

Smallpox and Bioterrorism Why the Plan to Protect the Nation Is Stalled and What to Do

by William J. Bicknell, M.D., and Kenneth D. Bloem

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The Iraq war is over, no weapons of mass destruction (WMD) have yet been found, and the president's smallpox plan, though sound, is running out of steam. Instead of being well on the way to protecting the nation's civilian population by vaccinating up to 10 million health, emergency, and public safety workers, we are stalled at 37,971 vaccinated civilians while the military has successfully and safely vaccinated more than 450,000 people. Moreover, whether or not WMD are found in Iraq, it is only one of a number of nations on the list of suspects.

Of all biological weapons, smallpox has the greatest potential for doing widespread harm. Given that the risk of death or serious harm to anyone from any form of terrorism is very low, we should live our daily lives normally, not in fear. However, to do that we need to be sure that our government is taking effective steps to reduce the chances of terrorism and, when it occurs, to minimize its consequences. Even though there is

enough vaccine for everyone, we are ill prepared to rapidly contain smallpox after a bioterrorist release.

Although Centers for Disease Control and Prevention (CDC) guidelines have recently improved, they continue to overstate the risk of side effects of the vaccine and erroneously suggest that, after an attack, the techniques used decades ago to eradicate smallpox will work well today.

Medicine and public health are very risk-averse professions in our risk-averse culture. We have not yet realized the complexity and difficulty of vaccinating millions of Americans rapidly after an attack. Nor have we come to grips with the need to make rapid, possibly draconian, post-attack decisions based on limited data of uncertain quality. That type of decisionmaking runs counter to the culture of public health.

The Bush administration needs to revitalize our preparations for a smallpox bioterrorist event.

William J. Bicknell, M.D., MPH, is a former commissioner of public health in Massachusetts and professor of international health at Boston University School of Public Health. Kenneth D. Bloem, former CEO of Stanford University Hospital and Georgetown University Medical Center, participated in the smallpox eradication program in the Congo and Bangladesh.

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The President's Plan

The September 11, 2001, terrorist attacks, followed by several anthrax mailings in the fall of 2001, forced many Americans to recognize their vulnerability to various bioterrorist threats. Smallpox, in particular, had a long history as a devastating disease before its eradication in the 1970s. Recently, it has captured the attention of homeland security planners, who view it as one of the most likely and deadliest agents for bioterrorism. Federal government officials initially considered a program of modest pre-exposure vaccination to protect against deliberate release of the smallpox virus by bioterrorists.¹ That approach was superseded when the White House announced a more ambitious plan on December 13, 2002.

Phase I of the president's plan called for the voluntary vaccination of approximately 500,000 health workers, 18 years old and older, by mid-January 2003.

Phase II called for the voluntary vaccination of up to 10,000,000 health and emergency workers in the following 90 days.

Phase III, to begin in mid-2003, would make the vaccine available to, but not recommended for, the general adult population.

The plan also called for the immediate vaccination of up to 500,000 members of the armed forces.² As of June 25, 2003, the military had vaccinated more than 450,000 individuals; the civilian program had vaccinated only 37,971 people by July 18. Some states had suspended their programs while awaiting guidance from the Centers for Disease Control and Prevention (CDC) on how to screen for cardiac conditions. In the District of Columbia, 105 people have been vaccinated, in Chicago 70, and in Massachusetts 120.³ The civilian numbers are not reassuring.

What Are the Specific Objectives of Pre-Exposure Vaccination?

We have not found the specific objectives clearly articulated in any one place. From various White House, Department of Health and Human Services, and CDC announcements, we glean these probable objectives:

Phase I

- Vaccinate sufficient vaccinators so that, if there is an attack using smallpox, the entire country can be vaccinated within 10 days.
- Vaccinate sufficient first responders to identify, pick up, and transport patients with suspected smallpox to hospitals.
- Vaccinate enough hospital workers in acute care hospitals so that, if a hospital receives a smallpox patient, it will be able to use staff personnel who are immune to smallpox to treat that patient.

Phase II

- Vaccinate as many additional acute care workers as possible to decrease the transmission of smallpox in hospitals and to ensure that essential emergency medical, police, and fire services can continue without emergency workers being either at risk of smallpox or at risk of transmitting smallpox. Once Phase II is completed, whether the event is small and inept or major and multifocal, the nation will be well prepared to rapidly respond to and stop an outbreak of smallpox.

Phase III

- In mid-2003, after Phase II is completed, permit, but do not recommend, vaccination of any healthy adult. This approach both allows informed adults to make their own risk/benefit decision and increases population immunity.

When Phases I and II are completed, whether the event is small and inept or major and multifocal, the nation will be well prepared to rapidly respond to and stop an outbreak of smallpox. If and as the general adult public opts for voluntary vaccination in Phase III, post-exposure control becomes even easier and faster. There will be fewer people to vaccinate, and, as the number of people susceptible to smallpox will be reduced, disease transmission will be slowed.

Does the President's Plan Make Sense?

The answer is yes. Why is the plan sensible?

First, it is phased and selective. Limiting vaccination to healthy adults dramatically reduces the risk of serious vaccine side effects. Second, by starting with 500,000 military personnel and a similar number of civilians, we develop current data about the risks of vaccination and can easily modify the plan if actual risks exceed those expected. Third, when Phase II is complete, there will be enough people vaccinated to vaccinate the balance of the population on a voluntary basis within 10 days from the time the first case is identified. Finally, and of great importance, hospitals and emergency services will be able to continue to operate while intensive mass vaccination is taking place. After an outbreak is recognized, the vast majority of people are highly likely to accept voluntary vaccination. At that point there will probably be no need for mandatory vaccination and its attendant problems.⁴

The pre-attack plan is correctly limited to healthy adults, as the risk of serious complications and death from vaccination is substantially higher in children. However, the age for vaccination could safely be dropped to 10 years, as the overwhelming majority of deaths and severe complications from vaccination occur in children 9 years of age or younger.⁵ If we are prepared to vaccinate rapidly after an attack, children can be isolated at home for a few days until they can be vaccinated. This approach avoids a number of serious and some fatal complications of vaccination in children that would likely occur if done pre-attack, while minimizing smallpox cases and deaths post-attack.

Why Is the Plan Stalled?

The problems are not exclusive to any one group or agency. The administration, as we discuss in more detail below, has never provided clear objectives or the rationale underlying the plan. Once announced, the plan was perceived by many people as not being a high priority for the administration. That perception was heightened when liability and compensation issues were addressed too late and little atten-

tion was paid to concerns about funding hospitals and health departments for costs related to vaccination. In addition, many medical and public health professionals continue to make three mutually reinforcing errors:

- Not distinguishing between the risk of vaccination in healthy, well-screened adults and the risk to children and high-risk adults.
- Not adequately recognizing the difference between naturally occurring disease and disease introduced by bioterrorism. For example, no one has epidemic-control experience with smallpox in a nonimmune, highly mobile population where exposure will be malicious rather than benign. The relevance of lessons from the eradication experience (characterized by very different circumstances) is limited.
- Not sufficiently appreciating that the decision to undertake pre-exposure vaccination is far more than a medical decision about the risks of vaccination. Of equal or greater importance, it involves social, economic, and national security considerations, as shown schematically in Figure 1.

It is important to emphasize that assessing the risk of attack is a national intelligence estimate, not a medical or public health estimate.

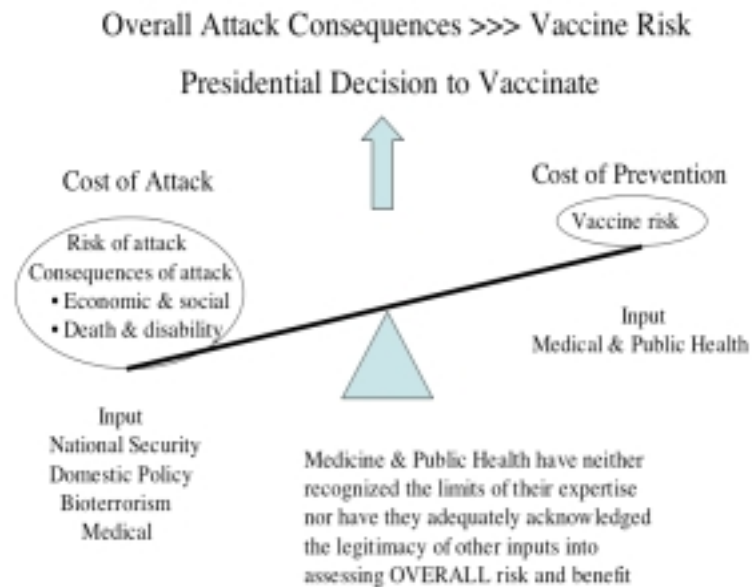
Before addressing in greater depth the reasons why the plan is stalled, it is necessary to review the nature of the threat and some facts about the risks of vaccination.

