BIOLOGICAL TERRORISM

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Bioterrorism, as it pertains to the civilian sector, has received little attention. Such planning as has been conducted has largely assumed that the impact of and response to bioterrorism would differ little from that following use of a chemical weapon or an explosive device. In fact, however, the scenario for a bioterrorist attack would differ substantially in terms of detection, the nature and duration of crisis management, the ramifications within the civilian population, the professional skills of those needed at virtually all levels of management as well as the nature of possible preparatory measures. Current misperceptions reflect the fact that very few who have had extensive experience in the practical realities of epidemic management have been involved to date in the planning process. In this presentation I would like to convey to you certain of the practical realities and differences in dealing with even modest epidemics of smallpox and of anthrax, based on field experience.

What is now generally accepted is that detection or interdiction of those intending to use biological weapons is next to impossible. Thus, the first evidence of intent to use such weapons will almost certainly be the appearance of cases in physicians' offices and hospital emergency rooms. The diagnosis of the early cases will almost certainly be missed for periods of days. 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. Moreover, from experience in various epidemics, it can be assumed that there may be substantial delays in even identifying the fact that an epidemic is in progress. The initial patients will undoubtedly be seen in a number of different clinic settings and hospital emergencies, admixed with a variety of other patients with symptoms of fever,

respiratory symptoms and rashes which may resemble the early symptoms of cases from almost any bioterrorist generated epidemic. The duration of delay in recognizing that an epidemic is in progress thus depends on how alert are those seeing patients and on the sensitivity of the disease surveillance systems at city and state levels. Clearly, the rapidity with which a proper diagnosis is made and the speed with which preventative or therapeutic measure are applied can well spell the difference between 1000s and perhaps tens of thousands of casualties. To date, little has been done to educate the medical community as to likely threats; state and local disease surveillance systems may well be at their weakest in decades; diagnostic laboratories outside of the few in the federal government are presently unable to confirm the presence of most suspected agents and, as yet, a coherant plan to address these problems has yet to be prepared.

Most persons reviewing the subject of bioterrorism 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, perhaps even a nation. 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; two bear recounting.

Before doing so, let me recall for you the disease, smallpox. It is caused by a virus which is spread from person to person, each infected person, in turn, experiencing the characteristic fever and rash. Infection caused by the virus invariably results in symptomatic disease. There are no mild, subclinical infections among unvaccinated persons. After an incubation period of about 10 to 12 days, the patient experiences high fever and aching pains. **(slide 1,2,3,4)** Then a rash begins with small papules developing into pustules about day 7-8 and finally changing to scabs

about day 12. Between 25 and 30% of all unvaccinated patients died of the disease. There was, and is, no specific treatment.

How concerned were the countries of the world about smallpox? Until 1980,essentially all conducted vaccination programs of some sort whether or not they had endemic disease (9). Until 1972, the United States mandated smallpox vaccination for all children at school entry despite the fact that the last cases had occurred in 1949, 23 years before. In the United Kingdom, there were four standby hospitals to be opened only in case of smallpox cases being imported and, in Germany, two state-of-the-art isolation hospitals were constructed in the 1960s specifically for the isolation of smallpox cases should they occur. No other disease has generated such fear and concern but the fears are not unfounded.

In 1962, the United States faced the question as to steps which it should take in the face of an importation. That year, a young Canadian boy returned from Brazil, traveling by air to New York and by train to Toronto by way of Albany and Buffalo (10). He developed a rash shortly after arrival and was quickly isolated in hospital. As Chief of CDC's Surveillance Section, I had immediately gone to Toronto to see the case and to review the situation with Canadian authorities. While there, I received an emergency call to come to Washington immediately to decide on measures to be taken. I was astonished on arrival to learn that a course of action had been all but finalized. It called for closure of the border with Canada, a mass vaccination campaign in all cities along a route extending from New York through Albany, Syracuse, Rochester and Buffalo, and the issuance of a public announcement asking all who had been in Grand Central Station on the day that the boy had taken the train to come forward and be vaccinated. All this in response to the occurrence of a single case.

You may also recall that on 10 March 1946, New York experienced its first death due to smallpox in over 30 years. Over succeeding days, other cases were discovered and traced and fears rose of the possibility of a major epidemic in a population which it was feared was not adequately vaccinated. The city mobilized and 6 300 000 persons were vaccinated over the course of one week. The eventual total

of cases -- 12; the deaths -- 2.

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. **(slide 5)** 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. The hospital had been closed to visitors for several days prior to admission of the patient because of an influenza outbreak. 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. **(slide 6)** Subsequently, 19 cases occurred in the hospital, including **(slide 7)** four in other rooms on the patient's floor of the hospital; eight on the floor above; and nine on the third floor. Two were contact cases. One on 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.

One of the 11 patients who acquired smallpox was a 30-year-old teacher who quickly became critically ill with the hemorrhagic form. **(slide 8)** This form of smallpox is not readily diagnosed even by experts. The Yugoslav teacher was first given penicillin at a local clinic but as he became increasingly ill he was transferred to a dermatology ward in a city hospital, then to a similar ward in the capitol city and finally, to a critical care unit because he was bleeding profusely and in shock. He died without a definitive diagnosis being made. He was buried two days before the first case of smallpox was recognized.

