Creating a smallpox vaccination program that adequately responds to the potential threat of a smallpox outbreak and which, at the same time, protects against the risks of such a program is a challenge for the public health system and for health care providers. The decision must balance the risks of not providing the vaccine (and thereby being unprepared for an outbreak) against the rare but real adverse side effects of the vaccine. This issue of CCC Forum offers a brief overview of the rationale for the Federal pre-event smallpox vaccination program; the smallpox agent and the disease it causes; the vaccine and its potential side effects; the legal issues faced by hospitals; and the compensation issues for individuals who receive the vaccine. The Federal program is part of a broad government effort to prepare the country for a possible bioterrorism attack that might use smallpox as an agent.

The threat - the rationale for the program

The United States in general, and New York City in particular, has been the target of several terrorist events over the past decade. Starting with the first World Trade Center attack in 1993, followed by the second World Trade Center attack on 9/11 and then the anthrax attack later in the fall of 2001, it has been clear that there are people, or groups of people, who wish the United States and its citizens serious harm. Unfortunately, but true, is the fact that these groups are patient (note the eight-year wait between the first and second World Trade Center attacks), apparently well organized and persistent. New York City, because of its prominence as a symbol of the United States and its economic power, has been a particular target for terrorists. Thus, for the country as a whole, and for New York City in particular, it is reasonable and rational to make some preparations, anticipating that biological weapons could be part of a future terrorist attack.

The biological agent and the disease it causes

The smallpox agent is a member of the orthopoxvirus family. It has caused disease far across the width and breadth of the globe. For several hundred years, major epidemics - sweeping across Africa, India, parts of Asia and the Americas - have been responsible for the deaths of hundreds of millions of people. There is no known treatment for smallpox.

Smallpox is a communicable disease that usually spreads by direct and fairly close face-to-face contact with an infected individual. Persons who have smallpox are asymptomatic for seven to 17 days. During most of this time, they are invisible to the rest of the population and are not infectious. At the end of this period, they develop
fever and prostration, feel quite sick and take to bed.

A rash develops during the initial phase of the disease. It is prominent on the face and mouth and moves first to the extremities and then centrally. The smallpox rash goes through an evolutionary process. Initially, it is a red, flat maculopapule. The rash then becomes a vesicle, and finally a thick, hard pus-filled lesion – a pustule – that goes deep into the dermis. The pustule eventually forms a scab and falls off, leaving the characteristic pitted smallpox scars.

A person who has smallpox is infectious and can transmit the disease from the start of the rash until the scabbing is complete. The person is most infectious during the earliest phases of the rash. At this time, the infected person has smallpox lesions in the mouth. These lesions may not be visible to others, but when the person coughs or exhales, smallpox virus is expelled into the air. It is said that close contact (six feet or closer) usually is required for efficient transformation of the virus. This is true, but there have been cases wherein some distant contact with persons carrying the virus can lead to infection by an airborne route. It is important to note that people in the latter stages of smallpox are considerably less infectious than those earlier in the disease progression. Clothing or bed linen containing smallpox scabs also is potentially infectious. Smallpox has 25 to 30% mortality and, currently, there is no effective treatment for this disease.

**Smallpox vaccine**

Over 200 years ago, Edward Jenner noticed that maidens who worked with cows in England developed a disease called cowpox and seemed less likely to come down with smallpox when a smallpox epidemic swept through the country. He deduced that somehow their contact with the cowpox protected them from smallpox. He then vaccinated or inoculated these women with infective material from the cows. It was his observation and a successful test of his concept that led to the creation of vaccines in general and a smallpox vaccine in particular.

Smallpox vaccine, as we know and use it today, is based upon the same principles and the same agent that Edward Jenner used in 1796. The smallpox vaccine is a live virus agent called vaccinia virus, which is the agent known to infect cows. This agent, which is similar to the smallpox virus, induces protective immunity against smallpox. People vaccinated with smallpox vaccine have high levels of protective immunity against smallpox for the first several years. This immunity wanes over time. The protection declines and is considerably less 20 years later, if not totally gone. Recent studies, however, suggest that there may be more long-lasting immunity than previously believed possible.

It is important to note that the vaccine will prevent acquisition of smallpox or lessen the severity of the disease even if given after exposure to smallpox itself. Thus, the vaccine protects against disease acquisition or significantly lowers the mortality rate of the disease if given within 72 hours after exposure to the virus. It is this property of the vaccine that allows for potential control of smallpox outbreaks.