The Threat

Smallpox (*variola major*) is a deadly scourge with, at present, no known treatment. It has an overall mortality rate in the unvaccinated of 30 percent and leaves 60 percent to 80 percent of all survivors permanently disfigured. Smallpox has death rates in the very young and the elderly approaching 50 percent. An effective live virus vaccine is available that rarely results in death but somewhat less rarely causes severe complications.

The decision to undertake pre-exposure vaccination is far more than a medical decision about the risks of vaccination. It involves social, economic, and national security considerations.

Figure 1
The Weight of the Evidence



The last naturally occurring case of smallpox was identified in 1977 in Somalia, and the last case, a laboratory accident, occurred in England in 1978.⁶ The United States and Britain already had stopped routine childhood vaccination in the early 1970s. The world was declared free of smallpox in 1980 by the World Health Organization.⁷

Smallpox had been weaponized by the Soviet Union.⁸ Weaponized virus may have been taken from the former Soviet Union, and stocks of virus may not have been destroyed by some countries, as called for by WHO in the late 1970s.⁹ The former WHO director of smallpox eradication, Dr. D. A. Henderson, summarized the threat 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 years of age has ever been vaccinated and older persons have little remaining residual immunity."¹⁰ The former deputy director of the Soviet Biological Weapons Program considers it certain that North Korea possesses the smallpox virus and probable that Iraq does, too.¹¹ Vaccination of North Korean and Iraqi troops has also been reported.¹²

Bioterrorism, particularly with smallpox, became a pressing U.S. and international issue after September 11, 2001. The call for pre-exposure vaccination came quickly. The head of Russia's Vektor Institute, which has functions similar to those of the CDC, urged widespread immunization against smallpox.¹³ The British government bought enough vaccine for 50 percent of the population. Germany purchased 6 million doses, and Israel vaccinated approximately 18,000 first responders and medical workers. The U.S. government considered the threat sufficient to purchase vaccine and vaccinia immune globulin (VIG) for all Americans in preparation for a possible smallpox attack. By late 2002 the United States had sufficient smallpox vaccine to immunize and VIG to manage the complications of vaccination for the entire population.¹⁴

It is tempting to think that, with the Saddam Hussein regime gone, the risk of a bioterrorism attack by any agent is substantially reduced. That may be the case. However, it is also plausible that the escaping Iraqi regime took away small but sufficient amounts of smallpox virus for bioterrorism purposes and has long since sequestered them

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in jurisdictions far from Iraq. Furthermore, the smallpox risk has never been thought to be limited to the Hussein regime. In any case, as was true before the Iraq war, the decision regarding post-Iraq smallpox as a national security risk is for the intelligence community to assess, not for medical and public health personnel. Those personnel need to consider other types of risks.

The Risks of Vaccination

What Is the Real Risk of Vaccinating Healthy Adults?

There are three particularly relevant historical data sources. The 1963 and 1968 U.S. national vaccination surveys include the number of persons vaccinated by age, vaccination status, and type of complication.¹⁵ The review by Lane et al. of vaccine deaths in the United States from 1959 to 1966 and 1968 details vaccine complications, but, as the data were not available for all years studied, it does not specify the total number of persons vaccinated.¹⁶ Considering all adults and children, both first-time and repeat vaccinees, 14,014,000 people were vaccinated in 1963 with seven deaths, and, in 1968, 14,168,000 with nine deaths. As vaccination was being done routinely, there is no reason to think that either more or fewer people were vaccinated in years other than 1963 and 1968. Lane found 68 deaths or an average of 7.5 deaths a year for the nine years he studied. It seems reasonable to conclude that the historical risk of death (adult and child) is closer to 1 death per 2 million than the 1 or 2 deaths per million that CDC continues to report.¹⁷

As the current national plan is limited to voluntary vaccination of healthy adults 18 and older, it is particularly appropriate to look at the probability of deaths and complications in this age group. Lane found two primary vaccinees in the 10-to-19-year age group who died of postvaccinial encephalitis (PVE). One of those was 14 and is reported in the 1963 data. The other death did not occur in either 1963 or 1968, and the age cannot be determined. To be

conservative, we assume this person was in the 15-to-19-year age group. Lane also found two revaccinated adults who died of PVE (a 33-year-old woman and a 64-year-old man), both without underlying disease. As previously noted, vaccination was routine and ongoing for the nine years Lane studied. Therefore, we assume roughly the same number of persons were vaccinated in each of the years studied. Extrapolating from the numbers reported in 1963 and 1968 for ages 15–19 and for ages 20 and older, 10,405,000 individuals were vaccinated, for an average of 5,202,500 per year, or a total of just over 46,000,000 for nine years.¹⁸ To be conservative, we round down to 45,000,000, giving an estimated risk of PVE in adults of 3 per 45,000,000 or about 1 per 15,000,000. This is an exceedingly low risk. Even if this estimate is too low by half, the risk is still extremely small.

What about other vaccine-related deaths in primary vaccinees and revaccinees in the 15-and-over age group? There were a total of five other deaths, all of revaccinees, for the nine-year study period: three had leukemia, one had Hodgkin's disease, and one had a connective tissue disease (scleroderma) and was on steroids. Today, because of our appreciation of their increased risk and the attendant careful screening, people with those and similar diseases should be screened out as ineligible for vaccination.

What about serious complications with long-term effects other than death? A careful review of historical and current data supports the conclusion that when healthy adults are vaccinated, persistent, serious side effects are extremely rare.

In summary, in a nine-year period, eight adults died (three of PVE with no underlying disease, five others with underlying disease). The death rate in healthy adults may be as low as 1 in 15,000,000 vaccinees. It is quite possible, and would not be surprising, that when Phase II of the national plan is completed, we will have no deaths of persons voluntarily vaccinated, and it is likely we will have fewer than five deaths. The current U.S. military experience with 454,856 vaccinated personnel as of

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The already low risk of accidental vaccination of another person can be reduced further by careful screening and the use of the inexpensive and readily available semipermeable membrane dressing.

June 11, 2003, (71 percent were primary vaccinees and 29 percent were revaccinees) with no deaths and no long-lasting complications strongly supports the conclusion that vaccination of healthy adults is safe.

Accidental Vaccination of Patients, Family Members, and Other Contacts

Accidental vaccination may occur when a recently vaccinated person (whose vaccination scab has not yet fallen off) comes into physical contact with an unvaccinated person and transfers vaccinia virus from the vaccination site to the unvaccinated person. That can happen when the site on a recently vaccinated person rubs against another person or a recently vaccinated person touches the site and then touches a susceptible person. The classic situation is two children playing together in a sandbox and rubbing up against each other.

Accidental vaccination is a particular concern today, because we have a far higher number of persons whom we would deliberately not vaccinate pre-outbreak (for example, transplant recipients, as well as many patients on cancer chemotherapy, on systemic steroids, or infected with HIV/AIDS). Further, it is believed that eczema¹⁹ is substantially more common in the general population today than it was 30 or 40 years ago. Individuals suffering from eczema are more likely to get accidentally infected with vaccinia virus by close contact with a recently vaccinated family member, friend, or caregiver.²⁰ The consequences could be very serious, even fatal.

How big is this risk? The 1963 and 1968 data show that there were 200 reported cases of accidental infections of other persons as a consequence of vaccinating 28,182,000 persons. Only 25 cases, or 12.5 percent, occurred in adults, with no deaths. Historically, well over 90 percent of accidental vaccination of others occurs either from child to child or from child to caregiver or vice versa.²¹ Lane reports one case of a recently vaccinated nurse caring for a child with severe eczema and one of a recently vaccinated adult woman who slept with and infected a man. Both the child

and the man acquired vaccinia.²² Today the nurse would use a double semipermeable membrane dressing (described in the next paragraph), wear long sleeves, and not be working on a unit with such a child until the vaccination scab had fallen off, by which time the nurse would no longer be shedding virus. The other case would be harder to prevent, but the semipermeable dressing would reduce the risk of transmission by 95 percent. Under the Bush plan, health care professionals are not vaccinating children today, and they are urging people with children who have eczema at home either not to get vaccinated or to avoid close contact with the children until their vaccination scabs fall off.

