
Bioterrorism Agent Fact Sheet

Smallpox/Variola virus

Disease

Smallpox is the disease caused by the Variola virus, a member of the orthopox virus family. After claiming more lives than any other infectious disease in human history, there have been no confirmed cases since worldwide eradication was achieved in 1978 by a WHO-sponsored campaign. Although natural disease has been eradicated, smallpox still remains a primary threat as a bioterrorism agent because of an expected case fatality rate of 30% and the potential for person-to-person transmission. A single confirmed case should be considered an international infectious disease emergency.

Clinical Features of Smallpox

Smallpox infection occurs following inhalation or direct contact between virus particles and mucous membranes. The asymptomatic incubation period is typically 10-14 days after exposure (range 7-17 days), during which virus is carried to regional lymph nodes, eventually leading to viremia. A prodromal phase follows, manifested by high fever, malaise, prostration, vomiting, headache and backache. Infected white blood cells then invade the oral mucosa and dermis giving way to the characteristic eruption. The rash begins as small macules then becomes papular, progressing to vesicles, pustules and then scabs over 1- 2 weeks. The lesions are round, 4-6 mm diameter, deep-seated and tense and distributed in a centrifugal pattern with concentration on the face and extremities, including palms and soles. Another distinguishing feature of smallpox is that all lesions in one area are in the same stage of development. In contrast, chickenpox lesions are usually oval, 2-4 mm, shallow, in various stages of development and predominantly involve the trunk. Pitting scars, or pockmarks, are common, especially on the face. Other, less frequent, complications include encephalitis, secondary bacterial infections, conjunctivitis and blindness. Death is usually caused by the massive inflammatory response and sepsis resulting from viremia. Partially immune individuals from prior vaccination usually have a less severe rash and course of illness. There are three categories of disease, each identified by the features of its rash. In an outbreak setting, the atypical presentations should be considered as smallpox until proven otherwise.

- *Classical*: accounts for >90% of cases and includes three sub-types of rash with mortality ranging from <10% for the discrete sub-type to 50-75% for the confluent sub-type.
- *Malignant (flat)*: has an atypical velvety rash which never matures into pustules and is associated with >90% mortality.
- *Hemorrhagic*: manifested by a more diffuse erythematous rash leading to petechiae and hemorrhages; often misdiagnosed as meningococemia. It is uniformly fatal.



Smallpox lesions on skin of trunk

Smallpox

Diagnosis

Diagnosis should be suspected in any patient who presents with the typical features. Clinical presentation alone is sufficient for a diagnosis in an outbreak setting after an index case has been positively identified. The characteristic centrifugal rash is distinct (see Clinical Features) and differentiates it from chickenpox, the chief alternative diagnosis. Clinical specimens should be obtained for confirmatory laboratory testing, which is only available at reference laboratories. Vesicular or pustular fluid, or scabs should be obtained with a cotton swab or glass slide by a recently vaccinated healthcare worker, or one who has no contraindications for vaccination, using proper infection control precautions. From these samples, an orthopox virus infection can be quickly distinguished from chickenpox by electron microscopy. Confirmation of Variola as the specific orthopox virus can be made by immunohistochemistry stains, polymerase chain reaction (PCR) or isolation of the virus.

Infection Control

Smallpox spreads person-to-person via respiratory droplets or through direct contact with contaminated clothing or bed linens. The secondary attack rate for unvaccinated contacts is estimated at 25-40% and is not affected by severity or form of disease in the index case. Although transmission typically occurs in 3-4 susceptible contacts per case, 20 or more secondary cases may arise from each primary case in a non-immune population. All suspected cases should be immediately isolated with airborne and contact precautions including the use of gowns, gloves and N-95 masks until all scabs separate or the diagnosis is excluded. Home isolation may be a preferred alternative for mild cases during an epidemic because of the high risk

Treatment

There is currently no known effective antiviral medication to treat smallpox. Supportive therapy such as electrolyte and volume repletion, as well as hemodynamic support should be offered. Antibiotics should be used for secondary bacterial infections as indicated. Idoxuridine may be useful as a topical agent if corneal involvement is present.

Post-Exposure Prophylaxis

Vaccination may be effective in preventing morbidity and mortality if given within 2-3 days of exposure. Exposure is defined as inhalation of viral particles from the initial release, household or face-to-face contact with a known case following fever development, or direct contact with contaminated linens or lab specimens from a known case. Cidofovir, an antiviral drug with substantial renal toxicity, may improve outcomes if given within 1-2 days after exposure; however there is no definitive evidence to suggest that it is better than vaccine alone. During an outbreak, all household or close contacts, hospital employees, other patients in the same hospital, laboratory and mortuary employees should be vaccinated.

Vaccination

Multiple versions of an attenuated-strain vaccinia virus vaccine are now available. It is expected that by early 2003, there will be enough vaccine available to immunize nearly the entire U.S., although much of it remains unlicensed. The vaccine is fully protective in all age groups when a primary "take" resulting in a scar is achieved with the bifurcated needle technique. Immunity lasts at least 5 years, and possibly up to 10 years after a single vaccination. Repeat vaccination may provide 20 or more years of protection. In 1972, routine childhood vaccination was discontinued, meaning that approximately half of the U.S. population has never been vaccinated. Unfortunately the vaccine has several adverse reactions. Common symptoms include local pain and swelling, headache, muscle aches and fatigue. Up to one third of primary vaccinees feel ill enough to miss at least one day of work or school. Live vaccinia virus can shed from the vaccination site prior to scab formation and cause accidental inoculation lesions in vaccinees or their contacts. Approximately 1-10 out of 100,000 will have more severe adverse reactions including encephalitis, progressive vaccinia (vaccinia necrosum) or eczema vaccinatum. Groups at highest risk for severe complications include the immunocompromised, pregnant women, infants less than 1 year old and those with eczema or other chronic skin disorders. All severe complications except encephalitis and vaccinal keratitis can be effectively treated with vaccinia immune-globulin (VIG), however the supply is very limited. Vaccine is currently not available to the public. Debates regarding mass vaccination prior to a bioterrorism event are underway.

Additional information and references available at www.bioterrorism.slu.edu

Infection Control (continued)

of nosocomial spread. All persons having close contact with a suspected case during the 3 weeks prior to presentation should be identified, vaccinated and monitored twice daily for development of temperature $>38^{\circ}\text{C}$ for 17 days post-exposure and subsequently isolated if fever develops. Laboratory specimens from suspected cases should be collected in sealed tubes with lids taped closed, placed in a watertight container, and then delivered to a designated reference laboratory with biosafety level 4 capability. Bodies of deceased victims should be cremated if possible.

Decontamination

In the event of an aerosol release, all virus will likely be completely inactivated or dissipated within 2 days. Buildings and/or exposed areas generally do not need to be decontaminated as index cases would not be identified until two weeks after the release. Standard hospital grade disinfectants such as quaternary ammonias are effective in killing the virus on surfaces and should be used for hospitalized patients' rooms or home care. Although less desirable due to damage to equipment and furniture, hypochlorite (bleach) is an acceptable alternative. Patients' linens should be autoclaved or washed in hot water with bleach added. Infectious waste should be placed in biohazard bags and autoclaved before incineration.

Reporting

Report suspected cases of smallpox or suspected intentional release of smallpox to your local health department. The local health department is responsible for notifying the state health department, FBI and local law enforcement. The state health department will notify the CDC.

Disclaimer

Information contained in this fact sheet was current as of November 2002, and was designed for educational purposes only. Medication information should always be researched and verified before initiation of patient treatment.