

The Smallpox Vaccination Plan: Challenges and Next Steps

Bill Number: Oversight Hearing

Hearing Date: January 30, 2003

Witness:

William J. Bicknell, MD, MPH

Boston University School of Public Health

Boston, MA

Testimony:

Mr. Chairman, members of the committee, colleagues and guests, it is an honor to be invited to testify before the Health, Education, Labor and Pensions Committee. My name is William J. Bicknell, I am a physician with a public health degree, have served as Commissioner of Public Health in Massachusetts, am Board Certified in Public Health and Preventive Medicine and have been a Professor of Public Health and International Health at Boston University's Schools of Public Health and Medicine for over 20 years. Most recently I have been a proponent of careful, selective, progressive and, ultimately, widespread, pre-exposure vaccination as the best way to protect the nation against the threat of a bioterrorist attack using smallpox as a weapon.

Issues of national security, economics and economic disruption, medicine, public health, and labor/management issues often get confused as we discuss smallpox. This is complicated by misunderstanding of the facts, confusion of fact and opinion and, finally, honest disagreements as to the correct course of action. And, as we consider smallpox, it is important to remember that it is just one of a number of bioterrorist threats.

CONTEXT

First let me provide some context. Smallpox (Variola) is very contagious with a 30% overall fatality rate in persons who have not been vaccinated. 60% to 80% of survivors are disfigured. There is no treatment. It is a terrible disease and an excellent weapon. The threat is widely believed to be real but cannot be quantified. However, as the consequences of a terrorist release of smallpox on an unprepared nation have the potential to be devastating, preparation is essential.

Many of us were vaccinated years ago. This decreases the likelihood of vaccine complications and may provide some very limited immunity to smallpox. From a personal or public health perspective the only significant benefit of vaccination 10 or more years ago is a further reduction in the already low rate of vaccine complications in adults. More about this shortly. The important point is anyone who has been vaccinated over 10 years ago cannot count on being protected from smallpox.

The nation is far better prepared today for a smallpox attack than it was even a few months ago. The three phase plan announced by the President in December is prudent and makes excellent sense. A tremendous amount has been accomplished and Drs. Fauci and Gerberding deserve to be congratulated for their leadership and excellent work. We now have sufficient vaccine to protect everyone and Vaccinia Immune Globulin (VIG) to treat the treatable complications of vaccination. The President's policy, as announced in December, if it is fully and well implemented and if we move rapidly with no discernable pause from Phase I to Phase II, will give us the ability to rapidly control a terrorist generated outbreak of smallpox. But we are not yet ready. Before addressing the

remaining issues and problems, I would like to summarize some facts about smallpox vaccination.

VACCINATION – SOME FACTS

Smallpox was eradicated in the 1970s after many years of great effort. At that time the immunity level of the general population was very high and most people in Africa and Asia were far less mobile than our population today. Today's American population is substantially non-immune and highly mobile. No one has any experience in dealing with an outbreak of smallpox in this very different and dangerous context. The unquantifiable but real risk of attack and our highly mobile and substantially non-immune population requires us to plan for a worst-case scenario, not a desirable or not too bad scenario. Managing less is easier. However, terrorists can do their job well. We know this. Planning for less than a worst case could be disastrous.

As we consider the possibility of attack, we must think beyond the tragedy of deaths and disfigurement and recognize the consequences of substantially shutting down commercial activity for weeks or more. In addition to domestic disruption, it would be reasonable for other countries to ban all arrivals from and departures to the United States. If panic, civil unrest and martial law were to ensue, the adverse consequences to the United States will be immense, horrible and incalculable. My most fundamental message to the Committee is we must rapidly complete Phase I and, without pause and with contemporaneous evaluation of Phase I results, move rapidly and without delay into Phase II of the President's plan. In my judgment, basic protection of the nation will not be sufficient until Phase II is completed.

As Dr. Henderson, former director of the worldwide smallpox eradication program, said in 1999: "One can only speculate on the probable rapidity of spread of the smallpox virus in a population where no one younger than 25 [now ~30] years of age has ever been vaccinated and older persons have little remaining residual immunity."

Does vaccination work? Yes, it is very effective and prevents smallpox. Dr. Henderson and his colleagues demonstrated this dramatically with great benefit to mankind.

The vaccine (vaccinia virus): We have enough for everyone living in the United States. The new Acambis product is expected to have a similar risk profile to the "old" recently relicensed Dryvax product. Newer vaccines that may be safer are still 2 or more years away. Drs. Fuci, Gerberding and Monath know far more about this than I. They too are far more qualified than I to comment upon the likelihood and risks of genetically engineered smallpox variants.

