# Smallpox: A Review for Health Educators

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**ABSTRACT**

*Since the declaration of the eradication of smallpox in May of 1980 concern about this virus has ebbed. However, recent world events, including the destabilization of governments, have raised concerns that smallpox could fall into the hands of nefarious individuals or groups who might attempt to use the virus as a weapon. In Centers for Disease Control and Prevention publications the threat of smallpox being intentionally released by bioterrorists is currently considered possible. Because health educators would likely be involved in public health prevention and response efforts to a release, it is our responsibility to be knowledgeable about smallpox. This article defines the disease, describes its history and the successful eradication effort, and discusses public health preparations for the possible return of this killer.*

Since the events of September 11, 2001, terrorism and especially bioterrorism-related concerns have increased. Bioterrorism is defined as the release or threat of release into the civilian population of a natural or altered disease-causing bacteria, virus, or toxin for the purpose of causing illness, death, or inculcating fear (Southern Nevada Area Health Education Center, 2003). For rogue nations, organizations, or individuals who do not possess conventional weapons the advantages of using biological weapons are numerous. Many biological weapons are accessible or easy to produce; can be disseminated over large areas; may cause secondary spread; are difficult to detect; would likely cause panic and fear; and the perpetrators would have the opportunity to flee the sites of their attacks before the effects are noticed (Southern Nevada Area Health Education Center, 2003). A frequently mentioned and potential bioterrorism weapon is smallpox.

Because health educators and public health personnel may be involved in bioterrorism prevention and response efforts (Garrett, 2000), and because the public may seek smallpox-related information from health educators, it is the responsibility of public health personnel to be knowledgeable concerning this potential threat. Further, a recent study found that a majority of Americans hold a number of beliefs about smallpox that are false. Authors expressed a need for public education about smallpox (Blendon et al., 2003). Health educators should play a role in improving the smallpox-related knowledge of Americans. This article provides a description of smallpox, a history of the disease, briefly describes the successful eradication effort, and discusses current threats and efforts to protect the population from and respond to a smallpox attack.

## WHAT IS SMALLPOX?

Smallpox is a serious, contagious, and sometimes fatal disease. Smallpox is a Category A bioterrorism agent as are anthrax, botulism, tularemia, plague, and viral hemorrhagic fever. Category A agents are those that pose a risk to national security because they can be easily disseminated or are transmitted from person to person, result in high mortality rates and have the potential for major public health impact, might cause public panic and social disruption, and require special action for public health preparedness (CDC, 2003a).

Smallpox is caused by the variola virus, which is an orthopoxvirus, as are cowpox, camelpox, and monkeypox. Smallpox is about 200 nm in size and contains a double-stranded DNA putative coding for more

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than 200 different proteins (WHO, 2001), making it one of the most complex and largest viruses (Henderson et al., 1999). It is known to have emerged in human populations centuries ago (CDC, 2003c). The name *variola* originates from the Latin word for "spotted" and describes the raised bumps that appear on the faces and bodies of those afflicted. Smallpox has two clinical forms, variola major, the most common and severe; and variola minor, which is less common and less severe and causes a disease called alastrim, which kills less than 1% of its victims (Bray, 1996). Within variola major there are four main types, with "ordinary" the most prevalent, accounting for at least 90% of cases before its eradication (CDC, 2003c). Three other types of variola major are "modified," a form that produces mild effects and usually occurs in previously vaccinated people; and "flat" and "hemorrhagic" smallpox. Flat and hemorrhagic variola major are rare but usually fatal (CDC, 2003a). Historically, variola major killed about 30% of the unvaccinated and 3% of the vaccinated, but has killed at higher rates. Approximately 80% of Indians in Santa Domingo succumbed in a 15th century outbreak. Case fatality rates were similar among North American Indians in the 17th and 18th centuries (Bray, 1996). Experts are concerned about the vulnerability of the U.S. population because America ceased vaccinations in 1980. It is estimated that only 10–15% of those who were vaccinated before the cessation of that procedure would retain residual immunity, and one-quarter of Americans have never been vaccinated (Garrett, 2000).