The already low risk of accidental vaccination of another person can be reduced further by careful screening and the use of the inexpensive and readily available semipermeable membrane dressing. Because there is appropriate concern about accidental transmission to others, particularly the immunocompromised, reducing the shedding of virus from the vaccination site into the environment to the lowest possible levels makes sense. Shedding of virus after vaccination can occur until the scab dries and falls off the vaccination site (about 21 days). The semipermeable membrane dressing, available commercially as “Tegaderm+Pad” from 3M and “OpSite” from Smith & Nephew, significantly reduces the shedding of virus. Those products combine a gauze pad with a membrane that allows the passage of air but not the vaccinia virus. Shedding is reduced by 95 percent and can be further reduced to 99 percent or more if a second layer of membrane with no gauze is applied over the first bandage.²³ CDC advises that “only persons working in healthcare settings should use semipermeable dressings”; members of public health response teams not involved in patient care can keep their vaccination sites covered with a porous dressing (e.g., gauze).²⁴

Since the semipermeable membrane dressing is simple to use, relatively inexpensive, and greatly reduces the already low risk of transmission to others, why not reduce the risk of accidental transmission everywhere to the

lowest possible levels? CDC might further reduce the risk of accidental vaccination by recommending that everyone who is vaccinated pre-exposure, whether in Phase I, II, or III, should use this dressing, wear long sleeves, and pay careful attention to hand washing, particularly after touching the dressing or touching anywhere near the vaccination site.²⁵

We have not yet specifically considered the immunocompromised, burn, dermatitis, chemotherapy, and similar patients who are in the category of persons at greatest risk. In the *New England Journal of Medicine*, Kent Sepkowitz recently reviewed worldwide case reports of vaccinia spreading to others in home and hospital settings from 1907 until 1975. He found 12 instances of spread in hospitals, with the last death in 1952 in France. Sepkowitz makes the point that today the number of patients at risk in hospitals is considerably greater than in the first two-thirds of the 20th century. He also notes, "The current plan for an occlusive dressing at the vaccination site and other now-routine infection-control procedures, including hand hygiene and isolation for any patient with unexplained fever and rash, should effectively limit potential spread."²⁶ The U.S. military operates multiple major hospitals with wards containing burn patients and neonates in intensive care, as well as transplant and chemotherapy patients. All are at a higher than usual risk for accidental vaccination. The military approach has been to use the semipermeable membrane dressing for personnel with patient care responsibilities, to encourage long sleeves over the dressing, and, where possible, to rotate workers off high-risk units until they are no longer shedding virus. Between mid-December 2002 and mid-June 2003, the military vaccinated more than 12,000 hospital workers and accumulated 27,700 worker-months of clinical contact time with no transmission from health workers to patients.²⁷ That is reassuring. However, there is no doubt that hospitals should carefully think through staff assignments and infection control procedures as their workers are vaccinated.²⁸

Assuming Phase II of the national plan is fully completed and 10 million healthy adults are vaccinated, we estimate the number of people who may die because of accidental vaccination by exposure to a recently vaccinated person at less than one. Stated somewhat differently, most likely, no one will die. As there are an increased number of immunocompromised persons at risk of death from accidental transmission today, it is necessary to correct and increase this estimate. However, the estimate must be increased by *more than* a factor of 20 to reach one death. (See Table 2, note 1, for a detailed explanation of this estimate of risk.)

Two things have changed since vaccination stopped in the 1970s. There are more people at risk of vaccine complications, and infection control techniques have also improved. We consider both, but in the estimate above we have given more weight to increased risk than to improved infection control.

The bottom line: Voluntarily vaccinating healthy, well-screened adults, using the semipermeable membrane dressing for all who get vaccinated—not just health care workers—and urging all vaccinees to wear long sleeves until their vaccination scab falls off makes the national plan safe for everyone.

What about Recent Reports of Heart Complications?

Two different types of vaccine complications involving the heart (heart attack or ischemic heart disease) and inflammation of tissues around the heart (myocarditis) have been widely reported in the recent news.

One member of the military and four civilians had heart attacks within 5 to 17 days of being vaccinated. Three died. The patients were all older (ages 54, 55 [two cases], 57, and 64), with known preexisting heart disease.²⁹ Heart attacks are expected to occur in this age group. The question is whether vaccination increases the risk of heart attack. If the number of heart attacks expected from historical data is unchanged after vaccination, then it is reasonable to conclude there is no causal relationship between vaccination and heart attack. The military data strongly support

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We can continue to expect occasional cases of myocarditis with uneventful recoveries. Some will be due to vaccination and some to other causes. Deaths, if they occur, will be rare.

this conclusion. Historically, on an annual basis, the military would expect several heart attacks per week, and that rate has not changed since the smallpox vaccination program began.³⁰ The evidence to date supports the conclusion that older people, who normally have more heart attacks, are continuing to have them at the same rate since we began smallpox vaccination. However, CDC and the U.S. military are being cautious and have temporarily advised that people with a history of heart disease postpone getting vaccinated until the data have been further studied.³¹ As the aims of both the military and the civilian vaccination programs can be met without vaccinating persons with a history of heart and certain other diseases, this caution poses no threat to the integrity of the overall vaccination program.

Myocarditis is different. Historically, there have been very occasional reports of myocarditis after smallpox vaccination. Those cases were mostly mild with full recovery.³² However, a total of four deaths reported from Finland, the United States, Australia, and

Great Britain since 1947 can reasonably be attributed to myocarditis secondary to vaccination.³³ The most relevant experience involved 126 Finnish military recruits with myocarditis admitted to the central military hospital and carefully studied between 1976 and 1981.³⁴ Ten percent (12 cases) were considered caused by smallpox vaccination, and the remaining 90 percent were attributed to various other viruses and bacteria. All recovered uneventfully. This is the case to date with the 42 probable and 1 confirmed cases in the U.S. military and the 10 U.S. civilian cases (as of June 11).³⁵ The Finns found a myocarditis rate of 1 per 10,000 in their recruits, and the U.S. military rate is very similar.³⁶ The strain of vaccinia used to make the Finnish smallpox vaccine is different from the U.S. strain. It is related to the Lister strain, which has more side effects than the strain used in the United States (New York Board of Health strain).³⁷ We can continue to expect occasional cases of myocarditis with uneventful recoveries. Some will be due to vaccination and some to other causes. Deaths, if they occur, will be rare.

**Table 1
Smallpox Vaccination: Risk of Death of Healthy Adults**

Risk Group	Estimated Total Persons at Risk	Deaths	Death Risk
Recalculated historical risk of death for all age groups ¹	126,000,000	68	.5/1,000,000 or 1/2,000,000
Recalculated risk of death for people 15 and older with historical screening ¹	45,000,000	8	.2/1,000,000 or 1/5,000,000
Recalculated historical risk of death for people 15 and older with improved screening ^{1, 2}	45,000,000	3	.07/1,000,000 or 1/15,000,000

¹Recalculated risk based on nine years of data (see text).

²This calculation excludes 5 deaths (3 leukemia, 1 Hodgkin's disease, 1 scleroderma). The 45,000,000 figure does not change because the number of people in the historical denominator with scleroderma, Hodgkin's disease, aplastic anemia, and chronic lymphocytic leukemia was small and the denominator has already been rounded down by 1,800,000. Further adjustments are not needed and would also suggest a greater degree of precision than is the case.

Comparing Everyday Risks and Vaccine Risks

Tables 1 and 2 summarize the vaccine risks discussed above. Table 3 compares vaccine risk to the risk of dying on a scheduled commercial U.S. airline flight or the risk of an adult in the United States dying from an accident of any type in the next 10 years. Given that vaccination is no more than a once-in-10-years event, the comparison with the risk of accidental death from all causes in 10 years is reasonable.

We would not expect adults to get revaccinated more frequently than once in 10 years since the protection lasts about that long. Over the same 10-year time period, the risk of death from an accident of any type for an adult in America is 3/1000 or 3,000/1,000,000.³⁸ Thus, a

healthy adult is 42,000 times more likely to die from an accident in the next 10 years than from a smallpox vaccination! The risk of death on a scheduled domestic major airline is between 1 in 8 million and 1 in 10 million.³⁹ A healthy adult has less risk of death from a smallpox vaccination than from flying from Denver to Washington, D.C. And, as flying is far safer than driving, when most of us drive to work, to the movies, or to a vacation destination voluntarily, we expose ourselves and our companions to far more risk than a smallpox vaccination does.