How safe is the vaccine? 14,168,000 persons were vaccinated in 1968, with 9 deaths, 7 of them in children. The 2 deaths in persons over 10 were a teen (age 16) with aplastic anemia and an adult (age 62) with leukemia. Using today's guidelines we would not vaccinate any children, and we would screen out and not vaccinate the teen and the adult. Deaths in children and sick adults can be expected not to occur today. In 1968 there were 114 cases of accidental vaccination of others with 1 death (a child). Mostly these were child-to-child transmissions (70%) and the balance (26%), with 2 or 3 exceptions, were between parent/grandparent and child. There is substantial historical evidence of safety in adults from the US military since World War II, the Israeli Military in the early to mid

1990s, and the recent Israeli civilian experience, There have been no reports of vaccine related deaths.

However, we do not have to rely entirely on historical data or recent Israeli experience. As of January 27, over 2000 military hospital workers have been vaccinated, including staff at Walter Reed. This very sophisticated, modern hospital has a hematology/oncology ward, transplant unit and neonatal intensive care unit. These are all areas where you would not want to accidentally spread vaccinia virus from recently vaccinated workers to patients. This has not happened. Vaccinated health care workers continued caring for patients using semi-permeable membrane dressings, long sleeves, and scrupulous hand washing. The semi-permeable membrane dressing reduces the shedding of vaccinia virus from the vaccination site into the environment by 95% to 99%. In addition, patient contact with recently vaccinated workers was minimized in the hematology/oncology ward, transplant unit and neonatal intensive care unit.

Primary or first-time vaccinees receive 3 jabs of the special bifurcated needle and 97% have a successful vaccination or take rate. Persons who had been vaccinated years ago (revaccinees) receive 15 jabs and have a 99% take rate. Sick leave day(s) off are taken by 4% of primary and 1.5% of revaccinees. Almost all sick leave has been 1 to 2 days off with 1 day being the most common. The military use the semi-permeable dressing for hospital workers but not for troops who use a band-aid. This is consistent with the CDC guidelines. Complications have been minor and are occurring at the expected rates. Full data on our military are still classified as to numbers but CDC and FDA have this information and, in terms of complications and absenteeism, there is nothing to suggest anything much different from the above.

It is very important to remember that many of the military are first-time vaccinees, a group at higher risk of vaccine complications than revaccinees, and similar to a well screened group of civilian health workers. In only a few weeks we will have recent hard, current data on serous complications, minor complications and absenteeism. However, everything to date suggests that the widely reported fears of some health workers either for themselves, their families or for their patients are not well founded.

As our recent experience with adult first-time vaccinees is somewhat limited, the plan to vaccinate 500,000 military and 500,00 civilian first responders will expand our experience base and, I believe, put to rest many fears. We are observing and evaluating as we go. We can contemporaneously, without pausing, adjust policy if the risks are greater than expected. Otherwise, we can and should rapidly move to 10,000,000 in Phase II, continue collecting data, recalibrate if needed, and finally make vaccination available to the general adult public. Anything less than completing Phase II is half-built protection. If a hospital, city or state chooses to do less, it is at higher risk, becomes a preferred target and weakens national defense.

It is worth remembering that those at greatest risk of vaccine complications are also at greatest risk of dying from smallpox. Thus, the more we do careful screening, education and vaccination pre-attack, the more the most vulnerable among us will be protected.

CHILDREN & SMALLPOX VACCINATION

Fatality rates from smallpox in children can approach 50%. Children are one of our most cherished assets. Gareth, my 2 and 1/2 year old grandson is certainly at the center of my life. So why not vaccinate children now, before an attack? The reasoning goes like this:

1 – The worst complications and the most deaths from vaccination, including deaths in otherwise healthy children, occur in children under 10.

2 – Arguably the worst complication – Post Vaccinal Encephalitis (PVE) - cannot be predicted and cannot be treated. This is rare and occurs most commonly in young children (15 of 16 cases in 1968). In 1968, 4,900,000 children under 10 were vaccinated for the first time, only 15 got PVE (0.0003%), but 4 died (26%) and 4 had complications including brain damage and paralysis of the arms and legs.

3 – Children are most likely to be accidentally infected or accidentally vaccinated by others. In 1968, with a total of 14,168,000 vaccinations (39% primary vaccinees) there were only 114 reported cases of accidental vaccination of others with 90 of these cases (79%) occurring in children. Children are most commonly infected by another child (70% of cases) or by an adult caregiver. 96% of the cases where one person accidentally vaccinated another were either child-to-child or between caregiver and child. Only one occurred in a hospital setting where a recently vaccinated nurse cared for a child with active eczema. This is also a good example of why it makes sense to use the semi-permeable membrane dressing and schedule recently vaccinated staff not to care for patients, such as eczema and immune disorder patients, at high risk of accidental immunization.