The transmission of smallpox is typically person-to-person via aerosol droplets that navigate from the lungs of infected humans to lungs of susceptible people. However, smallpox can be transmitted by contact with bodily fluids or contaminated fomites such as clothing or bedding. The well-known instance of British General Jeffery Amherst sanctioning the presentation of smallpox-laden blankets to American Indians in 1763, for the purpose of killing them (Fenn, 2001), underscores the effectiveness of intentionally spreading the disease via fomites. The disease is considered to be highly contagious, but is less transmittable than chickenpox and influenza, diseases that are also transmitted from infected human lungs to susceptible lungs (Bray, 1996). The variola virus can remain alive outside the human body, but 90% of aerosolized smallpox dies within 24 hours, and quicker in the presence of ultra violet light (CDC, 2003a).

Those in face-to-face contact (<6.5 feet) with smallpox victims and those in the same households are at high risk for infection. Others at risk include people who care for smallpox victims, smallpox response teams, and those who would transport smallpox sufferers such as emergency medical technicians. Law enforcement personnel, laboratory workers, and those who dispose of medical waste would also be in jeopardy of infection (WHO, 2001) in the event of a release.

The incubation period for smallpox is 7 to 17 days, with an average of 12 to 14 days. During the incubation period the infected feel fine and are not contagious. The initial symptoms of smallpox, which occur during the prodrome phase, are fever; malaise; headache, body aches, and especially backache; and sometimes vomiting. The headache can be splitting and the backaches excruciating. The fever is usually in the 101–104°F range and is followed by a rash. At this point the smallpox sufferer is usually very ill and incapable of moving about. This phase persists for 2 to 4 days (Fenn, 2001).

The third or "early rash" phase is appropriately characterized by a rash that emerges as small red spots on the tongue and mouth. It is during this phase, which persists for approximately 4 days, that the ill are at their most contagious. The susceptible that come near them risk their lives. As the sores on the mouth break open, a rash appears, starting on the face and spreading to the arms and legs, then the feet and hands, and finally to the remainder of the body, all occurring within 24 hours. As the rash appears, which will persist for about 15 days, the fever usually falls and the patient rallies. By the third day of this phase the rash develops into raised bumps, and by the fourth day the bumps fill with an opaque fluid that has a dip in the center. The fever frequently returns and stays elevated until scabs form over the bumps (Fenn, 2001).

The subsequent phase, called "pustular rash," usually lasts for about 5 days, but can continue for up to 9 days. The pustules become sharply raised and are usually round and firm to the touch. The infected remain contagious. Next comes a phase that is characterized by pustules and scabs that also persists for about 5 days (CDC, 2003a). If the smallpox case is a fatal one, it is usually at about this time that death occurs, which is 10–16 days after the first appearance of symptoms. By the conclusion of this stage most of the sores have scabbed over. Subsequently, the scabs begin to fall off but leave marks on the skin that usually scar. The infected remain contagious until the last scab falls off (Fenn, 2001).

There is no specific treatment for small pox, and the only prevention is vaccination (CDC, 2003c). The aftermath of small pox is either death or permanent immunity. Most survivors are indelibly scarred, and some are blind, especially those who were also starving while ill (Fenn, 2001). When the disease attacks the eyes, lungs, throat, heart, or liver, death is likely to occur. "Death is frequently caused by multiple hemorrhages that are sometimes complicated by bronco-pneumonia" (Bray, 1996, p.115). Smallpox can also produce secondary bacterial infections that can be as deadly as the smallpox symptoms. Severe dehydration is also common among sufferers, because the rash that occurs in the mouth and throat makes drinking difficult. Frequently a loathsome odor that is peculiar to smallpox is present as the pustules crack and begin to run. Survival rates are higher if the pustules remain discrete and do not run together into a single oozing mass. The oozing mass is characteristic of confluent smallpox, a condition from which 60% die (Fenn, 2001).

