# Biological Terrorism -- Epidemiological Realities

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Considering that discussions at this meeting have so far dealt primarily with chemical terrorism, it seemed to me that I might most usefully bring to your attention certain of the realities of and responses to serious epidemic disease. I suggest this because I strongly suspect that less than a handful of those attending this conference have had the experience of endeavoring to cope with a serious epidemic problem. It is far more difficult and problematic than one might imagine.

Not since the polio epidemics in the mid-1950s have we had epidemics of any kind in the United States of a size and severity which would seriously stress a large community. There have been such epidemics in other parts of the world, of course, although even the most severe pales in comparison with what might readily be anticipated following even a modest-sized dispersion of certain bioweapons. My reflections on possible scenarios are derived from a ten year personal experience as Chief of CDC's Epidemic Intelligence Service and 11 years as Director of the Global Smallpox Eradication Program.

A long list of potential bioweapons is conventionally offered but critical analysis tells us that, for the civilian sector, only a handful, in fact, are both practicable for use and sufficiently severe to make the type of statement which Stanley Bedlington characterizes as being that which is sought by a number of terrorist groups today. The subject of most probable agents was addressed formally at a meeting at the National Academy of Sciences in 1994. Vorobyev, a Russian bioweapons expert, presented to the Working Group on Biological Weapons Control a paper summarizing Russian conclusions as to the most likely agents to be used. The top three were, in order, smallpox, plague and anthrax. I would agree with that characterization with one

exception. Based on experiences with inhalation anthrax at Sverdlovsk, about which I will say more, I that anthrax would now be rated more highly than plague.

Today I should like to walk you through certain of the realities of epidemic smallpox

First, the disease of 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 classical smallpox 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, much like one has with a severe case of influenza. Then a rash begins to develop (SLIDES 1,2,3) with small papules developing into pustules about day 7-8 and finally changing to scabs about day 12. As abhorrent as these pictures may be, you should know that this young Pakastani boy actually had what we would call a mild case. A more typical case, called "ordinary smallpox" is shown in SLIDE 4. Between 25 and 30% of all unvaccinated patients died of the disease. There was, and is, no specific treatment. And some, after recovery, were left blind (SLIDE 5)

How concerned were the countries of the world about smallpox? Essentially all conducted vaccination programs of some sort whether or not they had endemic disease. 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. International travelers were obliged to carry an official vaccination card attesting to the fact that they had been successfully vaccinated within the preceding three years. 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. In fact, for the 1976 Innsbruck Olympics, a special 8 bed ward was constructed for use of smallpox cases should they occur. For no other disease was there any where near the international concern invoked by smallpox.

In 1962, the United States faced the question as to steps which should be taken 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. He developed a rash shortly after arrival and was quickly isolated in hospital. As Chief of the Epidemic Intelligence Service, I had immediately gone to Toronto to see the case and to review the situation with Canadian authorities when I received an emergency call to come to Washington immediately to decide on measures to be taken. I was astonished on arrival to be ushered into a meeting with many of our most senior Public Health Service officials and to be informed that the course of action they were seriously contemplating at that moment called for closure of the border with Canada, a mass vaccination campaign to be launched 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. After considerable discussion, it was decided that watchful waiting would suffice for the present given the fact that smallpox is not normally contagious prior to eruption of the rash. It is instructive, however, to note that there were many fully prepared to take heroic action involving the vaccination of hundreds of thousands of people threatened by spread of disease from a single patient. It is clear that smallpox terrified as no other disease.

What is the potential for smallpox as an aerosolized agent? This

(From IDSA paper)

How difficult would it be to prepare a smallpox weapon? Smallpox virus is readily grown on the chorioallantoic membrane of embryonated hens' eggs. It is a large virus and a stable one. It is so stable, in fact, that in the early 19th century, smallpox vaccine virus (a cousin of smallpox, if you will) was simply dried on small pieces of glass or on cotton threads and shipped from place to place on journeys of days to weeks. Dispersed in the air as an aerosol, the virus remains suspended for hours, especially in the dry, cool air of autumn and winter.

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 have continued to be vaccinated since.. Overall, however, it is doubtful that more than 10 to 15% of the population have any residual smallpox immunity at this time. Suppose that some modest volume of virus were to be released perhaps by exploding a light bulb containing virus on the tracks at Metro Center and perhaps in a departure lounge at Dulles. 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, most likely in a number of different cities, and by individuals who almost certainly had

never before seen a smallpox case, it is probable that several days would elapse before suspicions of smallpox would arise and an alarm sounded.