4 – Complications in children, ranging from mostly minor to, very rarely, severe, are quite common. For a mother often any complication is seen as severe, even though in the grand scheme of things it may be inconsequential. My own son had a smallpox vaccination complication in the 1960s, I don't remember it, his mother does! Based on 1968 data, children under 1 can expect to experience 1 complication for every 8,900 vaccinated, for children from 1 through 9 years of age the expected complications would be about 1 in 12,000. This is a lot of complications even though the vast majority would not be severe.

5 – Post-attack, children are far easier to isolate than adults. In a smallpox emergency we would say stay home until your local vaccination point is ready in somewhere between 1 and 5 days. Hopefully, this will be closer to 2 or 3 days. Then children will be rapidly vaccinated and protected before they are infected. The benefits of vaccination would now greatly exceed the risks.

6 – The more adults that are vaccinated pre-attack, the less likely it is there will be widespread transmission and transmission to children post-attack. In my judgment, this is a good reason to modify Phase III of the President's plan and move from allowing adults in the general public to be vaccinated to encouraging adults to be vaccinated.

What would I do for my family? I want the adults vaccinated or revaccinated so long as they had no contraindications. I'd say no for any children under 10. And I would want a tested and proven mechanism in place for rapid post-attack vaccination of every remaining unvaccinated adult and all children so that smallpox deaths would be reduced to a minimum (In a post attack scenario there are very few contraindications to vaccination.). In my judgment this approach offers the best protection with the least risk, pre- and post-attack, for children, adults and the nation.

A NOTE ABOUT MODELS

There are many mathematical simulations or models of a smallpox attack extant. They are confusing to many. However, it is my understanding, with the possible exception of one model, that, when the assumptions are well understood and corrections are made so

that the populations being considered are comparable, the results from various models are remarkably similar and favor the President's plan. If and as further modeling takes place and is used to inform policy and to test the feasibility of alternative program structures at the federal and state levels, it is vital that models be reality based and comprehensible with clear and explicit assumptions. The work of Ed Kaplan (Yale), Larry Wein (Stanford) and David Craft (MIT) is exemplary and their expertise represents a real national resource in this area.

JURISDICTIONAL ISSUES

These are non-trivial. The Homeland Security Act may have eliminated these concerns at the federal level, but perhaps not. At the state and local levels, jurisdictional issues remain. A colleague (Ken Bloem – He has led several leading academic medical center hospitals across the country) and I have been working on a concept that recognizes the unique problems in coordinating a response to bioterrorism events in the United States. Our constitutional division of responsibilities between the federal government and the states is only one complication. There are overlapping agency jurisdictions at the federal, state and local levels and we have a highly unusual blend of private and public organizations whose activities must be coordinated.

We are considering an approach that would use an incident command structure with incident commanders who may not be traditional public health professionals, but would simultaneously be federal and state employees reporting directly to the governor of a state and to a deputy or under-secretary in Homeland Security. These issues are not the subject of this hearing but they are of vital importance and I mention them only to highlight their importance. We now have all the material things needed to control a smallpox attack. It is time to imaginatively and realistically address the organizational and human issues that are essential for an effective response.

LIABILITY

I will not address liability as great progress has been made in this area and others are far more expert than I.

SERIOUS MYTHS & MISCONCEPTIONS

1 – The smallpox vaccine is so dangerous it should not be used before an actual case of smallpox occurs – WRONG.

There are differences of opinion. However, the historical data and current experience demonstrate that with careful screening, the use of the semi-permeable membrane dressing and limiting vaccination to healthy adults, the risks of severe vaccine complications and particularly deaths can be reduced to extremely low levels. These levels are far below the levels of many avoidable risks we all accept on a daily basis and far lower than what many health professionals are anticipating.

It is essential to distinguish between vaccine side effects in children under 10 and all others as well as between first-time vaccines and repeat vaccinees. Children under 10 are at highest risk, repeat adult vaccinees are at lowest risk. Deaths in healthy adults, whether previously vaccinated or not, can be expected to be extremely low.

2 - A contagious smallpox patient is always visibly sick with a rash so there is no risk to health workers if a person infected with smallpox is not obviously sick with a rash – WRONG.

CORRECT – Transmission can occur without a visible rash, with the person not feeling well but not so sick as to preclude travel and walking around.

3 - Vaccinating within a 2, 3 or 4-day window after exposure may/will prevent disease - WRONG.

CORRECT – Vaccination within 5 days of exposure may prevent death, and probably results in less serious disease (lower fatality rate), but there is little to no evidence that vaccination after exposure prevents disease.

4 - If doctors are just properly trained they will be able to quickly identify the first case or two of smallpox –WRONG.