## HISTORY OF SMALLPOX

The history and origins of smallpox are

topics of scholarly discussion, because it is difficult to determine when smallpox first appeared, but it can be argued with confidence that smallpox was causing illness in the Middle East during the 10th century (Bray, 1996). Because other diseases that caused symptoms similar to those of smallpox were endemic or epidemic in earlier times, and laboratory confirmation of the causative disease agents were centuries away, early claims of smallpox epidemics are disputed (Bray, 1996). It was not until around 910 AD that Arabian physician Rhazes drew the distinction between measles and smallpox (Marks & Beatty, 1976). However, there are reports that smallpox was present much earlier in ancient Egypt. The principal argument supporting this belief is that scars, which may have been caused by smallpox, have been noted on mummies (Bray, 1996).

Records suggest that smallpox was disseminated throughout Europe by several vehicles, including merchants who traveled along trade routes and those returning from the Crusades of the 11th, 12th, and 14th centuries. It is known that smallpox was endemic in mainland Europe by 1614 but did not reach London until 1628 (Marks & Beatty, 1996). Some epidemics were so devastating and sustained that parents did not name their children until after they had survived smallpox (Garrett, 2000).

During the 16th century Spanish and Portuguese explorers transported smallpox to Meso-America with devastating consequences. The disease killed at high rates among the natives, who had had no opportunity to gain immunity (Bray, 1996). Additional reasons for the high case fatality rates among American natives were poor nursing care, the common use of steam baths that compounded the effects of dehydration, and possibly differences in the immune systems of Native-Americans and Euro-Americans (Fenn, 2001). During one outbreak up to 80% of natives of Santa Domingo succumbed to the disease (Bray, 1996), and similar case fatality rates were seen among the Indians in current day New England (Watts, 1997).

Another potential explanation for higher death rates among Native Americans, as opposed to European immigrants, was that the practice of smallpox inoculation had been employed previously in Europe. Europeans were not the inventors of inoculation; it was employed by the Chinese as early as the 11th century. The Chinese version of inoculation entailed infecting children with smallpox by placing scabs that were taken from the infected, preferably from a person with a mild case, into the child's nostrils. The children usually survived the intentionally inflicted smallpox bout and were subsequently immune (Bray, 1996). The practice of inoculation did not reach Europe until Mary Wortley Montague accompanied her husband, the British ambassador, to Constantinople, where she observed "ingrafting." This frightening and fascinating procedure involved deliberately placing live smallpox virus into an incision, usually on the arm or hand. Similar to the Chinese method, the virus was optimally harvested from someone suffering with less severe symptoms. After a brief incubation period, smallpox ensued, but again the patient usually survived and suffered with mild effects. The reasons for the mild symptoms and low death rates are still not fully understood. This procedure is known as "variolation" and required the patient to survive an actual case of smallpox. To demonstrate the strength of her belief in the procedure Ms. Montague had her daughter successfully inoculated when she returned to England, and others followed her lead (Fenn, 2001).

At about this time Benjamin Jesty, a yeoman British farmer, observed that milkmaids were usually not affected by smallpox during outbreaks. It was known that milkmaids, in the course of their job duties, were prone to a disease called cowpox or vaccinia, which produced mild symptoms. Jesty reasoned that cowpox somehow protected the milkmaids during subsequent smallpox outbreaks. Later, when he noted that one of his bovines was suffering from cowpox, he removed infectious matter from the pustular eruptions that appeared on the teats and bags of cows and scratched the skin of his wife and children with that substance. During the next smallpox outbreak his wife and children survived without showing signs of the disease. In 1796 Edward Jenner, a British physician, learned of Jesty's work and coopted the procedure by performing an experiment to test the hypothesis that infection with the cowpox virus would protect one from smallpox. In a dangerous trial, Jenner intentionally infected an 8-year old orphan named James Phipps with the cowpox virus. Six weeks later, after Phipps had recovered from the vaccinia symptoms, Jenner intentionally infected the boy with the smallpox virus. The lad survived and showed no signs of illness. Jenner is thus credited with developing a safer method of shielding humans from smallpox. This new procedure became known as "vaccination," the word coming from *vaca*, which is Latin for "cow." The vaccination process does not oblige the patient to endure the actual disease as did variolation, thus greatly decreasing the risk for patients (Fenn, 2001).

