

# PUBLIC HEALTH REFERENCE SHEET

## Smallpox



<b>Name</b>	Variola virus EXCLUDES: Vaccinations and vaccine adverse events
<b>Reservoir &amp; Transmission</b>	Humans Droplet spread via respiratory tract or skin inoculation
<b>Incubation Period</b>	7–19 days
<b>Common Symptoms</b>	Acute onset of fever $\geq 101^{\circ}\text{F}$ ( $\geq 38.3^{\circ}\text{C}$ ), followed by a rash characterized by firm, deep-seated vesicles or pustules in the same stage of development without other apparent cause
<b>Gold Standard Diagnostic Test</b>	Culture, PCR
<b>Risk Groups</b>	Smallpox research scientists. Since smallpox has been eradicated, the general population is not at risk. However, in the event of a bioterrorism attack, anyone unvaccinated could potentially be at risk.
<b>Geographic Significance</b>	N/A

### What is smallpox?

Smallpox is a severe infectious disease caused by the variola virus, genus *Orthopoxvirus*.

### What is the occurrence of smallpox?

- Per the Centers for Disease Control and Prevention (CDC), the last documented case of naturally occurring (endemic) smallpox was in 1977. A single confirmed case of smallpox today could be the result of an intentional act (bioterrorism) and would be considered a global public health emergency.
- Infections with wild vaccinia-like viruses have been reported among cattle and buffalo herders in India and among dairy workers in southern Brazil and Colombia. Travelers touching affected bovines might acquire a localized, cutaneous infection. Immunosuppressed people or people with certain skin conditions are at an increased risk for developing systemic illness.

### How is smallpox transmitted?

- In 1980, the World Health Organization (WHO) officially declared smallpox eradicated; however, the threat of reemergence by intentional introduction (e.g., bioterrorism) persists. Before smallpox was eradicated, it spread from person-to-person principally through respiratory droplets. Contact with infectious skin lesions or scabs was a less common mode of transmission but sometimes occurred (e.g., when caregivers cared for patients or washed contaminated clothing). Rarely, smallpox spread through air in enclosed settings (airborne transmission).
- Vaccinia virus is the live virus component of contemporary smallpox vaccines. One of these vaccines, ACAM2000, is a replication competent vaccinia virus; occasionally, infection occurs from touching the fluid or crust material from the inoculation lesion of someone recently vaccinated against smallpox, or from touching contaminated materials like sheets and towels. Human infections with vaccinia virus have occurred in Brazil, Colombia, and India after contact with agricultural animals, often bovines, infected with sylvatic vaccinia-like viruses (CDC, 2023).

### Who is at risk for smallpox?

Immunocompromised patients or people with exfoliative skin conditions (e.g., atopic dermatitis or eczema) are at greater risk for severe illness or death. A person is considered at risk for

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# PUBLIC HEALTH REFERENCE SHEET



## Smallpox

contracting smallpox after prolonged, close contact with an infectious smallpox patient. Before smallpox was eradicated, the disease had a secondary household or close contact attack rate of approximately 60% among unvaccinated individuals.

### What are the signs and symptoms of smallpox?

Clinical signs and symptoms include acute onset of fever  $>101^{\circ}\text{F}$  ( $38.3^{\circ}\text{C}$ ), head and body aches, malaise, and sometimes vomiting; then, a characteristic, disseminated rash of firm, deep-seated vesicles or pustules in the same stage of development on each affected body site. Clinically, varicella (chickenpox) is the most common rash illness likely to be confused with smallpox. Lesions on the palms or soles and a centrifugal distribution of lesions on the body, which are characteristic of smallpox, can sometimes help distinguish *orthopoxvirus* infection from varicella.

### What are potential complications of smallpox?

Severe complications could include encephalitis, corneal ulcerations, and severe scarring from lesions. For the unvaccinated, smallpox can have a mortality rate of approximately 30%. Poor pregnancy outcomes, including fetal death, have been observed when pregnant people have had variola virus infections.

