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Smallpox: Technical Background on the Disease and Its Potential Role in Terrorism

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Summary

Smallpox, which kills approximately 30% of its victims, is estimated to have killed between 300 and 500 million people in the twentieth century before the World Health Organization's successful eradication program. The smallpox vaccine is effective at preventing smallpox but has a higher complication rate than any other currently used vaccine. The terrorist attacks of 2001 have increased fears that smallpox might be used as a weapon of terror. Smallpox has several properties that might make it desirable by terrorists, such as contagiousness and high lethality. These factors and its limited availability also make it difficult for a terrorist to use. Most experts agree that it is very unlikely that smallpox will be used as a weapon, but the high consequences of a successful attack have prompted exploration of methods to counter this threat. Also see CRS Report RL31694 *Smallpox Vaccine Stockpile and Vaccination Policy* and CRS Report RL31368, *Preventing Proliferation of Biological Weapons: U.S. Assistance to the Former Soviet States*. This report will updated as warranted.

Smallpox Virus

Viruses are essentially small pieces of genetic material in a protein coat. They cannot reproduce by themselves. To multiply, a virus must hijack the replication machinery in living cells by infecting another organism. Smallpox is caused by the Variola virus, which under normal circumstances only infects human cells. There are two types of Variola viruses. Variola *minor* causes a relatively mild disease that has less than a 1% fatality rate. Variola *major* causes what is generally thought of as smallpox, a very severe illness with a fatality rate of approximately 30%.[1] These viruses are part of the

[1] Some experts have estimated the fatality rate for unvaccinated victims to be approximately 50%. See T. Mack. "Smallpox in Europe,1950-1971." *Journal of Infectious Disease*. Vol. 125(2):161-9. February 1972.

Orthopox genus which also contains the viruses responsible for vaccinia, monkeypox, cowpox, camelpox and mousepox.[2]

Smallpox Disease

Before the last reported case of smallpox (a result of a laboratory accident in England in 1978), smallpox was considered to be one of the worst scourges in human history. Smallpox is estimated to have killed between 300 and 500 million people in the twentieth century alone.

Once infected, the victim incubates the virus for seven to seventeen days during which the victim feels and appears normal. This stage is followed by one to four days of high fever, malaise, headache, and muscle ache, often accompanied with nausea and vomiting. During this time the person looks and feels very ill, but is not yet contagious. After this stage, the characteristic sores develop; first in the mouth then over the rest of the body. If the victim survives, the sores scab over and turn to scars in three to four weeks. About 30% of unvaccinated victims die (some sources suggest up to 50%). Up to 80% of the survivors are disfigured by pockmarks or limb deformities.

Smallpox is contagious, but the Centers for Disease Control and Prevention (CDC)[3] considers it to spread less widely and less rapidly than chickenpox, measles, whooping cough, or influenza. The victim is most likely to infect other people when the sores in the mouth are most active. This is in the first week of the rash when virus comes out of the sores and into the saliva where they are easily aerosolized by coughing or sneezing. Although smallpox is usually transmitted by face to face contact, it can also be transmitted through the air over dozens of feet and by contaminated clothing or bedding.

Smallpox Vaccine

The vaccine works by infecting a person with vaccinia virus which is closely related to smallpox virus.[4] The vaccine triggers immunity against all closely related viruses, including smallpox. This immunity decreases over time; however, people who contract smallpox even thirty years after vaccination are much less likely to die than unvaccinated people.[5] Interestingly, the vaccine also helps reduce the severity of the disease if given to victims within a few days after smallpox exposure. This is the only known treatment for smallpox, although several antiviral drugs have shown promise in preliminary laboratory studies.

Although the vaccinia vaccine is very effective at preventing smallpox, it is not without risks. Its complication rate is higher than that associated with any routinely used vaccine. Based on historical experience, experts estimate that most vaccinees will

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[2] Chickenpox is caused by the Varicella zoster virus which is not a member of this family.

[3] The CDC is an agency within the Department of Health and Human Services charged with promoting health and quality of life by preventing and controlling disease, injury, and disability.

[4] Contrary to popular belief, the vaccinia virus is genetically distinct from the virus that causes cowpox which was first used by Jenner to inoculate his patients.

[5] T. Mack. *Op cite*.

experience only mild side effects such as low-grade fever, but 1 in 797 people will experience serious side effects. **Table 1** describes the historical complication rates.

Table 1. Historical smallpox vaccine complication rates (cases/million vaccinations)

Inadvertent Inoculation	529.2
Generalized Vaccinia	241.5
Eczema Vaccinatum	38.5
Encephalitis	12.3
Progressive Vaccinia	1.5

Source: CDC, Morbidity and Mortality Weekly Report, June 22, 2001, Vol. 50, No. RR-10, p. 8.

Inadvertent inoculation is the spread of the usually localized vaccinia infection to other parts of the body, causing sores and scarring most commonly on the face, genitals, and rectum. Generalized vaccinia causes vaccinia sores over the entire body. Eczema vaccinatum is a sometime fatal skin infection in people who have a skin disorder such as eczema or atopic dermatitis. Encephalitis is a very serious and sometimes fatal inflammation of the brain. Progressive vaccinia is an inexorable rotting away of the flesh around the vaccine site that can sometimes also be fatal. As a result of these complications, experts project 1-2 deaths per million vaccinations.

