Fact Sheet

Variola virus (Smallpox)

Unless otherwise noted, all information presented in this article is derived from the following two sources:

1. Henderson DA, Borio L, Grabenstein J. Smallpox and monkeypox. In Plotkin S and Orenstein W (eds), *Vaccines*. Philadelphia: W.B. Saunders Company; 2007.
2. Henderson DA, Inglesby TV, Bartlett JG, et al., for the Working Group on Civilian Biodefense. Smallpox as a biological weapon: medical and public health management. *JAMA.* 1999;281(22):2127-2137.

Background

Smallpox is a contagious disease caused by the variola virus.

The World Health Assembly declared smallpox eradicated in 1980, thirteen years after the Intensified Global Eradication Program began, and recommended that all countries cease routine smallpox vaccination. Today, the only potential source of smallpox infection is an unintentional laboratory release or a biological attack.

After the eradication of smallpox, the World Health Organization (WHO) recommended that all remaining stocks of variola virus be destroyed or sent to one of two designated reference laboratories at the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, or the Research Institute of Viral Preparations in Moscow, Soviet Union. It was discovered later that Russia moved its smallpox samples to VECTOR, a Siberian facility that had previously served as a biological weapons development plant.

In the 1980s, the Soviet government embarked on an extensive smallpox research and development biological weapons program, much of which was conducted at VECTOR. The program included methodology for industrial production of tons of smallpox virus annually for use in intercontinental ballistic missiles. Since the fall of the Soviet Union, Russian laboratories have had difficulty maintaining funding for their work and half or more of Russian scientists have left, some going to other countries. It is unknown whether they have taken samples of smallpox with them.

Smallpox as a Biological Weapon

Smallpox is considered one of the most serious bioterrorist threats to the population. It was first used as a biological weapon during the French and Indian Wars (1754-1767) when British soldiers distributed smallpox-infected blankets to American Indians.

Several factors contribute to the concern about the use of smallpox as a biological weapon:

- There is no treatment for the disease
- 30 out of 100 people who contract smallpox die
- Since routine smallpox immunization ceased in the United States in 1972 and in all other countries by 1983, the global population is extremely vulnerable to the disease. Much of the world's population has never been vaccinated or was vaccinated so long ago that immunity to smallpox has waned.

Smallpox would be relatively easy to disseminate in the form of an aerosolized biological weapon, and the virus is relatively stable as an aerosol. Furthermore, epidemiological evidence suggests that the infectious dose may be only a few virus particles. Since there are no symptoms at the time of exposure, a covert release of smallpox would likely not be detected until sick people begin showing up at doctor's offices and hospitals. (See "The History of Bioterrorism: Smallpox," a short video from the CDC: http://www.bt.cdc.gov/training/historyofbt/04smallpox.asp)

Transmission

Smallpox spreads from person to person, usually by respiratory droplets or through direct contact with body fluids. Contaminated clothing or bedding might also transmit the virus. Animals and insects are not known to carry or spread the virus to humans. The incubation period for smallpox is 7 to 17 days.

Infection Control Measures

Individuals diagnosed with or suspected of having smallpox should be isolated to prevent the spread of disease. Household and other face-to-face contacts of patients with or suspected of having smallpox should be vaccinated and placed under surveillance. Contacts who develop smallpox should be placed in isolation. (See CDC Isolation Precautions Guidelines: http://www.cdc.gov/ncidod/dhqp/pdf/guidelines/isolation2007.pdf)

For smallpox patients in the hospital, airborne precautions should be followed, and all hospital personnel should be vaccinated. Gloves, gowns, and masks should be worn, and patients should be placed in negative-pressure isolation rooms.

Signs and Symptoms

Diagnosis of smallpox is based on clinical presentation of symptoms in the patient and is confirmed by laboratory testing. Symptoms usually appear within 12 to 14 days after infection, and include high fever, severe malaise, and exhaustion with headache and backache.

A rash of small, pink bumps appears in the mouth, face and forearms, and then spreads to the trunk of the body and legs. Within 1 to 2 days, the rash becomes first fluid-filled and then pus-filled. Lesions are round, hard and deep; they begin to crust over on day 8 or 9. A person infected with smallpox is thought to be contagious from the time the rash appears to the time it heals (~2 weeks). Survivors are often left disfigured, with permanent scars on the face. (See photographs showing progression of smallpox in a child.)

Complications of smallpox include bacterial superinfections of the skin and organs, pneumonia, sepsis, arthritis, keratitis, and encephalitis. In contrast to smallpox, chickenpox is associated with a milder prodromal illness, and the rash is more superficial, usually appearing on the trunk first and spreading centripetally, evolving rapidly and in different stages, and only rarely appearing on the palms of the hands or soles of the feet.

Smallpox is caused by one of two viruses: variola major and variola minor. Clinically, the two viruses are indistinguishable except by polymerase chain reaction (PCR) testing. Variola minor infection (known as Alastrim) causes fewer systemic symptoms, a less extensive rash, less scarring, and fewer fatalities.