The basic mechanism for controlling smallpox over the years has been widespread vaccination to establish some level of baseline immunity, followed by what is called “ring vaccination,” wherein all people exposed to a case of smallpox are vaccinated, thus creating “rings” of protection around exposed cases.

The World Health Organization (WHO) applied these principles nearly 40 years ago in its campaign to eradicate smallpox. Widespread vaccination, combined with ring vaccination whenever a case or groups of cases appeared, gradually lowered the number of cases of smallpox occurring throughout the world. The last case of smallpox was identified in Somalia in 1977. In 1980, the World Health Organization declared smallpox eradicated, after noting that no cases had been reported anywhere in the world during the past three years.

As a consequence of the eradication of smallpox, vaccination with smallpox vaccine ceased throughout the world. Unfortunately, the lack of vaccination over the last two or more decades and the waning immunity of the previously vaccinated has left the world unprotected – without immunity and highly vulnerable to a smallpox outbreak. The large number of immunosuppressed persons, including those living with HIV/AIDS, those with cancer and those receiving steroids, enhances the risk to the population. Immunosuppressed individuals have a higher mortality rate from smallpox.

**The Federal Pre-Event Vaccination Program**

Due to the perceived threat of bioterrorism, the Bush administration formally undertook a three-stage, nationwide voluntary vaccination program in the late winter of 2003:

**Phase I.** Approximately 500,000 health care workers - those working mostly in hospital settings and departments of health - would be offered vaccination with smallpox vaccine. These 500,000 health care workers would then be responsible for the care of initial cases of smallpox should an outbreak occur.

The logic behind this plan was to create a cadre of physicians, nurses and other health care workers to care for initial cases of smallpox entering the hospital system. It would be unrealistic to otherwise expect unvaccinated, susceptible health care workers to care for documented cases of smallpox. In effect, health care workers who agreed to receive the vaccination simultaneously agreed to care for people with smallpox who came to the hospital.
The plan anticipated widespread vaccination after an outbreak, thus controlling the outbreak and permitting a larger number of persons to care for the sick. It is important to re-emphasize that this phase of the program – as with all parts of the program, with the exception of the military – was voluntary and optional. In addition to the hospital-based health care workers, designated people in the city, state and municipal departments of health also would be vaccinated so that they could operate safely in an outbreak environment.

Vaccinating hospital-based health care workers also would serve a second purpose. They would be the “strategic reserve” should a massive outbreak occur. If large numbers of persons acquired smallpox, New York City – or, in fact, any other municipality – would have to initiate widespread vaccination of anyone exposed to a potential case and, conceivably, vaccinate the entire populace. Such an undertaking would require a large number of resources, especially personnel, to accomplish widespread vaccination following a massive outbreak. The health care workers who signed up for the initial wave of the vaccination program would, if necessary, help vaccinate members of their own communities, as designated by the Department of Health.

**Phase II.** This stage of the vaccination program envisioned offering the smallpox vaccine to 10 million health care workers throughout the nation on the assumption that smallpox could start anywhere and that a wider range of health care professionals needed to be vaccinated (and not just selected providers in big-city hospitals).

**Phase III.** The Federal government would extend the vaccination program to reach the several hundred million persons throughout the country, should they want to be vaccinated. This phase of the program would not become operational until 2004.

In the spring of 2003, New York City initiated Phase I of the Federal smallpox vaccination program. Each hospital was asked to identify a team of approximately 100 to 150 volunteers from across the job spectrum. Again, the purpose of creating these teams was to create a group of volunteers willing to care for smallpox cases. Team members include doctors, nurses, respiratory therapists, transportation staff and security staff and others who might be needed to care for the patients. The vaccination program was under the tight control of the New York City Department of Health and Mental Hygiene. Strict control was necessary to ensure legal protection and coverage for hospitals acting as agents of the Department of Health by administering the vaccine.

New York City expected upwards of 10,000 hospital workers to receive the vaccine, but this was not to be. As of June 2003, only a few hundred hospital employees had been vaccinated. The turnout in most hospitals was typically fewer than 25 volunteers. Although the City now has a small cadre of vaccinated health care workers, the numbers fall below those planned for and initially desired. No doubt the vaccine’s well-publicized side effects limited the number of those willing to be vaccinated. New York City is currently reviewing the plan. An advisory group to the Federal government recently recommended significant revisions to the smallpox program.