Complications are not limited to people who get vaccinated. People who come into contact with those who have been vaccinated within two weeks may also be exposed to the live vaccinia virus and develop complications. Some experts estimate that up to 20% of the complications will occur in the unvaccinated contacts. Historically, for every million people vaccinated, about 65 people who were not vaccinated became infected and developed a serious complication simply by coming into contact with a vaccinee.[6] Because of the high rate of vaccine complications, in 1971, U.S. public health authorities rescinded the recommendation for universal domestic smallpox vaccination.

It is likely that the numbers in **Table 1** underestimate the current and future problem with the vaccine. Since these numbers were last compiled in 1968, the number of people predisposed to problems with the vaccine has increased. Some experts estimate that up to 25% of the population now have conditions that would make vaccination contraindicated. These conditions include a history of eczema or other exfoliative skin disorder, pregnancy, or any immunodeficiency which could be caused by AIDS, chemotherapy or anti-rejection drugs following organ transplant. Because of the serious risk of transferring the virus to a household member, it is recommended that people who live with someone with one of the above conditions not receive the vaccine. Excluding these people is complicated by the large number of people who are unaware that they have a disease that will produce a serious side effect. For example, a vaccinee could live with one of the estimated 300,000 people in the United States that do not know they are HIV positive.

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[6] J. Neff *et al*. "Contact Vaccinia–Transmission of Vaccinia from Smallpox Vaccination." *Journal of the American Medical Association*. Vol. 288(15):1901-1905. October 16, 2002.

The only product proven to counter some of the vaccine complications is vaccinia immunoglobulin (VIG). This is extracted from the blood of people vaccinated with the smallpox vaccine. It is only effective for treatment of eczema vaccinatum and certain cases of progressive vaccinia. Significantly, VIG provides no benefit in the treatment of postvaccinial encephalitis. Current civilian supplies of VIG are controlled by the CDC and are estimated to be enough to deal with the complications from about 27 million vaccinations. The CDC is in the process of procuring more VIG. Because the antiviral drug cidofovir has shown some anti-vaccinia activity in lab animals, it is available for use as an Investigational New Drug when VIG treatment fails.

Threat of Terrorist Use

Although smallpox was officially declared to have been eliminated from the wild in 1980, many countries maintained laboratory stocks of the virus obtained during outbreaks. By 1985, these stocks were supposed to have been destroyed or transferred to one of the official repositories; one in the Soviet Union and the other in the United States.

Russia inherited the smallpox stewardship following the break up of the Soviet Union. Although only the United States and Russia have declared stocks of smallpox, some experts have stated that although very unlikely, it is possible that some other countries have undeclared stocks. Countries that may have deliberately or inadvertently retained smallpox virus from naturally occurring outbreaks before eradication include: China, Cuba, India, Iran, Iraq, Israel, North Korea, Pakistan, and Yugoslavia.[7] A November 2002 CIA intelligence review added France to this list and reportedly states a "high, but not very high [level of] confidence" that Iraq and France have live smallpox samples and a "medium" level of confidence that North Korea does.[8]

The highest barrier to a non-state sponsored terrorist using smallpox is likely to be the difficulty in obtaining the virus in the first place. Because all countries have stopped smallpox vaccination programs, citizens of all countries are equally vulnerable to a spreading epidemic. Therefore, it is in the best interest of a country with even an undeclared smallpox stock to keep it very secure. Despite this, some fear that the Russian stocks may not be sufficiently secure due to the economic collapse that accompanied the break up of the Soviet Union.

Other than from a government controlled stockpile, some have suggested that it may be possible to acquire the virus from the bodies of smallpox victims buried in the Siberian permafrost in the 1800s. However, this is probably unlikely since Russian experts have been unable to acquire viable virus this way despite multiple attempts.[9] In 2002, American scientists successfully constructed infectious polio virus from mail-ordered

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[7] J. Tucker. *Scourge: the Once and Future Threat of Smallpox*. Atlantic Monthly Press, New York City. 2001. p. 205.

[8] B. Gellman. "4 Nations Thought to Possess Smallpox." *Washington Post*. November 5, 2002. p. A01

[9] Tucker, p. 162.

pieces of DNA.[10] However, most experts claim that it would be very difficult to construct Variola virus in this manner. For more information on this topic, see CRS Report RS21369 *Synthetic Poliovirus: Bioterrorism and Science Policy Implications*.

If a terrorist organization were able to obtain a sample of virus, it would also need the advanced technical knowledge, skill and facilities to maintain the virus without infecting themselves until the planned dissemination. It is considered to be quite difficult to "weaponize" smallpox.[11] However, in general, weaponization refers to developing advanced delivery systems such as missiles, artillery, or bombs to cause mass casualties. This technological barrier would be much lower for a terrorist. A terrorist, who was not concerned with his own survival could potentially use his own body as the delivery system, infecting dozens of people before succumbing to the disease.