Treatment and Prophylaxis

Post-exposure prophylaxis with vaccination within 1 to 3 days after exposure to smallpox can prevent infection with smallpox. Vaccination within 4 to 7 days post-exposure can reduce the severity of disease.

There is no U.S. Food and Drug Administration (FDA) licensed antiviral treatment for smallpox. The protease inhibitor SIGA-246 (SIGA Technologies, Inc.) was awarded orphan drug status by the FDA in December 2006 and is currently undergoing clinical trials.

Antibiotics may help treat secondary bacterial infections, and supportive therapy might also benefit patients.

WHO classification of smallpox types, based on a study of 3,544 patients in India, 1972*

Type of variola major	Characteristics	Case-fatality rate
Ordinary	• Most common form • 90% of cases in unvaccinated persons	30%
Modified	• Milder form • Produces fewer, smaller, and more superficial lesions • 2% of cases in unvaccinated; 25% of cases in vaccinated persons	Not available; however, cases of modified smallpox were rarely fatal.
Malignant or flat	• Lesions were flatter, evolved more slowly and coalesced • 7% of cases in unvaccinated persons	97%
Hemorrhagic	• Difficult to diagnose • Rash accompanied by bleeding into mucous membranes and skin • Less than 3% of cases	Near 100%
Variola sine eruption (without rash)	• Occurred in previously vaccinated contacts or in infants with maternal antibodies • Affected persons are asymptomatic or have a short-lived fever, headache, and influenza-like symptoms • Transmission of clinical smallpox has not been documented for variola sine eruptione	Not available; however, in cases of variola minor, death occurred in <1% of persons.

* *Derived from Fenner F, Henderson DA, Arita I, Ježek Z, and Ladnyi ID.* Smallpox and Its Eradication. *Geneva: World Health Organization; 1988. Page 4. Available at: http://whqlibdoc.who.int/smallpox/9241561106.pdf .*

Countermeasures

Rapid, point-of-care diagnostic tools and antivirals for smallpox are considered high priorities for the HHS Public Health Emergency Countermeasure Enterprise (PHEMCE). According to the PHEMCE Implementation Plan, development and acquisition of rapid diagnostics and smallpox antivirals are slated for 2009 to 2013. (See HHS Public Health Emergency Medical Countermeasure Enterprise Implementation Plan for Chemical, Biological, Radiological and Nuclear Threats. Washington, DC; 2007. U.S. Department of Health and Human Services: http://www.hhs.gov/aspr/barda/documents/phemce_implplan_041607final.pdf)

Two licensed vaccines for smallpox are currently in the U.S. Strategic National Stockpile (SNS) – ACAM2000 (Acambis) and "wetvax" (sanofi aventis). These vaccines contain live vaccinia virus, a relative of the smallpox virus. On rare occasions, immunization with these vaccine can cause serious and potentially life-threatening reactions. In June 2007, the U.S. Department of Health and Human Services (HHS) issued a contract to purchase a new smallpox vaccine that contains a highly weakened form of vaccinia virus, modified *vaccinia Ankara* (MVA, Bavarian Nordic) that cannot replicate in humans. The new vaccine will be for use in individuals with compromised immune systems, including chemotherapy patients and people with HIV/AIDS, as the current vaccine is contraindicated for these individuals except under emergency circumstances. (See HHS Buys Next Generation Smallpox Vaccine. HHS News Release. June 4, 2007.)

The SNS contains more than 300 million doses of live vaccinia virus smallpox vaccine, or enough to immunize every person in the U.S. The HHS contract for the new vaccine will add 20 million doses of vaccine, or enough to treat 10 million people with compromised immune systems (the vaccine requires a two-dose regimen per person). However, the date for delivery of this vaccine has not yet been announced.

The U.S. government does not currently recommend smallpox vaccination for the general public. In December 2002 the president announced the Smallpox Vaccine Program, to vaccinate voluntarily those persons deemed to be at highest risk should a smallpox outbreak occur, including first responders and healthcare workers serving on "smallpox response teams." In all, some 40,000 civilian employees were immunized in the first few months after the program was announced, but further vaccinations are not currently being promoted. Deployed military personnel continue to be vaccinated as well as laboratory staff engaged in work with vaccinia and related viruses.

Since smallpox no longer occurs naturally, a single confirmed case is considered an emergency and will prompt implementation of federal and state smallpox response plans for surveillance and containment.

See Also

Smallpox Web page. Centers for Disease Control and Prevention, Emergency Preparedness and Response. http://www.bt.cdc.gov/agent/smallpox. Accessed October 2, 2007.

Chemical and biological weapons resource page. Center for Nonproliferation Studies, Monterey Institute of International Studies. http://cns.miis.edu/research/cbw/index.htm. Accessed October 2, 2007.

Department of Defense Smallpox Vaccination Program Web site. http://www.smallpox.army.mil. Accessed October 2, 2007.

Guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings 2007 Web page. Centers for Disease Control and Prevention. http://www.cdc.gov/ncidod/dhqp/pdf/guidelines/Isolation2007.pdf. Accessed October 2, 2007.

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