Smallpox

Information for Healthcare Facilities

Adapted with permission from the Kansas Poison Control.

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Causative Agent

Variola major virus, which is in the orthopoxvirus family.

Hospital Precautions

In addition to standard precautions, both airborne precautions (requires N95) and contact precautions should be used.

Transmission

Patient-to-patient transmission is likely from airborne and droplet exposure, and by contact with skin lesions or secretions. In general, close person-to-person proximity is required for transmission to reliably occur. Strict quarantine with respiratory isolation should be applied for 17 days to all persons in direct contact with the index case. Smallpox infected patients become infectious at the onset of the rash and remain infectious until their scabs separate (usually 3 weeks). Patients are considered more infectious if they are coughing. Indirect transmission from infected bedding or fomites is possible.

Decontamination

Patient decontamination after exposure to smallpox is not indicated.
Items potentially contaminated by infectious lesions should be handled using contact precautions.
Strict quarantine of asymptomatic contacts for 17 days after exposure is recommended.

Mechanism

Viral infection resulting in acute illness.

Routes

Inhalation of either small or large droplets, or contact with skin lesions or secretions. It is estimated that 35% of exposed individuals will contract the disease.

Symptoms/ Onset

- Incubation period for smallpox is 7-19 days, with the average incubation period being 10 to 14 days. A prodromal phase of 2-4 days follows incubation period.
- Malaise, fever, rigors, vomiting, headache, and backache. Delirium is present in 15% of patients. Approximately 2-3 days after the onset of symptoms, lesions appear that quickly progress from macules to papules, and eventually to pustular lesions. Smallpox can be clinically distinguished from chickenpox: in chickenpox, macules, papules, and pustules/ vesicles may be present simultaneously; in smallpox, all lesions are in the same stage at the same time.

Treatment

- No current recommended treatments have been tested in patients with smallpox. Symptomatic and supportive care.
- Tecovirimat (TPOXX) and brincidofovir (TEMBEXA) are FDA-approved treatment for smallpox and maintained in the strategic national stockpile (SNS). These agents can also be used via an EIND for Mpox.
- Cidofovir has been shown to stop the grown of the virus in animals but is not FDA approved for treatment of smallpox.

Prophylaxis

3 smallpox vaccines are available from the SNS to be administered to high-risk individuals such as healthcare workers or to personnel exposed within 3 days after the exposure.

- ACAM2000 (Imvamune) and JYNNEOS (Imvanex) are licensed
- Aventis Pasteur Smallpox Vaccine (APSV) is available under an IND or EIND request

If more than 3 days has elapsed since time of exposure, vaccinia immune-globulin (VIG) can also be administered and is available via an EIND request on a case-specific basis. Contact the CDC at (770) 488-7100. Vaccines against smallpox does not confer life-long immunity, previously vaccinated patients (those patients who have been vaccinated more than 10 years ago or patients who have been vaccinated more recently who do not have a take scar) should be considered susceptible to smallpox.

REFERENCES

Medical Management of Biological Casualties Handbook. 9th ed. U.S. Army Medical Research Institute of Infectious Diseases. Fort Detrick Frederick, Maryland. September 2020.

Advanced Hazmat Life Support-Provider Manual. 4th ed. Arizona Board of Regents. Advanced Hazmat Life Support International Headquarters-Tuscan, Arizona. 2023.

Smallpox. Centers for Disease Control and Prevention. October 22, 2024. Available from: https://www.cdc.gov/smallpox/about/index.html.

About Smallpox Vaccine. Centers for Disease Control and Prevention. November 2, 2024. Available from: About Smallpox Vaccines | Smallpox | CDC