The bottom line: vaccination of healthy adults is safe. In our judgment, the best policy guidance that the CDC can offer is: if you are a healthy adult who does not worry about driving to work, you should not worry about getting vaccinated or accidentally vaccinating another person.⁴⁰

A healthy adult is 42,000 times more likely to die from an accident in the next 10 years than from a smallpox vaccination.

**Table 2
Smallpox Vaccination: Risk of Death of Persons Accidentally Vaccinated**

Risk Group	Healthy Adults Vaccinated	Deaths	Risk of Death for an Unvaccinated Person/1,000,000 Vaccinated Healthy Adults
Projected deaths from accidental transmission to account for increased number of immunocompromised, etc. ¹	10,000,000 ²	< 1	.09/1,000,000 or 1/11,000,000

¹Based on 200 cases of accidental transmission and 3 deaths from 28,000,000 vaccinations in 1963 and 1968. As we are not vaccinating children, reduce accidental infection by 70 percent to 60 cases and, as we can use the semipermeable membrane, reduce by another 95 percent to 3 cases of accidental transmission. When accidental transmission occurred, the death rate in accidentally vaccinated persons was 3 deaths per 200 cases or 1.5 percent. Therefore the number of deaths expected from accidental transmission today would be less than one (3 cases x 1.5 percent = .045 deaths). In 1963 and 1968, 10,400,000 persons aged 15 and older were vaccinated. This is close to the target number for the end of Phase II of 10,000,000. The estimated 0.045 deaths per 10,000,000 also can be expressed as 0.0045 deaths of an accidentally vaccinated person per million healthy adult vaccinees or 1 death of an accidentally vaccinated person per 222,000,000 healthy adult vaccinees. As this estimate does not take into account the increased number of persons at risk of death from accidental transmission, we increase the estimate by a factor of 20 and are still at just under 1 projected death of accidentally vaccinated persons after vaccinating 10,000,000 healthy adults.

Using the same assumptions, but stating the case somewhat differently, a 20-fold increase in susceptibles would lead to 4,000 cases (200 x 12). Eliminating children reduces this by 70 percent to 60 cases, and using the semipermeable membrane dressing reduces the number by another 95 percent with the same result—less than 1 projected death of accidentally vaccinated persons after vaccinating 10,000,000 healthy adults.

²If 10,000,000 people are vaccinated in Phase II, then, with proper precautions, the number of deaths from accidental vaccination could be as low as zero and is unlikely to exceed five.

Table 3
Smallpox Vaccination: Risks of Everyday Living Compared to Risks of Vaccination

Risk Group	Deaths per Million	Comparative Risk
Healthy adults vaccinated once every 10 years	0.07/1,000,000	One death per 15 million healthy adults
Projected deaths from accidental transmission to account for increased number of immunocompromised, etc.	0.09/1,000,000	One unintended death of an unvaccinated person per 11 million vaccinated healthy adults
Risk of death from flying once on a commercial airline	0.1/1,000,000	Flying once has a 1.4 times greater risk of death than getting vaccinated, or 1 in 10 million
Risk of death in 10 years from any accident for an adult	3,000/1,000,000	The risks of everyday living are 42,000 times greater than the risk of dying from vaccination, or 1 per 333

Note: See text and the notes to Table 1 and Table 2 for an explanation of the numbers in Table 3.

An In-Depth Look at Why the Plan Is Stalled

Determining the reasons why the current national plan to vaccinate healthy adults is stalled involves not just correcting misperceptions of the risks of vaccination. It requires analysis of both immediate or obvious contributing factors and the subtler but perhaps more important underlying factors that must be understood if there is to be a timely, effective, and enduring fix.

First, medical and public health practitioners and the general public have received inadequate and confusing information about the risk of smallpox vaccination to healthy adults. Because healthy adults are the only group targeted in the national plan, this is a serious omission. CDC has never adequately distinguished between healthy adults who are at low risk of complications from vaccination and sick adults and all children, sick or well, who are at far greater risk of vaccine complications. Nor has CDC promoted

the wide use of the semipermeable membrane dressing, which greatly decreases the risk of accidental vaccination of others. Finally, the ease of control after an event, particularly the value of vaccinating after exposure to smallpox, has been both overstated and misstated.⁴¹

Result: The perception of vaccine risk by many medical and public health practitioners, as well as by the public, is far greater than the actual risk. Misperceptions remain about the spread and control of smallpox after a bioterrorism event.

Second, the executive branch has been slow in proposing or putting in place sufficient coverage for liability and compensation for anyone who suffers a serious complication or death, including persons who may become accidentally vaccinated by close contact with a vaccinated person as well as the institutions and providers who do the vaccinating. This barrier has now fallen, and on April 30 the president signed into law the Smallpox Emergency Personnel Protection Act of 2003.⁴²

The perception of vaccine risk by many medical and public health practitioners, as well as by the public, is far greater than the actual risk.

Result: Widespread hesitation to vaccinate or accept vaccination due to fears of absent or inadequate compensation for care of vaccine-related complications that may result in work loss, severe illness, and even death. (It is still too soon to determine the degree to which SEPPA will help solve this problem.)

Third, a surprising silence on the part of leaders in the administration from just after the president's announcement of his plan on December 13 until the week of March 10, when CDC director Dr. Julie Gerberding, Dr. D. A. Henderson, and the surgeon general were very publicly vaccinated (President Bush was vaccinated previously, on December 21).⁴³ But there still has been no good, easily understood, widely available explanation of the national plan.

Result: A perception that the national plan is neither well designed nor a high priority.

When those three factors are combined, far too many people reasonably and understandably, but erroneously, are prone to conclude that vaccination before an attack is too dangerous, its complications may not be paid for, and it probably isn't very important anyway. After adding to the mix the natural and appropriate caution of physicians making recommendations to patients, it is little wonder that not many people are getting vaccinated. But deeper and more subtle factors stand in the way of the national plan.

Root Causes of Delay

The threat of bioterrorism extends beyond smallpox. Many other agents such as anthrax, botulinum toxin, and plague, to name just a few, are on the list of potential threats.⁴⁴ The root causes of delay that we present below, although relevant to the smallpox program, are not limited to smallpox. Thus, some of the lessons we learn from smallpox should be relevant to our overall approach to planning for and managing bioterrorism events by any agent.

Malicious dissemination, whether of smallpox or other bioterrorism agents, is different from naturally occurring disease.

Though obvious, this distinction is vital. What we know from naturally occurring disease may help in bioterrorism planning, but it is insufficient and, in some cases, misleading. For example, what worked during the final years of smallpox eradication when population immunity was high, population mobility was much lower, and there was no malicious intent to disseminate is not likely to work today with bioterrorism. In today's communication environment, public awareness of a single case of smallpox will be worldwide within minutes, and demands for swift action will run ahead of response capacity.

We emphasize that many members of the public health, medical, and nursing professions are participating actively and working with diligence to prepare the nation for a bioterrorism attack, whether it involves smallpox or another agent. Further, we are not conspiracy theorists and do not believe any one person, group, or agency is conspiring to undermine the president's plan. Rather, a variety of interacting and mutually reinforcing factors best explains the delay.

Risk and Public Health

Ours is a risk-averse culture. Physicians and public health personnel are particularly risk averse and, for the most part, appropriately so. However, the increasing threat of bioterrorism demands a new paradigm for balancing unknown but real risks against the various costs and benefits of preparedness. This type of assessment is particularly difficult for physicians who often feel they are violating an ethical canon if they endorse a certain risk today, however small, to obviate an uncertain and unknown risk tomorrow. The justification for this attitude is the oft-quoted *primum non nocere*, or "first do no harm." This belief structure and cultural attitude facilitate focusing on the potential risks of vaccination, without considering the magnitude or societal consequences of those risks, ways to mitigate them, or any benefits that might offset the risks.

The CDC Advisory Committee for Immunization Practices and the CDC National Immunization Program seem uncomfortable

The increasing threat of bioterrorism demands a new paradigm for balancing unknown but real risks against the various costs and benefits of preparedness.

Every day, patients are asked to comprehend extremely complex risks and make judgments about them as they consider medical and surgical choices much more difficult and with far greater risks to themselves and others than vaccination.

with the thesis that an unquantifiable and probably low risk of attack nevertheless poses a serious risk to the population. Such a stance impedes consideration of the following important question: If there were to be pre-event vaccination, what are the risks to different subsets of the population? This determination falls fully within the expertise of ACIP and NIP. However, neither body has any special expertise in assessing national security risk (i.e., the risk of attack) or the social and economic consequences of a bioterrorism attack. They also have no special expertise in determining an appropriate plan for either pre- or post-event control.