**Side effects and complications of the vaccine**

The smallpox vaccine is a live vaccine containing the vaccinia virus. It does not contain the smallpox virus. The vaccine is inoculated into the skin by bifurcated needle. The vaccinia virus multiplies in the dermis, and vaccinees develop a macule, vesicle and, finally, by days 7 to 10, a pustule, a raised, firm, round lesion in the area of vaccination. The pustule eventually develops a scab, which falls off, leaving the characteristic scar at the vaccination site. Vaccinated individuals may develop symptoms of fever, malaise, headache, chills and reactions at the vaccination site. The area around the vaccination site contains live virus and is infectious until the scab falls off.

Although the vaccination generally is benign in an otherwise-healthy person, there are individuals who should not be vaccinated because the vaccine poses an unacceptable risk. These include:

- Immunocompromised individuals, including those who are receiving steroids, are HIV-positive, have autoimmune diseases (such as SLE), have cancer, have received cancer chemotherapy or are organ transplant recipients. All of these people have compromised immune systems. There are well-documented cases in such patients of the vaccinia virus spreading in an uncontrolled fashion and causing progressive vaccinia resulting in death or severe disability.

- Individuals who have, or have ever had, any skin disease – in particular, eczema, atopic dermatitis or psoriasis. These people tend to have widespread dissemination of the virus in the skin, which may cause serious, potentially life-threatening reactions.

- Women who are pregnant, who anticipate being pregnant or could inadvertently become pregnant during the several weeks after vaccination should not be vaccinated because of the well-documented but exceedingly rare consequence of a fetal vaccinia.

The vaccine also is contraindicated for anyone who has a family member with any of the conditions noted above.
Inadvertent contact between family members and the vaccinated individual may result in transmitting the virus to an immunologically impaired person or a person with skin disease, with potentially serious consequences.

All of these reactions are relatively rare and are probably seen with decreased frequency in those who previously received the vaccine.

In rare instances (no more than roughly three to 10 per million in a manner that is unpredictable), persons who receive the smallpox vaccine develop a postvaccination encephalitis, which can cause death. This is an idiosyncratic reaction—it is not possible to predict and thus to screen for its occurrence. There is no effective treatment for the vaccinia-related encephalitis.

The Federal government’s smallpox vaccination campaign strongly emphasized the contraindications for the vaccine. The resulting intense media coverage of potential side effects or risks of the vaccine may have been partially responsible for the relative lack of enthusiasm for volunteering to be vaccinated.

Documented cases of heart disease in military vaccinees also may have contributed to the low turnout of vaccine volunteers. Approximately 10 to 15 cases of inflammation of the heart were reported among the first 300,000 military personnel who were vaccinated. This myopericarditis occurred in young people and appeared to resolve without residual damage.

In addition, there were reports of several cases of what appeared to be angina and several cases of heart attacks that occurred concurrently or within six weeks of vaccination. These episodes occurred in a somewhat older group of individuals—mostly over 45. Analysis suggested that the occurrence of the heart attacks in this group of people was not statistically higher than would be expected in an age-matched, non-vaccinated population. Thus, it was hard to link the heart attacks to any causal relationship with the vaccination. Nonetheless, as a precaution, the government advised that those with a history of coronary artery disease or significant risk for coronary artery disease forego volunteering for the vaccine. These last two side effects were documented just as the civilian vaccination campaign began and certainly did not enhance recruitment.

It is important to note that these contraindications to the vaccine are not absolute. In the case of a widespread outbreak of smallpox, nearly all persons potentially exposed to the virus would be vaccinated. There are two reasons: 1) The mortality of smallpox is much greater than the small risk of side effects or complications; and 2) vaccination of all exposed or at-risk persons might be needed to break the cycle of transmission and stop the outbreak.

### Legal and cost issues

The smallpox vaccination program created two categories of directly related costs: The costs associated with implementing the program itself, including creating and staffing the vaccination clinics; and the costs for compensating staff who lose time from work secondary to illnesses or reactions to the vaccine.