Assume that perhaps 100 persons have 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 hospital beds in the metropolitan D.C. area which provide adequate isolation. And who would care for the patients? Few hospital staff would 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, perhaps with few isolation precautions because an infectious disease was not suspected.

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, depending on how wide the net for possible contacts was extended. What measures should or would be taken to deal with them. Would they be isolated as in Yugoslavia and if so, where? Or would they simply be subjected to daily checks to determine if they had become ill? Where would one find the manpower to do this?

Logistics could be simplified if rapid, easily used laboratory tests could 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. It is urgent that vaccine be distributed as soon as possible because contacts can be protected even if vaccinated 3 to 4 days after exposure. Given the fact that cases may not be recognized for some few days after the rash begins and because of the time required to confirm cases and to trace contacts, there would almost certainly be no recourse but to launch a mass vaccination effort. Present reserves of vaccine would disappear within days 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. How have we prepared for this? Are infectious disease specialists and physicians in emergency rooms trained in early diagnosis of smallpox or have they even been alerted to the fact that smallpox might be a problem? Have provisions been made to provide training to laboratories in smallpox diagnosis? Is there a game plan as to how to manage an epidemic such as this? What is to be done if more vaccine is needed?

(IDSA PAPER)

Speculate upon the ramifications of even a modest-sized release of anthrax spores in a city of perhaps 1 000 000 persons. Emergency rooms would begin seeing a few patients with high fever and some difficulty breathing after perhaps 3 to 4 days following exposure. Although essentially all would be dead within 24 to 48 hours, it is probable that a delay of at least 3 to 5 days would elapse before a definitive diagnosis were made. No emergency room physicians or infectious disease specialists have ever seen a case of inhalation anthrax and would probably not suspect this diagnosis unless they had been forewarned of this possibility-- and few so far have been so warned. Medical laboratories have had effectively no experience in diagnosing anthrax and, except for a recent article describing the Sverdlovsk cases, pathologists have neither been alerted nor trained to recognize the classical picture of

inhalation anthrax.

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? Note, however, that there is, in fact, little vaccine available and no plan to produce more 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 should fever or cough, however mild, occur? Undoubtedly, there would be many persons with such symptoms, especially in winter, but 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 -- and what the reaction of that population might be toward health officials, most of whom at this point in time would have no idea as to what the appropriate responses might be?

To say that we are today ill-prepared to deal with a terrorist attack which employs biological weapons is to state the case optimistically. To date, the focus of concern for civilian populations has been on chemical weapons and a response which is, at most, a modest extension of existing hazmat capabilities. This is of special concern because 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 soon be directed to stabilization and recovery. Not so following use of smallpox or anthrax as biological weapons. Day after relentless day, additional cases could be expected -- and in new areas. The dimensions of the problem would not become clear for a matter of weeks. Meanwhile, demands that government respond decisively would rise. Innumerable false alarms could be expected suggesting that

the problem involved many more people and a far wider geographic area than was, in fact, the case. And, for both diseases, there are, at best, limited preventive or palliative measures which, at this time, could be taken. It is not a pretty picture and thus I echo Bill Nagle's concern that we are nowhere near being adequately prepared for biological terrorism. We have, in fact, not even seriously considered the implications of biological weapons if applied to civilian populations.

It is obvious that a great many steps need to be taken but little has been said at this meeting about many of the most important, including the need for:

1) A serious planning exercise to examine potential threats of biological agents as terrorist weapons, possible responses and needs.

2) Greatly expanded support for national reference, diagnostic and research capabilities, especially at NCID and USAMRIID

3) Strengthened state surveillance capabilities utilizing federal personnel as necessary.

4) Expansion of the capabilities of state health department laboratories for reference diagnosis and training.

5) Training of infectious disease specialists and emergency medicine physicians to recognize the principal diseases likely to be associated with bioterrorism.

6) Added research support to identify practical, simple, rapid diagnostic methods for use in major hospitals.

7) An expanded basic research capability in vaccine development and disease pathogenesis to facilitate provision of better methods for detection of agents and rapid production of vaccines

8) A greatly expanded collaborative international research program dealing with new and emerging infections to contribute to our knowledge as to what activities are being undertaken in the world's laboratories and what threats need to be anticipated.