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BIOLOGICAL TERRORISM

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Until recently, biological terrorism has been little discussed or written about in the medical literature or, for that matter, in the public press. Until recently, I personally had doubts about publicly discussing the subject because of concern that it might entice some to undertake dangerous, perhaps catastrophic experiments. However, events of the past 3 years have made it clear that likely perpetrators already envisage every agenda one could possibly imagine.

Over past years, there were three points of view which variously prevailed in national policy circles and in the academic community which served to discourage biological terrorism being considered as more than a theoretical possibility:

1)That historically, biological weapons have so seldom been deployed that precedent would suggest they would not be used.

2) That their use is so morally repugnant that none would deign to use them.

3)That it is technologically so difficult to produce organisms in quantity and to disperse them that the science is beyond the reach of any but the most sophisticated laboratories.

Each of these arguments is without validity.

We now know that there are nations and dissident groups who have both the motivation and access to skills to selectively cultivate some of the most dangerous pathogens and to deploy them in acts of terrorism or war. Three events contributed to an appreciation, gained only in the past 3 to 4 years, that the threat was more serious than had believed. Iraq was discovered after the Gulf War to have had a larger biological weapons program than any had surmised but not until the defection of Saddam Hussain's son-in-law was the true magnitude perceived. Iraq confirmed that

it had produced, filled and deployed bombs, rockets and aircraft spray tanks containing Bacillus anthracis and botulinum toxin (1,2). Its work force and technological infrastructure are still wholly intact. The Japanese cult, Aum Shinrikyo, in 1995, released the nerve gas Sarin in the Tokyo subway. However, as the New York Times recently divulged, this followed some 8 failed efforts to release anthrax and botulinum aerosols throughout central Tokyo.(3). The cult is still intact; it has financial reserves said to be in excess of one billion dollars; 18 000 followers are said to be present in Russia.

Russia's bioweapons capability, as defectors have increasingly made clear, was and is far more extensive and far more sophisticated than any had imagined at the end of the cold war. It is reported that Russia has in storage some 30 tons of dried anthrax spores and 20 tons of smallpox virus, among other agents. These had been weaponized on ICBMs. Over recent months, special concerns have arisen regarding the status of one of the largest and most sophisticated of the facilities, called Vektor, located in Central Siberia. Through the early 90s, this was a 4000 person, 30 building facility with ample BL-4 facilities, both for specimens and for isolation of human cases. It was protected by an elite guard. Here is where the smallpox virus is kept and here is where work has been going on using Ebola, Marburg and the hemorrhagic fever viruses. Visits last autumn disclosed a half-empty facility and a diminished number of guards who have not been paid for months. No one can say where the scientists have gone (4) nor is there confidence now that this is the only storage site for smallpox virus outside of the CDC.

An August issue last year of the Journal of the American Medical Association makes clear that biological terrorism is more likely than ever before and far more greatly to be feared than either explosives or chemicals. At a congressional hearing, Colin Powell said "Of all the weapons of mass destruction, biological weapons worry me most". Civilian preparations have scarcely begun and virtually no funds have yet been made available to strengthen our first line of defense, our public health and

medical infrastructures. Moreover, recognition that prevention of such episodes or countering them will be extremely difficult. Recipes for making biological weapons are now available on the Internet.

Thus, the first evidence of intent to use such weapons will almost certainly be the appearance of cases in hospital emergency rooms. The rapidity with which those manning the emergency rooms reach a proper diagnosis and the speed with which preventative and therapeutic measure are applied could well spell the difference between 1000s and perhaps tens of thousands of casualties. However, there are today few indeed who have ever seen so much as a single case of smallpox or plague or anthrax or, for that matter, would recall from the recesses of memory the characteristics of such cases.

Most persons reviewing this subject detail a long list of potential pathogens but, in fact, only a handful share the characteristics of being reasonably easy to prepare and to disperse and being able to inflict sufficiently severe disease so as to paralyze a city. In 1994, Vorobyev, a Russian bioweapons expert presented to a working group of the National Academy, the conclusions of Russian experts as to the agents most likely to be used (8). Smallpox headed the list followed closely by anthrax and plague. None of these agents has so far effectively been deployed as a biological weapon and thus, no real world events exist which provide the basis for suggesting likely scenarios. However, for smallpox, we have had several well-documented importations into Europe over recent decades;

Before doing so, let me recall for you that the disease, smallpox is caused by a virus which is spread from person to person, each infected person, in turn, experiencing the characteristic fever and rash. There are no mild, subclinical infections among unvaccinated persons. About 30% of all unvaccinated patients died of the disease. There was, and is, no specific treatment.