Further, there seems to be a belief among some health professionals that assessing risk of attack and risk of vaccination is just too much for the average American, let alone health care early responders, to handle and that such assessment must be kept in the hands of experts. That assumption is well illustrated by a passage from an article by Lane and Goldstein published in March of this year:

We might allow citizens to make individual choices about obtaining vaccination after they have been given information about the risks associated with vaccination and potential threat of smallpox. Public health authorities would thus cede decisions on a policy with considerable technical ramifications to persons with widely varying abilities to comprehend and weigh the risks and benefits. The media and the medical profession would have to communicate an accurate portrayal of the data and options. In the absence of a known threat of smallpox exposure, this option would be dangerous to many potential vaccinees, their contacts, and the public health initiative. It would subject the population to a known risk for severe adverse events. The publicity about such complications might subsequently keep some persons from accepting vaccination if the need actually arises.⁴⁵

Every day, patients are asked to comprehend extremely complex risks and make judgments about them as they consider medical and surgical choices much more difficult and with far greater risks to themselves and others than vaccination. There is neither any basis nor any right for anyone in the public health and medical professions to assume that the public is not competent to make such decisions. It is essential to remember that the principle of individuals making their own decisions lies at the heart of our social fabric and system of government.

In the words of Thomas Jefferson,

I know of no safe depository of the ultimate powers of the society but the people themselves; and if we think them not enlightened enough to exercise their control with a wholesome discretion, the remedy is not to take it from them but to inform their discretion.⁴⁶

Contributing to the confusion between national security risk and vaccination risk is the belief held by some that no one in his right mind would ever use smallpox as a weapon. After all, it would spread all over the world and would come back to bite those who released it. Yet we need only remember that Soviet premier Mikhail Gorbachev in the late 1980s ordered smallpox warheads to be put on Russian missiles to replace some nuclear warheads.⁴⁷ It is foolish and naive to assume our logic and values are the logic and values of others, let alone terrorists.⁴⁸ The fact that few observers would have believed, before it happened, that a terrorist attack on the scale and scope of the 9/11 attack was plausible did not keep it from occurring.

Turf Issues

The initial vaccination plan proposed by CDC in late 2001 and early 2002 was viewed by the administration as inadequate. Responsibility for development of what became the president's plan was removed from ACIP and CDC by HHS and the White House. Now the same organization and many of the same people whose advice was rejected have been asked to imple-

ment a plan they did not develop. That unusual history may help to explain some of the delay and hesitation shown by CDC.

There have recently been clear signs of positive change. Information from CDC is improving, but it is not yet fully correct or adequate. The CDC website, a primary source of information for the several thousand state and local health agencies in the United States and worldwide, is much improved but still hard to navigate. On March 7 HHS, CDC, and the American College of Preventive Medicine sponsored a “Clinician Communication Briefing Summary” with HHS secretary Tommy Thompson, CDC director Julie Gerberding, and Acting Assistant Secretary for Public Health Preparedness Jerome Hauer as speakers under the headline of “Need to Accelerate the Smallpox Vaccination Program.”⁴⁹ The briefing confirmed the following:

- Terrorists have demonstrated the intent to inflict mass casualties on the United States, and they more than likely have access to smallpox.
- The administration is concerned that we are not yet prepared to ward off a smallpox attack and that we will not be able to respond if there is an attack.
- Smallpox preparedness, including the vaccination of health care and public health personnel who would serve on response teams, is a national security issue.
- HHS and CDC remain committed to conducting the smallpox vaccination program as safely as possible but stress the need to scale it up and speed it up in the current context of the situation in the Middle East and the rest of the world.
- HHS and CDC are asking clinician leaders to support the smallpox vaccination program and to assist other clinicians in health care facilities in making informed decisions about their willingness to volunteer for the smallpox vaccination program.

Those and similar developments are encouraging. However, much more is needed, and the day-to-day actions and behavior of professional

staff within CDC must become far more congruent with the direction set by the director of CDC and the secretary of HHS (see the discussion of problems with CDC guidance below).

This neither suggests nor requires mindless obeying of orders. Rather, it requires that the professional staff raise and argue different viewpoints and, when a decision is made, either agree and support the decision, ask for reassignment, or resign. As decisions of this type are argued internally, the different opinions should be shared with the public. Such openness builds public confidence in the decision finally taken.

Spillover Concerns

Other Immunization Programs May Be Set Back. Many professionals in the NIP and on the ACIP have devoted their lives to getting parents to immunize their children against a wide range of childhood diseases as well as getting adults to accept immunizations such as the influenza vaccine. They are understandably concerned that adverse reactions to smallpox vaccinations will spill over and result in the public avoiding other types of vaccinations that have fewer side effects. Thus, they may fear that real risks of diseases that we know are present and can be prevented will be increased as a consequence of the public’s reaction to adverse events that may be associated with vaccinating for a disease that has yet to reappear. Paradoxically, CDC, by its alarmist attitude toward smallpox vaccination, may be inadvertently fanning irrational fears of all vaccinations.

Smallpox and Bioterrorism Initiatives Undercut Far More Important Public Health Efforts. Some public health professionals feel that the entire bioterrorism initiative, and its smallpox focus in particular, take away from other far more needed public health programs and, without more specific additional funding for smallpox and bioterrorism, the fabric of public health is at risk. Certainly more funding dedicated for bioterrorism would be welcome, but these concerns are exaggerated. One of us (WB) is a former state commissioner of public health, who knows what it takes and is taking to

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respond to bioterrorism and smallpox. For example, it is frequently said that “everyone is working on smallpox.” That is a substantial exaggeration. The chronic cries of bureaucrats need to be dramatically discounted.

Budget cuts in public health funding, sometimes very severe, have occurred in many states. However, it does not follow that federal bioterrorism funds are or could be fungible and available for general support of public health at the state and local levels. Although a number of reports have observed that the unit cost of administering vaccine pre-event is high and possibly prohibitive, that is partly due to the inaccurate information about vaccine safety that keeps clinics operating at very low volumes. If clinic volumes were higher and integrated into routine immunization and other medical care activities, unit costs would be much lower.

Smallpox and bioterrorism are often seen as an opportunity to get new money. However, when public health officials make the unsubstantiated assertion that, for bioterrorism initiatives to succeed, it is necessary to strengthen the rather vaguely defined “public health system,” the argument is weak. What is the exact logic that links the “public health system” to effective response to bioterrorism? Further, what exactly is the “public health system,” and which parts of it are essential to an effective bioterrorism control program? Until those questions are answered convincingly and with precision, substantial new money is unlikely to flow to public health agencies.

There actually are some convincing answers. We strongly support enhanced public health laboratory capacity at the state level; enhanced disease surveillance and early warning systems; and strengthened, proactive, epidemiologic intelligence capacity at the state and local levels. Investing in those public health activities makes sense for an effective bioterrorism response, and it is a good example of a dual-use investment. For example, investment of this type could help with SARS and monkeypox today as well as in the identification and management of other diseases totally unrelated to bioterrorism but of public health importance.

Problems with CDC Guidance

Although we believe the burden of bioterrorism on state and local health agencies has been overstated, it is true that state and local efforts have been greater than needed because guidance from CDC has been confusing, needlessly complex, and sometimes wrong. One example will suffice. Because of serious errors in content, long known to CDC, the entire national post-event federal planning guideline for state and local health agencies was removed from the CDC website on January 27.⁵⁰ Then, for one additional month, the nation was without any national post-event guidance. On February 27 new guidance was posted without either explanation or any clear statement about what was new and how the guidance to state and local health agencies had changed. It is unfortunate that all post-event state plans were developed within the framework of CDC guidance to the states that was known to be flawed.

Since February 27, 2003, CDC guidance has substantially improved.⁵¹ However, as erroneous information was posted for over a year and widely disseminated in the media, public and professional awareness of changes remains limited. Therefore, major changes need to be highlighted and brought to the attention of professionals and the lay public through the media. In clearing up continuing misperceptions, the following points are of particular importance:

1. Transmission of smallpox is very possible and should be assumed before the appearance of any visible rash.
2. In a bioterrorism outbreak states should plan to move to local mass vaccination as they also identify and vaccinate easily identified contacts of the first case or cases.
3. Vaccination after exposure, particularly within three to five days, is likely to prevent death but is unlikely to prevent disease and further spread of smallpox. Therefore, though valuable for individuals, it has limited value in planning for post-event control in the general population.

4. Fast and effective post-event control is critically dependant upon completing substantial pre-event vaccination as called for in Phase II of the president's plan.