First case(s) will be diagnosed late: Smallpox doesn't look like much until day 3 or 4. Confirming may take another day or two. Once the first case is confirmed, there will be over-diagnosis. No amount of training can prevent this. As rapid diagnosis cannot be assured, and it would not be surprising if it took longer than 3 or 4 days, this is an additional compelling reason for rapidly completing Phase II of the President's plan.

5 - Identifying individual cases, tracing contacts with targeted vaccination of contacts, isolation and quarantine (Often called “Ring Vaccination”) is the preferred strategy to contain a smallpox attack – WRONG.

In any serious terrorism scenario, this will not work. See the comparison of post-attack ring vaccination and immediate mass vaccination by Kaplan, et al. With ring vaccination, we can also anticipate failure of quarantine, serious disruption of commerce and quite possibly civil unrest. As the first case or two are identified and obvious case contacts are vaccinated, we should simultaneously ramp up for local mass vaccination in the area of the first case(s) and be ready for more widespread national mass vaccination if a case occurs in a second geographic area.

All of the above have substantial implications for planning pre- and post-attack national control strategies.

I submit as part of my written testimony a recent article by Dr. Ken James and myself that carefully reviews and considers many of the issues I have been raising during this hearing. It proposes a framework not only for the US but also for other countries to consider as they, too, face the possibility of smallpox. I also include a recent article by Warren Kaplan, Esq. that, although using Massachusetts as an example, takes a national perspective on federal and state legal issues as they impinge upon mounting an effective response to the bioterrorism threat.

THE PREFERRED NATIONAL STRATEGY

1 – Pre-Attack: Implement the President's plan in a timely manner with real-time evaluation of Phase I results as we move immediately to Phase II. There is no argument for delay and protection is not adequate until Phase II is complete. I would more actively encourage vaccination of the general population once first responders have been vaccinated. This will decrease post-attack transmission, decrease panic and make post-attack control much easier. I would also consider using the semi-permeable membrane dressing for everyone who is vaccinated not just hospital workers. Why not decrease the risk of accidental vaccination to the lowest possible levels?

2 – Post- Attack: With one or two cases in the nation, I recommend: A) in the area where the first case(s) occur immediately vaccinate obvious contacts and simultaneously initiate mass vaccination; B) mobilize for national mass vaccination; and C) move to national mass vaccination if there are any cases in a new geographic area. .

REMAINING PROBLEMS

Clear, concise, accurate information to the public and to the medical and public health community is needed. This is getting better but further improvement is essential. Open, honest, direct and forthright communication including acknowledging uncertainty and errors are essential to gain and maintain the trust of the public in government.

Although we have all the material to control an outbreak of smallpox, administratively, we are far from ready. Mass vaccination tomorrow would be chaotic. Who is in charge and who should do what are often not clear. Plans should emphasize simple methods and procedures that recognize we will be vaccinating in a big hurry. To do this well requires not just advance planning, but the elegance that comes from simplicity.

Finally, the public health system is, by its nature and culture, not an emergency response system and never has been. We need to consider an integrated federal-state incident command structure with Emergency Medical Services and the acute care system taking the lead role for mitigating the adverse health impact of any bioterrorism event. In this conceptualization, public health, particularly laboratories and epidemiologic intelligence, would play an essential supportive, but not directive, role.

Of the utmost importance, if smallpox or some other bioterrorist threat becomes a reality, we must be certain our plans will work. Therefore, we must move to rapidly complete Phase II of the President's plan, and whatever our ultimate organizational structure, we must realistically and regularly test our post-attack plans.

CONCLUSION

This is a terrorist threat we have anticipated and can largely prevent. The nation has made tremendous strides in the past 16 months. The President's plan is sound, takes the teeth out of the smallpox weapon and decreases the smallpox risk for us and the rest of the world. But we must keep moving. We can simultaneously be prudent, avoid needless risk and move ahead rapidly.

Putting the President's smallpox control plan into effect is but one step in a long and arduous journey on the road to improved national protection against a variety of bioterrorist threats.

Finally, as was the case with the interstate highway program and the space program, I believe we can look forward to many positive and unanticipated benefits to our bioterrorism preparedness initiatives.

Thank you for offering me the opportunity to testify. I welcome questions.

William J. Bicknell, MD, MPH

Professor of International Health, Socio-Medical Sciences, and Community Medicine

Department of International Health

Boston University School of Public Health

715 Albany Street, T4W

Boston, MA 02118-2526

USA

Cell Phone: (1) 617-283-5775 (with voice mail)

Email: <wbicknel@bu.edu>

Main Office Phone: (1) 617-638-5234

Fax: (1) 617-812-5834