

Variola (Smallpox) Virus as a Bioterrorist Agent

Agent: Variola (smallpox) virus could be used as a biological weapon in aerosol form or inoculated onto fomites. Since smallpox vaccinations were discontinued in the 1980s, the use of the smallpox virus as a weapon constitutes a serious threat, especially because certain countries may be secretly harboring stockpiles of the virus. The virus is usually spread by the respiratory route and is stable in the environment,. It may also be spread through direct contact.

Disease: Smallpox

Incubation Period: 7-17 days

Signs/Symptoms: The prodrome lasts 2-4 days and includes malaise, fever, rigors, headache and backache. This is followed by defervescence and the appearance of a typical skin eruption (macules to papules to vesicles to pustules and scabs over 7-14 days). Unlike the lesions of chickenpox, the lesions will all be in the same stage of development. The centrifugal distribution of lesions, more numerous on the face and extremities than the trunk, and their presence on the palms and soles of the patient are important diagnostic features. Fever may reappear 7 days after the onset of the rash. There is a 20-50% mortality rate. Flat-type smallpox characterized by slow evolution of flat, soft, focal skin lesions and severe systemic toxicity has been noted in 2-5% of patients. Mortality for flat-type smallpox was 66% in vaccinated patients and 95% in unvaccinated. Another form seen in about 3% of patients is hemorrhagic-type smallpox. It is characterized by the appearance of extensive petechiae and mucosal hemorrhage. Death usually occurs before development of the typical pox lesions.

Diagnosis:

Differential Diagnosis: Chickenpox and monkeypox should be included in the differential diagnosis for smallpox along with allergic contact dermatitis, erythema multiforme with bullae, secondary syphilis, and atypical measles.

Differential between smallpox and chickenpox

Sign & Symptoms	Smallpox	Chickenpox
Eruptions	Centrifugal	Centripetal
Development of Eruptions	Synchronous	Different Stages
Papules	Firm and Deep	Soft and Superficial
Scarring	Yes	Usually No

Monkeypox is difficult to distinguish from smallpox, although generalized lymphadenopathy is a more common feature of monkeypox. Person-to-person spread of monkeypox is rare.

Laboratory: Skin samples (scrapings from papules, vesicular fluid, pus or scabs) may be collected for rapid identification of pox viruses (smallpox, cowpox, and monkeypox) by electron microscopy (EM). Skin samples may also be used for agar gel immunoprecipitation, immunofluorescence, or polymerase chain reaction (PCR) assay. Pox viruses cannot be rapidly distinguished from one another except by PCR. In the event of known exposures, early postexposure (0-24 hours) nasal swabs and induced respiratory secretions may be collected for viral culture, fluorescent antibody assay, and PCR assay. After 2 days, blood may be collected in a tiger-top (SST) or red-top tube for viral culture. Serological tests may be useful for confirmation or early presumptive diagnosis.

Variola, vaccinia, monkeypox and cowpox can be identified in the laboratory by a number of methods although they cannot be rapidly distinguished from one another except by PCR. Transmission electron microscopy can be used to demonstrate characteristic virions, which can be recovered from scabs throughout convalescence. Aggregations of virus particles called Guarnieri bodies may be seen using light microscopy. Black cytoplasmic inclusions appear when stained with Gispens's modified silver stain.

Send specimens for laboratory confirmation in a triple to the Oregon State Public Health Laboratory, 1717 SW Tenth Avenue, Portland, OR 97201. Prior notification is requested by calling the laboratory at (503) 229-5882 and Acute and Communicable Disease Prevention at (503) 731-4024.

Supportive Tests: Leukopenia is often found in severe cases. The differential count shows granulocytopenia and a relative increase in lymphocytes. Early in the hemorrhagic form, severe thrombocytopenia, global reduction in clotting factors, circulating antithrombin, and a marked increase in immature lymphoid cells in the peripheral blood are present.

Treatment: Antivirals for use against smallpox are under investigation. Cidofovir has proven effective *in vitro* and shown to be effective *in vivo* in experimental animals. Supportive treatment should be given.

Vaccine/Prophylaxis: Limited quantities of vaccine may be available in the case

of a bioterrorist attack. The vaccines, Wyeth Calf Lymph Vaccine and DOD cell culture derived Vaccinia must be given by scarification. Smallpox vaccination should be given, if available, irrespective of prior vaccination status. Most authorities state that, with the exception of significant impairment of systemic immunity, there are no absolute contraindications to *post-exposure* vaccination of a person who experiences *bona-fide* exposure to variola. However, concomitant administration simultaneously with vaccinia immune globulin (VIG) 0.6(one source says 0.3) ml/kg IM is recommended for pregnant and eczematous persons in such circumstances.

Infection Control: Patients should be considered infectious until scabs separate, which usually takes about three weeks from the time of infection. Isolation with droplet and airborne precautions should be exercised for patients and all contacts for a minimum of 16-17 days following exposure. Isolation in the home or other non-hospital facilities should be considered where possible, since the risk for transmission is high, and few hospitals will have enough negative-pressure rooms for proper isolation. Immediate vaccination, if available, should be given to all medical personnel. Outside of the hospital setting, patients and household contacts should wear a N95 or better mask. Caregivers should wear disposable gowns and gloves, as well. Bed linens, clothing, and other exposed articles must be autoclaved or incinerated.

Report: Immediately report any suspect cases to your local health department or the Oregon Health Division at (503) 731-4024 during working hours (8:00 am to 5:00 pm Monday through Friday) or (503) 731-4030 nights, weekends and holidays.

Adapted with permission from the Texas Department of Health