In addition to the threat posed by terrorist groups, it is possible that another nation may choose to use smallpox against the United States. Some experts suggest that of the countries that might have undeclared stocks of smallpox virus, Iraq may pose the most danger to the United States. Some experts believe that it is very unlikely that Iraq has smallpox since they did not use it during the Gulf War. However, those who feel that Iraq has the smallpox virus counter that it would not have been used because it is not well suited for battlefield deployment since it is contagious and likely to infect troops on both sides. Some experts also believe that Iraq was dissuaded from using chemical or biological weapons by what could have been interpreted as a thinly veiled threat of nuclear retaliation.[12] In the current situation of rising tensions, some experts have stated that if Iraq has the capability, Saddam Hussein may unleash smallpox as a weapon of last resort, particularly if he can deploy it covertly on United States soil.[13] In December 2002, the Administration reserved the right to use nuclear weapons to respond to the use of weapons of mass destruction against the United States or its allies.[14]

Nonetheless, most experts feel that the barriers posed by acquisition and successful deployment of smallpox virus are high enough to make such an attack very unlikely. Furthermore because of these hurdles, most experts feel that a terrorist organization would require a state sponsor in order to successfully obtain and deploy smallpox.

Policy Implications

Although most experts deem the risk of a smallpox attack to be very low, the high consequences of a release have led the President to order the vaccination of approximately

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[10] J. Cello, A. Paul, and E. Wimmer. "Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template." *Science Express* 10.1126. July 11, 2002.

[11] For more information about biological weapons see CRS Report RL31059 *Biological Weapons: A Primer* and CRS RL31332 *Weapons of Mass Destruction: The Terrorist Threat*.

[12] J. Miller, S. Engelberg, and W. Broad. *Germs: Biological Weapons and America's Secret War*. Simon & Schuster, New York City. 2001. p. 121.

[13] "Pentagon's Worry: Iraqi Chemical Arms." *New York Times*. May 19, 2002. p.12.

[14] Executive Office of the President, "National Strategy to Combat Weapons of Mass Destruction." Washington, DC. December 2002. Available online at: [http://www.whitehouse.gov/news/releases/2002/12/WMDStrategy.pdf]

500,000 people in the armed forces and to initiate a voluntary program to encourage as many as 10 million medical workers and first responders to be vaccinated. By the middle of 2003, the vaccine will be available on demand to any American adult who is not in a high-risk group for complications. However, the Administration will not recommend vaccination for members of the general public because of the high complication rate.[15]

Scientific research may be able to further limit the threat posed by smallpox. If a safer smallpox vaccine could be produced, for instance, public health officials would be less reluctant to recommend mass vaccination. The development of such a vaccine is stymied by several factors. One is that it is difficult to predict before making a large investment whether a new vaccine will be safer and still effective against smallpox.[16] Another factor is the uncertain market of a therapeutic agent that is designed to protect against what most experts agree is a very unlikely event. Without a guaranteed market, the commercial sector may be reluctant to make such investments.

Some experts suggest that, in general, it may be better to develop treatments rather than relying on prophylactic measures for the many potential biological agents that could be used to attack the United States. They suggest that the financial and societal costs of multiple mass vaccination programs may make a vaccines-only approach impractical. Some scientists are working on producing antiviral drugs as a cure for smallpox and several have shown promise in preliminary studies.[17] However, more work needs to be done to improve animal models of smallpox so that the efficacy of new therapeutics can be tested.[18] Another potential advantage of this approach is that these drugs may be effective against other viruses and therefore might be marketable as treatments for influenza or AIDS.

The United States might be better equipped to defend against a smallpox attack if the status of any undeclared smallpox stocks could be determined with greater certainty. For example, if it could be determined that Iraq does not have any smallpox then focus could be shifted to preventing terrorist access to other sources. Unfortunately, it is possible that Iraq could successfully hide a smallpox program from any inspection regime.

The United States is helping to increase the security of the former Soviet Union's biological weapon stockpiles. By focusing on the physical security of the agents and the economic security of the scientists, these programs simultaneously reduce the threat posed by all of the agents in the former Soviet Union's arsenal. For a comprehensive discussion of these programs, see CRS Report RL31368 *Preventing Proliferation of Biological Weapons: U.S. Assistance to the Former Soviet States*.

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[15] C. Connolly and D. Milbank "U.S. Revives Smallpox Shot." *Washington Post.* December 14, 2002. Also see CRS Report RL31694 *Smallpox Vaccine Stockpile and Vaccination Policy*

[16] S.R. Rosenthal *et al.* "Developing New Smallpox Vaccines." *Emerging Infectious Diseases*. Vol. 7, No. 6. November – December 2001. pp. 920- 926.

[17] Ibid.

[18] JW LeDuc and P. Jahrling. "Strengthening National Preparedness for Smallpox: An Update." *Emerging Infectious Diseases*. Vol. 7. No. 1. January – February 2001. pp. 155- 157.