Points 1 and 2 are now clearly and consistently expressed in current guidance. Point 3, as previously noted, remains flawed,⁵² and current CDC guidelines, though modified, still use the words "will prevent" in guidance to state and local agencies and to the general public.⁵³ As yet, Point 4 does not appear to be acknowledged.

Silence of Most State and Local Health Officials

State and local health officials, with some notable exceptions, have been silent about the inadequacies of CDC plans and information. Yet many of those professionals have perceived the plans as confusing and not feasible. Why have they been silent? Smallpox is a new area for most state and local agencies, while CDC has people who have seen and worked with smallpox. Thus, it is reasonable to give CDC the benefit of the doubt. Further, CDC provides money to state and local agencies. Speaking out is perceived as putting funding at risk and degrading otherwise good and collegial professional relationships. Finally, state and local officials are part and parcel of a risk-averse culture that discourages making waves and rocking the boat. Given that the constitutional authority for protecting the public's health remains at the state, not the federal, level, this is particularly troubling.⁵⁴

Political Concerns

The smallpox threat was seen by some as a Bush administration ploy to gain support for the war against Iraq. Therefore, any support of vaccination was seen as an endorsement of war. Variants of this theme include concerns such as, "If I support vaccination I am supporting the president's social policies and legislative program, which undermine public health." It is not necessary here to debate the pros and cons of the administration's positions on other issues. It is only necessary to

realize that individual political opinions on topics that really are not related to the smallpox threat are shaping the judgments and recommendations of some public health and medical practitioners.

Systems Thinking and the Culture of Public Health

To fully understand why the president's smallpox vaccination plan has been delayed, we must dig even deeper and consider how public health professionals think and the extent to which the culture of public health is relevant or antithetical to national preparedness for bioterrorism.

Smallpox expert Dr. D. A. Henderson warned as early as 1999 that malicious dissemination of smallpox by bioterrorists could be disastrous.⁵⁵ There is much to support his opinion, and it is not unreasonable to conclude that this risk is the primary rationale behind the president's plan.⁵⁶ However, there are powerful voices that still say smallpox is difficult to transmit and maintain that the lessons of control from the eradication years are valid today.⁵⁷

It is essential to recognize that eradication took place over a period of more than 10 years when the level of population immunity was growing, populations were far less mobile than today, and there was no malicious intent to disseminate smallpox.⁵⁸ The persistent inability of many public health professionals to grasp the importance of these points suggests that systems thinking—seeing how the pieces fit and interact—is not sufficient in the profession. Consider the CDC director's statement that the true measure of the president's pre-event vaccination plan is whether the entire nation could be vaccinated within 10 days of an attack. Juxtapose that with the words of others in CDC: "It would be a success if no one receives the vaccine, but we offered this opportunity to all the right people."⁵⁹ Because the speed of post-event vaccination is directly dependent on the number of vaccinators willing to expose themselves to

Eradication took place over a period of more than 10 years when the level of population immunity was growing, populations were far less mobile than today, and there was no malicious intent to disseminate smallpox.

The smaller the number of immunized vaccinators, the faster smallpox would spread across the country.

the risk of smallpox, the smaller the number of immunized vaccinators, the faster smallpox would spread across the country. Further, if neither health care workers nor the general population are immunized, our hospitals and medical care system will be at grave risk of being swamped and losing significant capacity after a smallpox attack. That is exactly what the president's plan was designed to prevent. It is difficult to comprehend how no pre-event vaccination can be called a success.

The above is but one example of inadequate systems thinking in moving from the macro level—the overall approach to pre- and post-event smallpox planning—to the micro level of how clinics will work and determining what exactly must take place to avoid bottlenecks in the distribution and administration of vaccine. For example, having prepositioned at the state level vaccine supplies that are sufficient to begin substantial vaccination as soon as a case is identified would speed up initiating a control program by at least 12 to 24 hours. As demonstrated by Kaplan, Craft, and Wein, many public health officials fail to realize the importance of response logistics in determining the outcome of a bioterrorism event.⁶⁰ That misunderstanding is emblematic of the widespread but dangerous devaluation of the benefits of applying sophisticated yet pragmatic systems approaches to smallpox and bioterrorism planning.

Inadequate systems thinking about smallpox lies within a larger construct. Public health, by its very nature, prefers to deal with events once full data are available. It eschews making proactive decisions when nothing has yet happened, as is the case with the threat of smallpox when there is no attack and no illness.

However, in emergencies with lethal potential, far-reaching decisions may have to be made on the basis of very limited data.⁶¹ That type of emergency situation requires thinking that is completely contrary to the usual thinking of public health professionals. Typically, a good public health professional

collects good and complete data, analyzes with care,

plans and involves concerned constituencies, prepares within the framework of the plan, acts if needed, and evaluates and revises.

That is a time-consuming and risk-minimizing approach for the public and for the professional. It is consistent with the risk-averse culture that permeates public health and medicine. It works well for much of public health decisionmaking, but it is not correct for decisionmaking with regard to bioterrorism, whether it involves smallpox or another agent, where decisions may need to be made with little data and less time.

Sweeping decisions based on limited data run counter to the culture of public health. Opting for pre-event national vaccination is just such a sweeping decision. Post-event decisions will also have to be made on the basis of fragmentary, inadequate data and will require fast, even draconian, action without the certain knowledge that the action will, in hindsight, be correct. This too is antithetical to the culture of public health. We posit that such will be the case whether we are dealing with smallpox, anthrax, or other agents.

Once you take your pick of several underlying forces and mix them with more immediate causes for delay, it becomes easy to understand why the national pre-event vaccination plan is stalled. Is the situation serious? Yes. Is it catastrophic? No. We have enough vaccine to vaccinate the entire country in case of an attack. But instead of vaccinating rapidly within 10 days, with our current level of preparedness, we could easily take one to two months, with needless spread of disease, avoidable deaths, and much suffering and economic loss. We can muddle through. But muddling through at the expense of hundreds, perhaps thousands, of lives is not good enough.

We are focusing only on the limitations of public health with regard to bioterrorism and are not making a sweeping indictment of public health. However, we submit that much of what is good about public health may stand in

the way of effectively planning for and responding to bioterrorism. Rather than ask a workhorse to be a racehorse or vice versa, let's debate the desirability of creating a structure that draws only on those elements of public health that can contribute to an effective response to all bioterrorism agents. We are concerned about efforts to make the public health apparatus into something it isn't and shouldn't be. This is exemplified by the recent letter to the director of CDC from the Institute of Medicine's Committee on Smallpox Vaccination Program Implementation.⁶²

The Institute of Medicine Committee letter, though containing some useful recommendations, is flawed. Equating smallpox preparedness with chronic disease and obesity and suggesting that responses to such diverse threats to health should be integrated strains credulity. The statement that "... a high level of preparedness may well be possible without vaccinating any personnel pre-event" is wrong, irresponsible, and dangerous. In another part of their letter, the committee suggests that individual states may have goals of vaccinating their populations in 2 to 10 days. The impossibility of achieving either with no pre-event vaccination is not mentioned. Later, the committee says, "It is unclear ... how numbers of vaccinated personnel relate to the ability to respond effectively to a smallpox attack." These and other inconsistencies and contradictions are obvious yet not addressed by the committee. In yet another place the committee suggests that in a post-event situation it may not be possible to immediately vaccinate everyone, so plans should be made for "prioritizing categories of vaccinees ... pre-event" or rationing access. We can only speculate about the problems of crowd control when access to vaccine is needlessly denied in the face of a disease with a 30 percent fatality rate. Although the committee mentioned the military have vaccinated over 450,000 people, they failed to comment on the fundamental finding from the military experience that smallpox is a safe vaccine when administered with care to healthy adults. In brief, the IOM letter illustrates poor risk assessment and inadequate systems thinking that

neither serve good public health nor support sound national preparation for a possible terrorist release of smallpox.

What to Do?

Short Term

The CDC needs to clearly articulate the rationale for the president's three-phase plan and, within that rationale, specifically include the basis for the number and categories of people to be vaccinated pre-event. It must develop and publicize a fair, understandable, well-documented assessment of vaccination risk that is updated as new information becomes available. Since CDC has, so far, been unable to accomplish either objective, it is likely that rigorous oversight by HHS and Congress will be required to make this happen.

Another important short-term measure involves reducing the risk of accidental vaccination of others by recommending the use of the semipermeable membrane dressing for everyone who is vaccinated, not just hospital workers.

