175 cases with 35 deaths.

An outbreak of smallpox today could be catastrophic. Vaccination ceased in the United States in 1972 and, by 1980, throughout the world. Thus, half or more of the population is fully susceptible to the disease, as are many of those who were vaccinated before 1980, since vaccination immunity decreases over time. The disease spreads from person to person and, because so few are now protected, each patient would probably infect 10 to 20 others if an epidemic were to occur today. Thus, every 10 to 14 days, there would be a new wave of patients that, if uncontrolled, would be at least an order of magnitude larger than the previous one. There is no treatment; 30 percent of patients die. The only effective measures that could be taken would be vaccination and isolation of patients so they could not spread the disease. Vaccination protects within about seven to eight days after administration. In an epidemic, efforts are made to immediately vaccinate all persons who have been in contact with patients since they first became ill—in the hospitals where patients are housed as well as contacts in the family, school and work place.

But there is an even larger problem. The only available vaccine was made and stored before 1980, and while some of it remains potent today, there is very little available. There are no manufacturers anywhere in the world today. Although the US Centers for Disease Control and Prevention (CDC) have recently negotiated a contract to produce 40 million doses of smallpox vaccine, the first product will not be ready until 2004. If an outbreak of as few as 50 patients were to occur, demands for vaccine supplies would exhaust the limited available stocks within four to six weeks.

The Public Health Response

Effective management of an epidemic is a complex and difficult task, often compounded by high levels of public anxiety and even, on occasion, panic. Presently, there is little experience upon which to build management skills. Large-scale epidemics with high death rates are now uncommon in most parts of the world, and there are few, if any, who have had experience with any of the diseases identified as potentially the most dangerous biological weapons. The last smallpox epidemics occurred more than 25 years ago and the details of the only known epidemic of inhalation anthrax—which resulted from a 1979 accidental release of anthrax spores from a Soviet bioweapons plant—are incomplete.

The medical and public health infrastructures in most countries are marginal at best and nonexistent at worst. Hospitals today are usually full to overflowing and have little capacity to deal with even a small, sudden surge of patients. Few would be able to prevent in-hospital disease transmission, and most are short of staff for almost every important task. The public-health infrastructure in most parts of the world has been steadily eroding over several decades as principal investments have been directed to tertiary curative care facilities and therapeutic drugs.

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Surveillance to detect disease outbreaks is seriously deficient everywhere, including in the United States, primarily because of the lack of public-health expertise. Those who know well the status of public health in the United States suspect that New York's West Nile encephalitis outbreak would probably have gone undetected in 90 percent of US cities and without preventive measures until so late in the autumn as to be of no value. Internationally, surveillance is even poorer. Who knows how many other new or emergent infections as serious as AIDS are now spreading through remote villages of Africa or Asia?

In efforts to cut costs, pharmaceutical firms have reduced inventories of both antibiotics and vaccines with the result that shortages of both are occurring regularly. Thus, absent special measures being taken, there would be no way to deal with an epidemic such as plague or anthrax that required a surge in use of antibiotics. A fundamental problem is that public-health and medical-care systems are poorly equipped today to deal with any sudden surge of cases, whether naturally occurring or propagated by a terrorist. Any emergency large-scale vaccination or drug-distribution program would far exceed the capacity of most public-health departments. This is especially true in the developing world where, even today, simple programs to provide daily doses of drugs to treat a growing tuberculosis epidemic, for example, are beyond the capacity of most health systems.

What Can Be Done

Perhaps the most important principle to be recognized is that for nearly a generation, we have become increasingly complacent about the threat of the ever-changing, ever-mutating microbial world. However, as Nobel Prize laureate Joshua Lederberg has pointed out, viruses and bacteria are man's only serious competitors for dominion of the planet--and the ultimate outcome is by no means a foregone conclusion. A grim scenario, for example, would be an epidemic of an HIV/AIDS-like virus that spreads as rapidly as influenza but does not produce serious symptoms for many years. How prepared would we be to detect, diagnose, and deal with such an occurrence with either drugs or vaccines? Epidemics, whether occurring naturally or as a result of deliberate release, are serious threats to the well-being of peoples everywhere. There are serious penalties to be paid by the unprepared.

Consideration must be given to the development of an international surveillance network of epidemiologists and laboratories, prepared to quickly investigate and determine the cause of disease epidemics wherever they might occur. Disease epidemics in the modern world are more than national problems; they are potentially threats to international security. The essential component of disease surveillance for infectious diseases at a local level is that clinicians treating patients in emergency rooms or health centers accustom themselves to contacting public-health officials immediately whenever they encounter suspiciously severe cases of common illness or an unusual cluster of cases. This will undoubtedly require an expansion of public-health capacities, but it is a small price to pay for the possible prevention of a catastrophe.

Prevention of bioterrorism, to the extent that this is possible, should be a high priority. It is imperative to build a universal consensus, particularly among scientists, that the development, production, or dissemination of biological weapons by any persons, laboratories, or governments would be regarded by the world community as one of the most serious of all crimes. Strengthening the Biological and Toxin Weapons Convention to provide for some means for verification of compliance is also desirable, but it is unlikely to be sufficient. Plans and preparations for dealing with outbreaks of severe disease and other catastrophes involving large numbers of casualties should be a basic responsibility of national and local governments in all countries.

In the United States, some planning has begun to respond to bioterrorism. A network of laboratories equipped to deal with the principal agents is taking shape. A few states and some localities are developing plans for responding to a problem; the CDC has begun stockpiling critical drugs and equipment, and greater attention is now being paid to various groups who might be motivated to attempt the use of a biological agent. However, there is no coherent national plan and no clear delineation of responsibilities of the different federal and state agencies. No satisfactory teaching materials have been made available either to the medical or to the public-health communities. In most areas, hospitals have yet to be brought into the planning process to assess what should be done in case of an emergency. Fragmentary research programs have already been instituted by several agencies, but many have little understanding of the problem involved or what research might contribute.

The good news is that some active discussion is already beginning to take place. The bad news is that this discussion is a modern tower of Babel, with many groups talking at the same time, each with different objectives that are incomprehensible to others. The world at large is only beginning to recognize that bioterrorism is a threat equivalent to, and perhaps greater than, the threat of nuclear weapons. We are only now becoming familiar with a threat that will be with us for many years to come. H