The potential for smallpox as an aerosolized agent was vividly demonstrated in an outbreak in Germany in 1970 (11). That year, a German electrician returning from Pakistan became desperately ill with high fever and diarrhea. On January 11, he was admitted to a local hospital and isolated in a separate single room on the ground floor because it was feared he might have typhoid fever. He had contact with only two nurses over the next three days. On January 14, a rash developed and on 16 January, the diagnosis of smallpox was confirmed. He was immediately transported to one of Germany's special isolation hospitals and more than 100 000 persons were promptly vaccinated. After the diagnosis of smallpox was made, hospital patients and staff were quarantined and remained so for four weeks. Patients and staff were vaccinated, very ill patients receiving VIG first. However, the patient had had a cough, a symptom seldom seen with smallpox and, as you know, coughing can produce a large volume. small particle aerosol much as one would expect were smallpox to be used as a terrorist weapon. Subsequently, 19 cases occurred in the hospital, including four in other rooms on the patient's floor of the hospital; eight on the floor above; and ~~nine~~ seven on the third floor. One of those afflicted was a visitor who had spent less than 15 minutes in the hospital and had only briefly opened a corridor door, easily 30 feet from the patient's room, to ask directions. Three of the patients were nurses, one of whom died. And this was in a well-vaccinated population. One needs no better illustration than this to understand that smallpox virus in an aerosol has a considerable capacity to spread over a considerable distance and to infect at low dosages.

The experience of Yugoslavia in February 1972 is also instructive in comprehending the havoc created even by a small outbreak. Yugoslavia's last previous case of smallpox had occurred 45 years before, in 1927. Nevertheless, Yugoslavia, like most countries throughout the world had continued population-wide vaccination to protect itself should an importation occur. In 1972, a pilgrim returning from Mecca became ill with an undiagnosed febrile disease. Friends and relatives visited from a number of different areas and two weeks later, 11 of them developed

high fever and rash. None were aware that others were ill and physicians who saw the patients failed to make a correct diagnosis. Few had ever seen a case of smallpox.

The first cases were correctly diagnosed four weeks after the first patient became ill but, by then 150 persons were already infected. The cases were occurring in widely separated areas of the country. By the time of diagnosis, the 150 secondary cases had already begun to expose yet another generation and, inevitably, questions arose as to how many undetected cases there might be. Each of the neighboring countries closed its borders to all traffic. The country was in panic.

Government health authorities saw no alternative but to launch a nation-wide vaccination campaign. Mass vaccination clinics were held and check points along roads were established where vaccination certificates were examined. Twenty million persons were vaccinated. Hotels and residential apartments were taken over, cordoned off by the military and all known contacts of cases forcibly moved into these centers under military guard. Some 10 000 persons spent two weeks or more in such isolation. Nine weeks after the first patient became ill, the outbreak was stopped -- 175 patients had developed small pox and 35 had died -- and this was in a generally well-vaccinated population and it was, in fact, a small outbreak.

What might happen if smallpox were to be released today in a U.S. city? First, it is important to recall that routine vaccination stopped in the U.S. in 1972, 25 years ago. Thus, there are large numbers who have never been vaccinated and, for virtually all others, vaccine immunity has been waning for more than 25 years. Based on what we know, it is unlikely that more than 25% would have any residual protection. A release of smallpox would go unnoticed until cases with rash began to appear perhaps 9 or 10 days later. With patients being seen by different physicians in different clinics none of whom had ever before seen a smallpox case, it is probable that days would elapse before the diagnosis of smallpox was confirmed and an alarm

sounded.

Assume that 100 persons had been infected and required hospitalization. As soon as smallpox was suspected, this number would soon be submerged among a group of patients many times larger, perhaps 200 or 300 persons, all with illnesses with fever and rash but whose diagnosis was uncertain. Some would be reported from other cities and other states. Where would all of these patients be admitted? It is doubtful that there are more than perhaps 100-150 hospital beds in the New York area which provide negative pressure isolation. And who would care for the patients? Few hospital staff have any smallpox immunity.

What of contacts? Based on experience in other outbreaks, the number of contacts of confirmed or suspected cases would number in the thousands, if not tens of thousands. Would they be isolated as in Yugoslavia and if so, where?

Predictably, there would be an immediate clamor for mass vaccination such as occurred in Europe. Present U.S. stocks of smallpox vaccine are nominally listed at 15 million doses but, as it is packaged, the useful number of doses is perhaps half that number and for other reason, it may in fact be a great deal less. Present reserves of vaccine would rapidly disappear and there is, at present, no manufacturing capacity anywhere to produce additional vaccine. Under emergency circumstances, 30 to 36 months would elapse before significant new stocks became available.