CDC and other health policy officials in the Bush administration should explain clearly to the public the key details of recently approved vaccine compensation coverage and how it is linked to workers' compensation and other disability income insurance. It should be emphasized that very few people will have events that trigger the need for compensation.

The secretary of homeland security and the White House should reaffirm the importance of the National Smallpox Vaccination Program and meet with leaders of medical, hospital, and nursing associations and relevant unions, to stress that this is a national security issue, the risk to healthy adults is minimal, there is a good approach in place for liability and compensation, and the nation needs their help.

Medium Term

To ensure that bioterrorism response plans are adequate, President Bush should require CDC and HHS to jointly empanel an advisory

The CDC needs to clearly articulate the rationale for the president's three-phase plan and specifically include the basis for the number and categories of people to be vaccinated pre-event.

In the case of bioterrorism, thorough investigation and retrospective analysis prior to taking fast and sweeping action is more likely to ensure failure than lead to success.

group that has expertise in systems analysis and operations research, public administration, public health and behavioral science, hospital and medical care administration, law, epidemiology, and clinical medicine, including infectious diseases. The panel should have military representation as well. Most of the members should be fresh faces, not people drawn from existing committees and agency working groups. The charge to the panel and its staff would be to critically examine and test all bioterrorism plans—not just those for smallpox—to identify weaknesses, propose changes, and ultimately ensure their adequacy. The underlying question should be: Are the plans adequate for a worst-case scenario? That requires analysis of pre- and post-event plans as well as of the interaction between federal and state plans. It cannot be limited to federal plans alone.

Though bioterrorism is a public health issue, the primary impact of bioterrorism will fall on the acute care system, particularly hospitals. That is where people go when they are sick or think they are sick. We must recognize that our hospitals, especially their emergency rooms, are a critical first line of defense against bioterrorism. But after two decades of reimbursement policies driven by managed care competition in the private sector and administered pricing for public-sector programs, hospitals are operated on a “just-in-time, just-what’s-required” basis. For an adequate hospital-sector level of preparedness, critical issues of surge capacity and shortages (staff, equipment, and facilities) and the need for adequate government funding for bioterrorism preparedness and response must be addressed.

What can be learned from our approach to smallpox? What must be done to ensure that we are adequately prepared, not just for smallpox, but for all bioterrorism hazards? What can we learn from the recent military experience with vaccination? Are there ways to capitalize on the strengths of CDC and state and local public health agencies while addressing weaknesses in systems thinking and communication? Is the culture of public health sufficiently malleable to allow, even to foster, rapid decisionmaking with vast consequences based

on very limited data? As the best possible preparation for and protection against bioterrorism is in all our interests, those questions and more merit public discussion and debate.

A Note on SARS, Monkeypox, and Public Health

The onset and spread of Severe Acute Respiratory Syndrome and monkeypox have dominated public health headlines in recent months. SARS, although infectious and communicable and thus akin to smallpox, has been appropriately addressed by the application of classic public health epidemiologic and laboratory methods. SARS is less infectious than smallpox and has a lower mortality rate. Its impact develops far more slowly than that of anthrax and botulinum toxin. An understanding of SARS, what it is, and how to control it can be determined only by rapid, but not precipitous, epidemiologic and laboratory investigation that pays exquisite attention to all possibly relevant details. SARS differs subtly but significantly from bioterrorism, and it exemplifies where classic public health can shine. In the case of bioterrorism, thorough investigation and retrospective analysis prior to taking fast and sweeping action is more likely to ensure failure than lead to success. SARS does dramatically demonstrate that hospital workers may be particularly vulnerable and hospitals can serve as epidemiologic pumps contributing to the spread of disease as they struggle to control the same disease. Most notably, the economic and social consequences of even a small epidemic like SARS already have been vast.

Monkeypox reminds us that we must expect the first case of smallpox to be identified slowly. Initiating civilian vaccination at our current state of preparedness will be neither easy nor fast.

Finally, SARS and monkeypox demonstrate the ease with which infections can be transmitted in our era of easy, worldwide air travel and the impact of rapid, global communication on how citizens and governments respond.

Conclusion

With sufficient vaccine and VIG, the nation now has the material, but not the human, capacity to rapidly control a bioterrorist smallpox outbreak. Pre-event vaccination of 10,000,000 medical, public health, and emergency workers is central and essential for rapid post-event control. However, few health and emergency workers have opted for voluntary vaccination. The overt reasons are

- inadequate and misleading vaccine risk information provided by CDC,
- delay in passing liability and compensation legislation, and
- insufficient education about and support for vaccination by key leaders in the administration directed to the public and key professional groups.

Further, a variety of subtle but powerful underlying reasons is delaying vaccination and weakening post-event planning. Perhaps the most important are deficient systems thinking in public health and a public health culture that prefers to be reactive rather than proactive.

In the near term, far better information about the risk of vaccination along with a clear rationale for the president's plan are needed. With the passage of compensation legislation, the administration now needs to reemphasize that vaccination is safe and that our nation's security requires the timely completion of the national pre-event plan. Those actions will effectively neutralize the weapons potential of smallpox. The only reason for less preparation would be that the national intelligence assessment supported a conclusion that the threat of dissemination is significantly reduced or absent.

In the medium term, the adequacy of our pre- and post-event response plans for all bioterrorism agents should be subjected to critical, multidisciplinary analysis. Those of us in the health professions need to consider if and how public health expertise can be made more relevant to planning for and managing bioterrorism events. However we

organize to combat bioterrorism, further questioning of premises and conventional wisdom is likely to illuminate weaknesses and suggest more robust approaches.

Notes

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In the near term, far better information about the risk of vaccination along with a clear rationale for the president's plan are needed.

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15. Lane et al., "Complications of Smallpox, National Surveillance in the United States 1968"; and Neff et al., "Complications of Smallpox Vaccination, National Survey in the United States, 1963."
16. J. Michael Lane et al., "Deaths Attributable to Smallpox Vaccination, 1959 to 1966 and 1968," *Journal of the American Medical Association* 212 (1970): 441-44.
17. CDC, "Vaccine Overview," March 31, 2003, www.bt.cdc.gov/agent/smallpox/vaccination/facts.asp.
18. The data for 1963 and 1968 are aggregated for the 15-to-19-year age group and cannot be broken out. Therefore, the age group starts at 15 even though the national plan begins at 18. However, because vaccine risk increases with decreasing age, if this introduces error, it will be conservative and show increased risk.
19. Eczema or atopic dermatitis is a skin condition that tends to wax and wane. It occurs more commonly in children than adults, and, whether it is active or not, it is thought to place the person at higher risk of a vaccine complication. If the dermatitis is active in an unvaccinated person, that person is at higher risk of being accidentally infected by coming into close contact with a recently vaccinated person.
20. Bartlett et al.
21. Neff et al., "Risk of Transmission of Vaccinia Virus to Contacts."
22. *Ibid*.
23. Robert B. Belshe, Presentation at CDC, May 8, 2002, reporting no detectable viral shedding when a double-thickness semipermeable membrane was used over a folded gauze pad.
24. Melinda Wharton et al, "Recommendations for Using Smallpox Vaccine in a Pre-Event Vaccination Program," *Morbidity and Mortality Weekly Report* (CDC), February 26, 2003, www.cdc.gov/mmwr/preview/mmwrhtml/m2d226.htm.
25. Hand washing, a cornerstone of good infection control, is very important until the scab at the vaccination site falls off, often around 21 days after vaccination. It should be done after changing the dressing covering the vaccination site or whenever the vaccination site is touched. The

dressings is typically changed every 2 to 4 days.

26. Kent A. Sepkowitz, "Current Concepts: How Contagious Is Vaccinia?" *New England Journal of Medicine* 348, no. 5 (January 30, 2003): 439–46.

27. Personal Communication with Col. John Grabenstein.

28. For details of the military experience, see U.S. Department of Defense, "Smallpox Vaccination Program Safety Summary, as of May 16, 2003."

29. "Update: Adverse Events Following Smallpox Vaccination—United States 2003," *Morbidity and Mortality Weekly Report*, April 4, 2003, pp. 278–81; and www.smallpox.army.mil/event/SPSafetySum.asp, as of March 31, 2003.

30. Personal Communication with Col. John Grabenstein.

31. CDC, "Interim Smallpox Fact Sheet, Smallpox Vaccine and Heart Problems," www.bt.cdc.gov/agent/smallpox/vaccination/heartproblems.asp (accessed June 8, 2003); U.S. Department of Defense, "Smallpox Vaccination Program, Resources Regarding Cardiac Adverse Events," www.smallpox.army.mil/event/cardiac.asp (accessed June 8, 2003); and U.S. Department of Defense, "Smallpox Vaccination Program Safety Summary as of March 31, 2003."