The first smallpox epidemic in the Western hemisphere occurred in the late 1400s or early 1500s (Marks & Beatty, 1976). As stated earlier, the effects of smallpox in the New World were devastating, largely killing off the Aztec and Inca civilizations and the indigenous peoples of North America, which in effect cleared the way for settlement by Europeans (Bray, 1996). During the early 1600s there were approximately 25 million Native Americans in North America alone; by 1870 their numbers had been reduced to less than one million, largely because of the dreaded effects of smallpox. Some European-Americans, in misguided notions of supremacy, believed that God was acting on their behalf by ridding America of the Indians and allowing for their unfettered settlement of the New World. Some referred to the massive Native-American deaths as, "the secret judgment of God" (Marks & Beatty, 1976).

During the late 1700s a variolation procedure was used in America. The American version was a 2-week long event that included extended periods of bed rest and drinking a mercury-laced, milk-based

preparation that sometimes caused a loss of teeth. In the course of this procedure, which was similar to the Turkish method, live variola was placed in an incision and the variolated subsequently suffered a case of smallpox. Again, most survived because the symptoms were usually mild. Those surviving then held lifetime immunity from smallpox. There were considerable risks involved with this routine. In instances of the failure to inject sufficient virus, inoculation did not occur; injecting too much could be lethal, and it was possible to transmit and thus cause a lethal case of smallpox. Further, patients could be infected with other blood-borne diseases such as syphilis. Vaccination was controversial in late 1700s America and was an illegal practice at times. Angry mobs rioted in Marblehead and Salem, MA, closing one variolation hospital and razing another. Others burned the home of a physician who practiced smallpox inoculation in Williamsburg, VA (Fenn, 2001).

Concurrent with the American Revolutionary War a smallpox epidemic swept North America, causing the deaths of more people than were killed in the war. That epidemic is the subject of the recent book, *Pox America* (Fenn, 2001). This text details, among other events, the significant impact the disease had on formulating the military strategies used by General George Washington, himself a smallpox survivor. Washington contracted smallpox as a young man while in Barbados, where he had taken his older half-brother to convalesce from tuberculosis. Fortunately for Washington, he survived with little more than scars on his nose. During the times of our first president 90% of the people who attained the age of 21 years had survived smallpox (Fenn, 2001).

Because Washington had witnessed the havoc caused by smallpox and knew the risks of inoculation, he was hesitant to require this procedure of his troops. Because the inoculated would be ill or very ill for 3 or 4 weeks, the decision to variolate the troops was an important one. The general feared that the enemy would learn of the American plan and attack during the period when the troops would be too ill to effectively fight. The British, on the other hand, were not nearly as concerned about smallpox, because most of their citizens were inoculated as a matter of course as children, the vaccination of children having become law in England during the 1830s (Bray, 1996). After struggling mightily with the decision, Washington ordered all Continental troops to be inoculated in 1777. This was the first large-scale state sponsored public health program in American history (Fenn, 2001).

## THE ERADICATION EFFORT

Smallpox was endemic in America for about 150 years after the Revolutionary War, and worldwide caused the deaths of more people in the 20th century than any other disease (Garrett, 2000). During the 1950s an estimated 50 million cases worldwide occurred annually (WHO, 2001). The possibility of eradicating smallpox had been discussed in the early 20th century, but it was not until 1958 that the Soviets proposed the idea to the World Health Assembly (Green & Ottoson, 1994). Eight years later the United States signed on to aid in the endeavor (Watts, 1997). The rationale behind the eradication efforts was strong, because the disease has no known animal reservoir, it is only found in humans. This fact made the identification and elimination of animals hosting the virus unnecessary. Three additional factors made smallpox an even more enticing target for annihilation. Because all smallpox sufferers develop a distinguishable rash, they could easily be identified and isolated. Thus, it was a straightforward matter of determining who had smallpox, where it was occurring, and identifying those to be quarantined. Additionally, the ill were infectious for short periods of time, which allowed limited opportunities for the virus to find new human hosts. Finally, there was a safe, inexpensive, and effective vaccine that did not require refrigeration. This allowed those involved in the eradication effort to vaccinate the susceptible in the earth's most remote and undeveloped regions. Further, the vaccine was effective against all strains of smallpox (Bray, 1996).