In addition, given the known side effects of smallpox vaccination, it could reasonably be assumed that any large-scale, mandatory smallpox vaccination program would result in a number of vaccination-related injuries. These injuries could range from relatively insignificant to very disabling, including death. Addressing the questions of who should bear such costs, and what provisions should be made to compensate those who are injured, are important aspects of the smallpox vaccination program. There have been various efforts to address these issues on both state and federal levels.

The Homeland Security Act § 304 was the Federal government’s first response to issues of smallpox vaccination liability. The Act provides an exclusive remedy for those who suffer vaccination-related injuries. It also provides liability coverage for all hospitals and health care workers who administer the vaccine and sets forth procedures for those who believe they have been injured as a result of the vaccination.

The Act does not provide for compensation for every vaccination-related injury. It does not cover those injuries that are known to be risks of the vaccination itself. It is not a “no fault” procedure. Establishing injury alone does not entitle a vaccinee to compensation. Rather, following the procedures of the Federal Tort Claims Act, those injured must prove negligence in accord with state liability law. Thus, a showing that an individual developed progressive vaccinia alone would be insufficient to merit compensation. Rather, to be entitled to compensation, the “injured” individual would have to prove that the screening process was insufficient or make some other showing of negligence in the vaccination process. In addition, the Act provides no coverage for liability due to gross negligence or willful misconduct of vaccination manufacturers. Thus, if there were injuries caused by “bad vaccine” that was allowed into the marketplace due to a manufacturer’s willful misconduct or gross negligence, “injured” individuals would have to seek compensation from the manufacturers.

If the United States “makes a payment on a claim that is based partly or wholly on willful misconduct or gross negligence, the U.S. may recover that part of the payment, in addition to interest and litigation costs, from the manufacturer.” The Act also requires the cooperation of all defendants, including manufacturers. Should defendants fail to
cooperate, the Federal government will not defend or indemnify them. Under the limited provisions of the Homeland Security Act, there was no recovery for lost wages nor could those injured through inadvertently acquired vaccinia from a vaccinee recover damages. Because of the deficiencies in the Homeland Security Act Provisions, Congress passed the Smallpox Emergency Personnel Protection Act of 2003, which President Bush signed into law on April 30, 2003. This law protects all those who have been inoculated as part of their roles in an emergency response plan, as well as individuals accidentally inoculated through contact with those who have been directly vaccinated. The Act provides for lost wages up to the amount of two-thirds of pay, with an annual cap of $50,000. There is a provision for additional compensation for lost income if the eligible individual has one or more dependents, which increases the lost wages claimed by 8 1/3 percent. The Act also provides $262,100 in benefits to those who either die or suffer total and permanent disability as a consequence of vaccination. This benefit is in addition to whatever other benefits, such as life insurance or long-term disability insurance, the individual or survivors receive. The Act also provides for supplemental medical insurance benefits in addition to those already available to the injured individual. All these benefits are secondary to other benefits available to the injured individual.

In addition to the Smallpox Emergency Personnel Protection, New York State workers are entitled to protection under the New York State Workers' Compensation Law. Compensation is capped at $400 a week, representing no more than two-thirds of the average annual wage. There is no compensation available for the first seven days of disability, unless the disability lasts for more than 14 days. Medical costs to treat a vaccine-associated injury are covered by...
compensation law. Workers’ compensation also provides for scheduled compensation for covered workplace injuries and disabilities. However, it is not clear whether these benefits will be available to those who lose wages due to secondary transmission.

The future

The smallpox vaccination program was but a prelude to the interaction needed between the hospital community and public health authorities as we seek to craft a response to the emergence or re-introduction of dangerous biologic agents. Before the smallpox vaccine program, there was anthrax, and afterwards, there was SARS. We can be assured that more threats will come and that more preparation will be needed. Ongoing and expensive preparedness will be required for many years.² Who should pay the costs, how the programs will be implemented, the relative roles of hospitals and public health authorities all are part of the ongoing dialogue needed to meet this challenge.

1. The Act covers both those who are directly vaccinated and those who are inoculated through contact with others who have been vaccinated.
2. A survey by the Greater New York Hospital Association found that from September 11, 2001, through the end of 2002, its hospitals were spending an average of $1.7 million in emergency preparedness. Those hospitals anticipated spending an additional $2 million in 2003. Of this amount, less than 7 percent was being covered from sources other than general operating revenue.

For More Information . . .