What of anthrax which has been so enthusiastically embraced by both Iraq and the Aum Shinrikyo? Their interest, in part, stems from the fact that the organism is so easy to produce in large quantity. In its dried form it is extremely stable. What the effect of aerosolized anthrax might be on humans once had to be inferred from animal experiments and the occasional human infection among workers in factories processing sheep and goat hides (13) What was clear is that inhalation anthrax is highly lethal. Just how lethal became evident in the 1979 Sverdlovsk epidemic (14).

In all, 77 cases were identified with certainty of whom 66 died. It is suspected that the actual total was considerably more than 100. The cases lived or worked somewhere within a narrow zone extending some four kilometers south and east of a military bioweapons facility. An accidental airborne release of anthrax spores occurred during a single day and may well have lasted no more than minutes. Further investigations revealed anthrax deaths among sheep and cows in six different villages ranging up to 50 kilometers southeast of the military compound.

Some cases experienced the onset of disease as late as six weeks after exposure but whether the onset of illness occurred sooner or later, death almost always followed within one to four days after onset.

Meselson and his colleagues who documented this outbreak calculate that the weight of spores released as an aerosol could have been as little as a few milligrams or as much as "nearly a gram". Note that Iraq acknowledged producing at least 8000 Liters of solution with an anthrax spore count of 10^9/ml. Recall also that Russia has a reported 30 tons of dried anthrax spores in storage.

The ramifications of even a modest-sized release of anthrax spores in a city are profound. Bear in mind that the small particle aerosol penetrates interior spaces such that the risk is roughly equivalent whether an individual is inside or outside. Emergency rooms would begin seeing a few patients with high fever and some difficulty breathing perhaps 3 to 4 days following exposure. Once the diagnosis was made, one would be faced with the prospect of what to do. Should provision be made to treat all with antibiotics for 6 or 8 weeks? Could this be done logistically? Should Vaccine be administered to those who might have been exposed? Unfortunately, there is at present, little vaccine available and no plan at present to produce any for civilian use. Should one be concerned about additional infections occurring as a result of anthrax spores being subsequently resuspended and inhaled by others?

Finally, when does one permit any in the population to return to the affected area. This is a serious concern given the fact that anthrax spores may persist in the environment for 40 years or more and methods for decontamination are extremely costly and conceivably impossible for many settings. There is as yet no agreed technical guidance.

We are today ill-prepared to deal with a terrorist attack which employs biological weapons. To date, the focus of concern with respect to countering civilian terrorism has been almost wholly on chemical and explosive weapons. A chemical release or a major explosion is far more manageable than the biological challenges posed by smallpox or anthrax. Following an explosion or a chemical attack, the worst effects are quickly over; the dimensions of the catastrophe can be defined; the toll of injuries and deaths can be ascertained; and efforts can be directed to stabilization and recovery. Not so following use of smallpox or anthrax as day after day, additional cases can be expected -- and in new areas.

The specter of biological weapons use is an ugly one, every bit as grim and foreboding as the picture which has been painted of a nuclear winter. As was done in response to the nuclear threat, I believe that we, as a medical community, bear a responsibility to educate the public and the policy makers as to the nature of that threat. There is a need to build on the 1972 Biological ~~Warfare~~ Weapons Convention to strengthen measures prohibiting the development and production of biological weapons and to assure compliance with agreements which are made. In a broader sense, there is the need to build a strong moral consensus utterly condemning biological weapons.

we know tactics and conventions have their limits

But this is not enough. In the near term, we need to be as prepared to detect and diagnose, to characterize epidemiologically and to respond appropriately to biological weapons use as we need to be prepared to respond to the threat of new and emerging infections. In fact, the needs are convergent. Most important of all, we need at international, state and local levels, a greater capacity for surveillance; we need a far better network

of laboratories, ~~and better diagnostic instruments~~, we need a more adequate cadre of trained epidemiologists, clinicians and researchers.

We are in urgent need of a funded research ~~and training agenda~~ program. Until recently, all too little research has been done with respect to any of the agents and virtually none in the civilian sector. Such new funds as have been made available for that have been assigned to the Defense Department and to the national laboratories of the Department of Energy. NIH may get $10 million if a supplemental appropriations bill is passed but, so far, that is it.

To strengthen adequately our public health and medical infrastructure and to undertake a needed program of research will require a great deal of money. However, if we can and are willing to spend tens of billions to deal with the threat of nuclear weapons, as is now the case, we should be more than prepared to devote hundreds of millions to cope with the greater threat of new and emergent infections, whether naturally occurring or induced by man.

~~In my opinion, bioterrorism represents one of the most serious threats we have faced in this century. We need to faceup to the realities of that threat and prepare the medical and public health community accordingly. To that end a Center for Civilian Biodefense Studies has just been established with a base at Johns Hopkins but with the participation and involvement of state and local health departments as well as medical and public health associations. Ultimately, our best defense is an educated and informed citizenry. There is much to be done.~~