Does smallpox still pose a threat?

**Background and epidemiology:** The terrible effectiveness of smallpox as a biological weapon was demonstrated in the 1760s, when British troops deliberately distributed blankets that had been used by patients with smallpox among the Iroquois. The resulting epidemics wiped out many tribes. Four decades later, the threat of smallpox as a biological weapon was substantially diminished by the development and dissemination of an effective vaccine. Two centuries later, in 1979, after an unprecedented global effort to support worldwide vaccination, the World Health Organization declared smallpox eradicated. The last naturally occurring case occurred in Somalia in 1977.

In 1980 the World Health Assembly recommended that all countries cease smallpox vaccination. All remaining known laboratory samples of the virus went either to the US Centers for Disease Control and Prevention, in Atlanta, or to the Institute for Viral Preparations, in Moscow. The specimens in Moscow were subsequently moved to the more secure Russian State Research Centre of Virology and Biotechnology, in Koltsovo. In 1996 the 49th World Health Assembly unanimously approved a resolution to destroy remaining stocks of the virus at both sites by June 1999, but in May 1999 this date was pushed back to 2002 — amid reports from Ken Alibek, a former deputy director of the Soviet Union’s civilian biowarfare program that, in 1980, the Soviet Union had begun producing large amounts of the smallpox virus and adapting it for use in bombs and missiles.

Although these reports are difficult to confirm, the recent collapse of the Soviet Union has resulted in mounting concern that existing stocks of the virus, along with the intelligence information and the equipment needed to deliver it, may have passed into non-Russian hands. This has raised once again the spectre of the potential use of smallpox as a biological weapon, and it means that, in light of the terrorist acts on Sept. 11, physicians once more have to be taught about this potential threat. Smallpox is caused by the DNA virus variola, a member of the genus orthopoxvirus. There are 2 strains: variola major, with a case-fatality rate of 30%, and variola minor, a much milder form. Smallpox is unique to humans and highly contagious. There are no known animal or insect vectors or reservoirs. To sustain itself the virus must pass from person to person; it is spread by inhalation of air droplets or aerosols. Contaminated clothing or linens can also spread it.

On exposure, the virus lodges on the oropharyngeal mucosa and subsequently migrates to regional lymph nodes. Two to 3 days after infection an asymptomatic viremia develops, followed by viral multiplication in the spleen, bone marrow and lymph nodes. The virus, packaged in leukocytes, then localizes in small blood vessels of the dermis and beneath the oral and pharyngeal mucosa. Infected macrophages migrate to the epidermis, causing edema, necrosis and splitting of the dermis. A maculopapular rash erupts and progresses to vesicles and then pustules. Pock marks result from the destruction of sebaceous glands, followed by the shrinking of granulation tissue; blindness can result from scarring in the conjunctiva. The lesions rarely become secondarily infected. Death, which typically occurs in the second week of illness, usually results from the toxemia produced by circulating immune complexes and soluble viral antigen.

**Clinical management:** Twelve to 14 days after infection the patient becomes febrile and has severe aching pain and prostration. About 2 days later the papular rash erupts. Unlike the rash that accompanies chickenpox, the smallpox rash develops at the same pace on all parts of the body: papules, vesicles and pustules do not occur simultaneously. The rash is denser on the face and extremities than on the trunk. Laboratory specimens should be collected by someone wearing gloves and a mask who has been recently vaccinated. Vesicular or pustular fluid can be collected on a cotton swab, and scabs can be picked off with forceps. Specimens should be deposited in a vacucontainer tube, sealed at the juncture of the stopper and tube with adhesive tape, and then placed in a second watertight container. Laboratory examination should be undertaken only in designated facilities; Canada has a level 4 laboratory in Winnipeg. There is no treatment.

**Control and prevention:** Suspected cases must be reported immediately to the local or provincial public health authority. All patients suspected of having the disease should be isolated in a hospital room that is under negative pressure and equipped with high-efficiency particulate air filtration. All laundry and waste should be placed in a biohazard bag and autoclaved before being laundered or incinerated.

Vaccination within the first 4 days after exposure may prevent or significantly ameliorate illness. The immune status of those vaccinated more than 25 years ago is unclear, although neutralizing antibodies have been shown to decline over 5–10 years, which suggests that immunity wanes. It must be assumed that the population at large is highly susceptible to infection. A number of countries and the World Health Organization have stockpiled small amounts of smallpox vaccines produced in the 1970s. There are currently no manufacturers equipped to produce the vaccine in large quantities.

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**References**