The original eradication strategy embraced by the international team was "mass" or "saturation vaccination." The intent of the plan was to vaccinate every person on earth. The need for vaccination was strongest in developing countries, because cases were rarities in the industrialized world. The last American smallpox case was diagnosed in Texas in 1949 (CDC, 2003a).

A shortage of vaccine in Eastern Nigeria in 1967 spawned a clever and ingenious strategy that eventually replaced mass vaccination as the strategy of choice. Dr. William Foege, who was originally in Africa on a church-based medical mission, signed on to assist in the eradication effort. Facing the vaccine shortage, the thoughtful Foege imagined himself as a virus determined to survive (Griffin, 2001). Foege formulated a plan that became known as "surveillance and containment," or "ring vaccination." In employing this tactic every smallpox case was identified, geographically mapped, and placed under strict quarantine for at least 20 days (Watts, 1997). Next, people living within the confines of the geographic "ring" were vaccinated. The first to be vaccinated were family members and those who went to the village markets. The Foege scheme was determined to be a success in Nigeria. Health authorities originally believed that 80–100% of individuals would need to be inoculated to halt the spread of smallpox, but the Foege strategy was able to do so with less than 50% vaccinated. This tactic, was at first not accepted by some others involved in the effort, but the success of the technique was recognized as effective following its use in triumphs over smallpox in South Asia and other parts of Africa, where the final cases were occurring. The last person on earth to naturally contract smallpox was Ali Maow Maalin, a hospital cook from Merker, Somalia, in September of 1977. At that point a disease chain of at least 1,000, and up to 3,000 years, had been broken (Fenn, 2001). The entire project cost from 1967–1979 is estimated at $3 billion, one of the greatest bargains in human history (Green &

Ottoson, 1994).

Ring vaccination is a part of current response plans should a smallpox outbreak occur. The size of the ring would be decided by federal and state officials and would depend on the size of the outbreak, personnel resources, effectiveness of other outbreak control measures, and vaccine availability (CDC, 2003c).

## THE FUTURE

Although smallpox was officially declared eradicated in 1980 (Fenn, 2001), the potential for future smallpox outbreaks is unknown, because the location and control of remaining samples are questioned. Following the successful eradication effort, the World Health Organization (WHO) designated two repositories of the virus, one in Atlanta, GA, at the Centers for Disease Control and Prevention, and the other at the Virology Institute in Moscow (Garrett, 2000). This agreement appeared to function as designed until political unrest in Russia during the 1990s raised questions about the security of that country's smallpox stockpile. At that time it was learned that the Union of Soviet Socialist Republics had already relocated their smallpox supply to the Research Institute for Viral Preparations in Novosibrsk, which is located in the Ural Mountains. This move took place without other WHO partners being informed (Watts, 1997). With the ultimate disintegration of the Soviet Union and resulting job losses of up to 50,000 scientists who had worked at a minimum of 47 bio-weapons laboratories and testing sites, the security of the Russian stockpile was again questioned. It is feared that smallpox could fall into the hands of extremists, terrorists, or militia groups, who could intentionally initiate an outbreak. No one is sure who has the virus, but in 1999 the United States Congress released a report stating that Iraq was in possession of the virus, a report that has yet to be substantiated. Scientists have proposed that the secretary-general of the United Nations should be responsible for the containment of smallpox at the international level. Scientists also recommend efforts be made to locate and question all persons who had access to the virus since 1977 to ensure that no stores have been maintained (Breman, Arita, & Fenner, 2003).

Because of the changes in world circumstances in the late 1990s, U.S. governmental officials saw the need to evaluate the stockpile of smallpox vaccine. Checks of existing vaccine identified potential problems. About 15.4 million doses were located in the United States, with approximately 60 million available worldwide. Further examination of the vaccine caused additional anxiety, as it appeared that the vacuum pressure used to store the freeze-dried and crystallized vaccine had been lost (Garrett, 2000). The pressure loss could have caused deterioration of the vaccine, making the quality and potency questionable. Also, there were only one million specialized bifurcated needles available, which are used to deliver smallpox vaccinations, and no company was manufacturing them. Further, only 675 doses of variola immunoglobulin, which is needed in cases of life-threatening reactions to the vaccine, were on hand (Garrett, 2000).