32. Jouko Karjalainen et al., "Etiology of Mild Acute Infectious Myocarditis," *Acta Medica Scandinavica* 213 (1983): 65–73; and Brian J. Feery, "Adverse Reactions after Smallpox Vaccination," *Medical Journal of Australia* 2 (1977): 180–83.

33. L. R. Finlay-Jones, "Fatal Myocarditis after Vaccination against Smallpox: Report of a Case," *New England Journal of Medicine* 270 (1964): 41–42

34. Karjalainen et al.

35. "Cardiac Adverse Events Following Smallpox Vaccination—United States 2003," *Morbidity and Mortality Weekly Report*, March 28, 2003, pp. 248–50; www.smallpox.army.mil/event/SPSafetySum.asp, as of March 31, 2003; and personal communication with Col. John Grabenstein

36. *Ibid.*

37. *Morbidity and Mortality Weekly Report*, March 28, 2003.

38. "Risk of Death: Assigning Numbers to Health Risks," *New York Times*, July 7, 2002.

39. Arnold Barnett and Alexander Wang, "Are Some Airlines Safer Than the Others?" <http://web.mit.edu>

[/~msey/www/are some airlines safer.html](http://web.mit.edu/~msey/www/are%20some%20airlines%20safer.html); see also "Flying? No Point in Trying to Beat the Odds," *Wall Street Journal*, September 9, 1998.

40. This assumes that everyone vaccinated uses the semipermeable membrane dressing and health workers who have contact with patients for the 21 days during which they may accidentally infect another person have their work assignments modified so that they are not working in patient care areas with high-risk patients (immunocompromised, burns, etc.).

41. Cyril W. Dixon, "Smallpox in Tripolitania, 1946: An Epidemiological and Clinical Study of 500 Cases, Including Trials of Penicillin Treatment," *Journal of Hygiene* 46 (1948): 351–77 (see particularly Table 6, p. 369); Philip P. Mortimer, "Can Postexposure Vaccination against Smallpox Succeed?" *Clinical Infectious Diseases* 36 (2003): 622–29; and William Bicknell and Kenneth James, "Smallpox Vaccination after a Bioterrorism-Based Exposure," Letter to the editor, *Clinical Infectious Diseases*, August 2003, p. 467.

42. CDC, "Smallpox Emergency Personnel Protection Act: Benefits and Compensation for Smallpox Vaccine Injuries," June 6, 2003, www.bt.cdc.gov/agent/smallpox/vaccination/bene-comp.asp. The law established a no-fault program to provide benefits and/or compensation to certain individuals, including health care workers and emergency responders, who are injured as the result of administration of smallpox countermeasures. The program will also provide benefits and/or compensation to certain individuals who are injured as a result of accidental vaccinia inoculation through contact. The Homeland Security Act of 2002 already had protected physicians and other health care workers from lawsuits by those they vaccinate. It deemed entities and individuals involved in the manufacture, distribution, and administration of the smallpox vaccine to be "employees" of the Public Health Service for tort liability purposes. That legislation effectively transferred liability to the federal government under the Federal Tort Claims Act (which limits remedies for those seeking redress). See Robin J. Strongin and Eileen Salinsky, "Who Will Pay for the Adverse Events Resulting from Smallpox Vaccination? Liability and Compensation Issues," National Health Policy Forum Issue Brief no. 788, March 12, 2003, p. 5. However, Strongin and Salinsky observed that section 304 of the Homeland Security Act did not appear to provide liability protection for hospitals or other health care organizations that ask their employees to volunteer for the vaccine but are not directly responsible for administering the vaccine. The liability status of health care workers who are vaccinated and may inadvertently pass the vaccinia virus to an unvaccinated person also remained unclear, at best. In addition, the 2002

- legislation did not establish a clear avenue of compensation for individuals who incur injuries caused by administration of the vaccine. Ibid, pp. 6–7; see also “Smallpox Vaccine: Easing Fears on Inoculations,” *American Medical News*, May 12, 2003, www.ama-assn.org/sci-pubs/amnews/amn_03/edsa0512.htm.
43. CNN.com/Health, “Surgeon General Vaccinated against Smallpox,” March 11, 2003, www5.cnn.com/2003/HEALTH/03/11/smallpox.surgeon.gen.ap.
44. Alibek, *Biohazard*.
45. J. Michael Lane and Joel Goldstein, “Evaluation of 21st-Century Risks of Smallpox Vaccination and Policy Options,” *Annals of Internal Medicine* 138 (2003): 492. See also de Rugy and Peña; and Bicknell.
46. Quoted by Dr. Gregory Saathoff speaking at the King’s College conference on “Communicating the War on Terror,” London, June 5, 2003.
47. Alibek, *Biohazard*.
48. To the extent that smallpox is in the hands of nations other than Russia and the United States, there is always the chance of accidental release without malicious intent. Moreover, we should not assume that everyone who possesses samples of the virus will be as diligent or capable as designated WHO repositories in storing and handling the virus. An exposure of this type would be easily confused with bioterrorism but, we hope, easier to control.
49. American College of Preventive Medicine, “Clinician Communication Briefing 6 Summary, Special Smallpox Preparedness Program Update Telephone Briefing,” March 7, 2003, www.acpm.org/hhs_smallpox.htm.
50. Personal communication with Dr. Larry Anderson, CDC, January 26, 2003.
51. CDC, “Smallpox Response Plan and Guidelines (Version 3.0).” See particularly Draft Guide A—Smallpox Surveillance and Case Reporting; Contact Identification, Tracing, Vaccination, and Surveillance; and Epidemiologic Investigation (May 21, 2003) and Guide B—Vaccination Guidelines for State and Local Health Agencies (February 27, 2003), www.bt.cdc.gov/agent/smallpox/response-plan/index.asp.
52. Dixon; Mortimer; and Bicknell and James, “Smallpox Vaccination after a Bioterrorism-Based Exposure.”
53. CDC, “Smallpox Fact Sheet: Vaccine Overview,” www.bt.cdc.gov/agent/smallpox/vaccination/facts.a sp (accessed August 3, 2003).
54. To give the reader a sense of the power of peer pressure, as we write these words both authors are uncomfortable, not with the truth of the facts set forth in this article, but with the knowledge that what we are writing may seem like airing dirty linen in public.
55. Henderson.
56. Bicknell; and Edward H. Kaplan, David L. Craft, and Lawrence M. Wein, “Emergency Response to a Smallpox Attack: The Case for Mass Vaccination,” *Proceedings of the National Academy of Science* 99 (2002): 10935–40, published online before print as 10.1073/pnas.162282799.
57. Thomas Mack, “A Different View of Smallpox and Vaccination,” *New England Journal of Medicine* 348 (January 30, 2003): 5; Lane and Goldstein; and www.bt.cdc.gov/agent/smallpox/response-plan/index.asp.
58. Edward H. Kaplan and Lawrence M. Wein, “Smallpox Eradication in West and Central Africa: Surveillance—Containment or Herd Immunity?” *Epidemiology* 14 (2003): 1–4; and Bicknell and James, “The New Cell Culture Vaccine Should Be Offered to the General Population.”
59. Ceci Connolly, “Bush Smallpox Inoculation Plan Near Standstill: Medical Professionals Cite Possible Side Effects, Uncertainty of Threat,” *Washington Post*, February 24, 2003, p. A6; and David McGlinchey, “Smallpox: CDC Says It Never Aimed for 500,000 in First Phase,” *Global Security Newswire*, February 26, 2003, www.nti.org/d_newswire/issues/newswires/2003_2_26.html#4.
60. Kaplan, Craft, and Wein; and Lawrence M. Wein, David L. Craft, and Edward H. Kaplan, “Emergency Response to an Anthrax Attack,” *Proceedings of the National Academy of Science* 100 (2003): 4346–51, published online before print as 10.1073/pnas.06 36861100.
61. William Bicknell and Daniel C. Walsh, “The First ‘Red Tide’ in Recorded Massachusetts History: Managing an Acute and Unexpected Public Health Emergency,” in *Proceedings of the First International Conference on Toxic Dinoflagellate Bloom* (Boston: Massachusetts Science and Technology Foundation, 1975), pp. 337–45.
62. Institute of Medicine, “Review of the Centers for Disease Control and Prevention’s Smallpox Vaccination Program Implementation,” Letter Report #4, August 12, 2003.