### How is smallpox diagnosed?

- Diagnosis involves evaluating patients with acute onset of fever followed by a rash. The CDC provides a detailed algorithm and clinical criteria for evaluating and categorizing the risk of smallpox in patients presenting with vesicular or pustular rash illnesses, which can be found at <https://www.cdc.gov/smallpox/clinicians/diagnosis-evaluation.html>.
- PCR testing or virus isolation can confirm an *orthopoxvirus* infection. For patients with a high risk of having smallpox, the state health department will contact the CDC to conduct laboratory testing to confirm or rule out smallpox. In the absence of known smallpox disease, the predictive value of a positive smallpox test diagnosis is low, so only cases that meet the clinical definition of the disease should be tested.

### How is smallpox treated?

- Treatment of smallpox is mainly supportive care through hydration, nutritional supplementation, and prevention of secondary infections.
- To diminish the chances of spreading virus to other parts of the body or to other people, advise people to keep all pox lesions covered until the scab detaches and to avoid touching their eyes before proper hand washing. Topical antivirals (e.g., trifluridine drops) have been used to treat ocular involvement.
- Tecovirimat (TPOXX), brincidofovir (Tembexa), and vaccinia immune globulin have been licensed by the U.S. Food and Drug Administration to treat smallpox or vaccinia complications and are stocked in the U.S. government's Strategic National Stockpile (SNS).
- Vaccination within 2 to 3 days of exposure can prevent or lessen the severity of the disease and may decrease symptoms if given within the first week of exposure.

### How can smallpox be prevented?

- There are vaccines to protect people from smallpox. Currently, smallpox vaccines are not recommended for the general public because smallpox has been eradicated. If there were a smallpox outbreak, health officials would use smallpox vaccines to control it.
- Two vaccines are licensed for the prevention of smallpox in the United States. The Advisory Committee on Immunization Practices only recommends preexposure prophylaxis for people

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# PUBLIC HEALTH REFERENCE SHEET

## Smallpox



at occupational risk for *orthopoxvirus* infection (e.g., since healthcare delivery to a patient or laboratory work involves orthopoxviruses). Members of the U.S. military are required to receive the vaccine.

### What are some public health considerations?

- When reporting smallpox in the Disease Reporting System internet (DRSi)—
  - Document the source of infection, if known.
  - Document the circumstances under which the case patient was exposed, including duty exposure, occupational activities, environmental exposures, or other high-risk activities.
- The deliberate release of smallpox as an epidemic disease is a remote possibility, and the United States is taking appropriate precautions. Smallpox is classified as a Category A agent by the CDC. Category A agents are believed to pose the greatest potential threat for adverse public health impact and have a moderate to high potential for large-scale dissemination. The public is generally more aware of category A agents, and broad-based public health preparedness efforts are necessary.
- For patient and clinician smallpox comprehensive resources and for Department of Defense Smallpox Vaccination Program (SVP), military and civilian healthcare personnel can access the Defense Health Agency (DHA)'s online Smallpox Resource Center at <https://www.health.mil/Military-Health-Topics/Health-Readiness/Immunization-Healthcare/Vaccine-Preventable-Diseases/Smallpox-ACAM2000/Smallpox-Resource-Center>.

### References:

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- Heymann, David L. ed. 2022. *Control of Communicable Diseases Manual*. 21st Edition. Washington, DC: APHA Press.
- Rao, Agam and McCollum, Andrea. "Smallpox & Other Orthopoxvirus-Associated Infections." *CDC Yellow Book 2024: Travel-Associated Infections & Diseases*. Centers for Disease Control and Prevention, 2023.  
<https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/smallpox-other-orthopoxvirus-associated-infections>
- "Smallpox," Centers for Disease Control and Prevention (CDC), last reviewed July 12, 2017  
<https://www.cdc.gov/smallpox/>

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