However, recently the federal government took action to improve readiness for a smallpox release. A Cambridge, MA, company, OraVax, was commissioned to produce smallpox vaccine and will also manufacture the bifurcated needles (LeDuc & Jahrling, 2001). The first phase of the plan demands mandatory vaccination of about 500,000 military troops, who would potentially be exposed in an event. The second phase involves the voluntary vaccination of civilian health care workers, whose skills would be critical in responding to any bioterrorism event. Those workers refusing vaccination could be quarantined. The government's plan will offer the vaccine to all Americans by 2004, and currently the United States has sufficient smallpox vaccine for every American (CDC, 2003c).

The vaccine, however, does carry rare but serious risks. It is estimated that 15 of every million vaccinated for the first time would face life-threatening complications, and one or two would die. Severe reactions are less common among those who were previously vaccinated. Typical reactions include a sore arm, fever, and swollen glands. The most frequent severe reaction occurs when the vaccine escapes the inoculation site, often because the person vaccinated intentionally touched the site and then touched either themselves or someone else. This "secondary vaccinia" can cause blindness if it spreads to the eyes (CDC, 2003d). Risks of secondary vaccinia are reduced by properly caring for the vaccination site, which involves covering it with a bandage, properly disposing of bandages, and hand washing. The bandage should be changed every 1–3 days, and used bandages should be placed in sealed plastic bags and discarded. Vaccinees should keep the site dry, cover it with a waterproof bandage while bathing, and change back to a dry gauze bandage after bathing. Gauze bandages should be changed whenever they become wet. Additionally, it is recommended that vaccinees wear long-sleeved shirts that cover the vaccination site. Hands should be washed thoroughly with antimicrobial soap and water after any contact with the vaccination site or materials that have come into contact with the site (CDC, 2003d).

The federally supported vaccination program, however, is off to a slow start. The government had hoped to have about 450,000 people who are part of smallpox response teams vaccinated by March 1, 2003. Recent data suggests that only 12,404 had received a vaccination by March 4, 2003. The goal of phase two is to vaccinate about 10.5 million health care and emergency responders. One possible reason for the slow response is that some labor unions have cautioned workers against getting the vaccination, because no compensation plan had been established for those becoming ill or dying as a result of the procedure. This is because drug manufacturers expressed concern about litigation that could result from use of the vaccine. In response, as a part of Section 304 of the Homeland Security Act, protection from liability of the U.S. government and vaccine manufacturers was

granted (CDC, 2003b). However, in early March 2003 the administration laid out a plan to compensate those who are negatively affected by the vaccine. This plan, which must be approved by Congress, calls for paying $262,100 in cases of death or permanent and total disability, and up to $50,000 for those less seriously harmed, plus medical expenses. Civilians volunteering for the program will not be eligible to receive monies from the fund (Meckler, 2003).

As stated earlier, the vaccine is delivered by a bifurcated needle that has been dipped into the vaccine. When removed, the needle retains a drop of vaccine, and then is used to rapidly prick the skin about 15 times, usually on the upper arm. The needle pricks are not deep, but the spot will be sore and a few drops of blood may form (CDC, 2003a). If the procedure is a success, which is called "a take," a red and itchy bump develops at the vaccination site in three or four days. During the first week the bump becomes a large blister, fills with pus and begins to drain. Health officials will examine the vaccination site for a take 6, 7, or 8 days after the inoculation. During the second week postvaccination the blister will begin to dry up and scab over. The scab will fall off during the third week and leave a small scar. It is estimated that the protection will persist for 3 to 5 years (CDC, 2003d) but some believe benefits will be sustained for at least 10 years. Delivery of the vaccine up to 4 days postexposure, and before the rash appears, does provide protective immunity or amelioration of the severity of disease symptoms (WHO, 2001).

Those who have compromised immune systems, such as the pregnant, the HIV positive, cancer victims, and organ transplant recipients should not be vaccinated. Additionally, people with eczema risk serious and permanent rash if vaccinated (CDC, 2003c).

The challenges of preparing for a smallpox attack are enormous. It is clear that health educators will play roles in prevention and response efforts and should be knowledgeable about this disease. As with all potential catastrophic events, we will not know if we are prepared for that incident until it occurs.

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