(slide 9) The first cases were correctly diagnosed four weeks after the first patient became ill but, by then 150 persons were already infected. Among them were 38 who were infected by the young teacher, including two physicians, two nurses and four other hospital staff. The cases occurred 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 other yet undetected cases there might be. 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. Meanwhile, each of the neighboring countries closed its borders to all traffic. 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 recognize that routine vaccination stopped in the U.S. in 1972, 25 years ago. Some travelers were vaccinated over the following 8 years and many military recruits as well as a handful of laboratory workers. Overall, however, it is doubtful that more than 10 to 15% of the population today has significant residual smallpox immunity. Suppose that some modest volume of virus were to be released perhaps by exploding a light bulb containing virus in a Washington subway. The event would almost certainly go unnoticed until the first cases with rash began to appear perhaps 9 or 10 days later. With patients being seen by different physicians in different clinics and by individuals who almost certainly had never before seen a smallpox case, it is probable that several days would elapse before the diagnosis of smallpox would be ~~confirmed~~ considered and an alarm sounded.

Assume that perhaps 100 persons had been infected and would require hospitalization. As soon as smallpox was suspected, this number would soon be submerged among a group of patients many times larger, 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 50 to 75 hospital beds in the metropolitan D.C. area which provide adequate isolation. And who would care for the patients? Few hospital staff have any smallpox immunity. Couple this with the problems posed by the one or two severe hemorrhagic cases which typically have very short incubation periods and would have already been admitted to hospital before smallpox was suspected. They would have been cared for by a large, unprotected intensive care team.

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. What measures should or would be taken to deal with them. Would they be isolated as in Yugoslavia and if so, where?

Logistics could be simplified if rapid, easily used laboratory tests could rapidly confirm or rule out smallpox among suspected cases. At present, however, such tests are known only to scientists in two government laboratories

Predictably, there would be an immediate clamor for mass vaccination such as occurred in the cited outbreaks in Germany and Yugoslavia. 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. How widely does one apply this vaccine and how quickly? Comparatively few doses might be needed were vaccine able to be limited strictly to close contacts of confirmed cases. However, the realities of dealing with even a modest-sized epidemic would almost certainly preclude such a cautious, measured vaccination effort. Present reserves of vaccine would rapidly disappear and there is, at present, no manufacturing capacity anywhere to produce additional vaccine. If an emergency effort were made to produce new stocks of smallpox vaccine, many months to a year or more would be required.

It is apparent that even a modest-sized outbreak offers an agenda replete with problems.

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).

(slide 10) 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 along the same axis as the human cases.

(slide 11) Of the 58 cases with known dates of onset, only nine experienced symptoms within a week after exposure and some experienced the onset of disease

as late as six weeks after exposure. Whether the onset of illness occurred sooner or later, death almost always followed within one to four days after onset. However, there did appear to be a somewhat higher proportion of survivors after the fourth week. This almost certainly resulted from the widespread application of penicillin prophylaxis and anthrax vaccine both of which were distributed in mid-April throughout a population of 59 000 persons.

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 and cell count of 10^9/ml.

The ramifications of even a modest-sized release of anthrax spores in a city are profound. Emergency rooms would begin seeing a few patients with high fever and some difficulty breathing perhaps 3 to 4 days following exposure. By the time they were seen, it is almost certain that it would be too late for antibiotic therapy. Essentially all would be dead within 24 to 48 hours. No emergency room physicians or infectious disease specialists have ever seen a case of inhalation anthrax; medical laboratories have had virtually no experience in its diagnosis. Thus, it is probable that a delay of at least 3 to 5 days would elapse before a definitive diagnosis were made

Once the diagnosis was made, one would be faced with the prospect of what to do over the succeeding six weeks. 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 antibiotics be administered prophylactically? If so, which antibiotics and what should be the criteria for exposure? What quantity would be required to treat an exposed population of perhaps 500 000 persons over a 6 week period? Should one be concerned about additional infections occurring as a result of anthrax spores being subsequently resuspended and inhaled by others? Does one request everyone who has been anywhere near the city to report to his or her local physician for treatment at the first occurrence of fever or cough, however mild? Undoubtedly, there would be many

persons with such symptoms, especially in winter. How does one distinguish these from the premonitory symptoms of anthrax which may proceed to death within 24 to 48 hours? Can one imagine the reaction of a large population confronted with this array of problems?

We are today ill-prepared to deal with a terrorist attack which employs biological weapons. As I noted at the beginning, the focus of concern with respect to countering civilian terrorism has been almost wholly on chemical and explosive weapons and a response which is, at most, a modest extension of existing protocols to deal with a hazard materials incident. 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. Day after relentless day, additional cases could be expected -- and in new areas.

But anthrax poses yet one more dilemma. When can individuals be permitted to reenter the affected area? We know that a well-placed anthrax aerosol cloud can drift for miles. It penetrates buildings with alacrity and in concentrations comparable to those outside. The spores are remarkably hardy and are able to be recovered from surfaces in viable form for 50 years or more. Decontamination is extremely difficult and logistically and financially is probably impossible for most structures, including subways. What recommendations should be made under such circumstances?

It is abundantly clear that if we are to be prepared to deal with a bioterrorist attack -- and, as you will recall, it was Sam Nunn's judgment that it is not a question of if but when -- we will have to make major investments in the civilian sector. As a beginning step, decisions are needed as to which are the likely threats which could seriously compromise the functioning of a city, if not a geographic area or indeed the country. An immediate strategy needs to be decided with respect to vaccines, antibiotics and other necessary material for crisis response and cleanup. Only when this is done will it be possible to undertake the necessary planning and training for

management of an epidemic crisis at federal, state and local level. There are other needs. Education of the medical community, especially infectious disease specialists and emergency room personnel, is essential; the capacity for infectious disease surveillance at both city and state level must be strengthened; laboratory capacities need to be expanded; and research programs need to be decided and funded. I could continue but the bottom line is that we have a lengthy agenda which we have scarely defined, let alone begun to address.