



SMALLPOX

1. **Agent:** Variola virus, a member of the poxviridae family. (This is the agent for both variola major—classic smallpox—and variola minor, a less serious form of the disease.)

2. **Identification:**

a. **Symptoms:** Most significantly, the rash of smallpox is preceded by a prodrome consisting of 1 to 4 days of high fever, malaise, head and body aches, prostration; sometimes nausea, vomiting, abdominal pain, and backache. In 90% of cases, smallpox (variola major) presents as an acute infectious disease characterized by a maculopapular rash (usually starts as small red spots on the tongue and in the mouth), which becomes vesicular on day 3 or 4, then slowly evolves into pustular lesions, deeply embedded into the dermis, by day 6. Fourteen days after the initial appearance of the rash, most of the lesions have developed scabs. The rash in smallpox usually appears as a single crop with all lesions progressing from the macular to the pustular stage at about the same time.

The mortality rate for smallpox may be as high as 30% in unvaccinated persons and 3% in those with a history of vaccination sometime in the past. (Patients with variola minor have similar signs and symptoms but the disease is less severe and the mortality rate is only about 1%.)

In a minority of instances, smallpox can present as “flat type” smallpox where lesions remain flush with the skin, never becoming elevated even during the pustular stage. This type of presentation is seen in 5% to 10% of cases and results in very severe disease. Another severe form of smallpox is “hemorrhagic smallpox” which involves extensive bleeding into the skin and almost always results in death. This form of disease, which can be seen in less than 3% of cases, can easily be mistaken for meningococcal sepsis.

Milder disease with a less severe prodrome and a more rapid evolution of

lesions can be seen in previously vaccinated individuals.

b. **Differential diagnosis:** Although there are other causes of generalized rash illness which present as vesicles and pustules, the severe prodrome along with the nature of the rash and its evolution distinguishes smallpox from other diseases. The diseases, which can look similar to smallpox, include: varicella, disseminated herpes simplex, disseminated herpes zoster, impetigo, drug eruptions, contact dermatitis, erythema multiforme, enterovirus, scabies, molluscum contagiosum, and monkeypox.

c. **Diagnosis:** The clinical case definition for smallpox is: an illness with an acute onset of fever of 101°F or higher followed by a rash characterized by firm, deep seated vesicles or pustules in the same stage of development on any body part, without other apparent cause. Laboratory diagnosis is aided by a negative result on one of the rapid diagnostic tests for **varicella** (i.e., DFA, electron microscopy, and PCR). Laboratory diagnosis of smallpox can be made by PCR, culture of vesicular or pustular fluid, or culture of the scab; it should only be performed by the LAC Public Health Laboratory, California Viral & Rickettsial Diseases Laboratory, and Centers for Disease Control and Prevention (CDC). (After appropriate consultation to ensure safe packaging and handling, specimens can be sent to the local public health laboratory for forwarding to the state laboratory and then to CDC.)

Electron microscopy of vesicular or pustular fluid, or of the scab, as well as acute and convalescent serologic testing through CDC, can also be performed for diagnosis.

3. **Incubation:** Usually 10-14 days (range 7-19 days).



4. **Reservoir:** Officially, only in designated laboratory repositories in USA and Russia. Humans are the only natural host.

Naturally occurring smallpox no longer exists, although the threat of smallpox release remains due to concerns that variola virus might exist outside the two official repositories.

5. **Source:** Macules, papules, vesicles, pustules, and scabs of the skin and lesions in mouth and pharynx.
6. **Transmission:** Direct and fairly prolonged face-to-face contact is required to spread smallpox from one person to another. Smallpox also can be spread through direct contact with infected bodily fluids or contaminated objects such as bedding or clothing. Rarely, smallpox has been spread by virus carried in the air in enclosed settings such as buildings, buses, and trains. Transmission may more easily occur in a hospital setting if isolation of the case is not implemented immediately. The virus is most likely to be disseminated in an aerosol cloud if used in biological warfare. Smallpox is not known to be transmitted by insects or animals.
7. **Communicability:** A smallpox case becomes infectious to others when rash lesions first appear in the mouth and pharynx, which usually occurs 24 hours before the rash is noted on the skin. Patients can transmit the virus throughout the course of the rash illness until all scabs have separated.
8. **Specific treatment:** Tecovirimat is the only medication approved by U.S. Food & Drug Administration to treat smallpox.
9. **Immunity:** Infection is felt to confer lifelong immunity. Immunity from vaccination with the smallpox vaccine (vaccinia virus) gradually wanes over time beginning 5 years after vaccination. Usually no protection against disease is observed for persons 30 or more years post-vaccination, although they can have less severe illness if infected. Vaccination of the U.S. general public ceased in 1972 after the disease was eradicated in the U.S.

REPORTING PROCEDURES

1. **Report any case or suspect cases by telephone immediately** (Title 17, Section 2500. *California Code of Regulations*).
 - A. Call ACDC during working hours; after working hours, contact Administrative Officer of the Day (AOD) through County Operator.
 - B. Any laboratory that receives a specimen for smallpox testing is required to report to the State Microbial Diseases Laboratory immediately (Title 17, Section 2505, *California Code of Regulations*).
 - C. ACDC must notify the CA Dept. of PH Division of Communicable Disease Control (CDPH DCDC) immediately upon receiving notice of a case of suspected smallpox by calling the Duty Officer at (916) 328-3605 (available 24 hours).

ACDC will supervise investigation and control measures.

2. Report Form:

- A. [Worksheet: Evaluating Patients for Smallpox](#)
(For Internal ACDC Use)
- B. [FORM 1: Smallpox Post-Event Surveillance Form](#)
(For Internal ACDC Use)

CONTROL OF CASE, CONTACTS & CARRIERS

ACDC will coordinate all contact investigations for smallpox. Personnel designated for case interviews and contact investigation must be effectively vaccinated prior to initiating face-to-face interviews with the case and contacts. If vaccinated personnel are not available, then only those without contraindications (including but not limited to atopic dermatitis, active exfoliative skin conditions, and conditions associated with immunosuppression. Please refer to [CDC website](#)¹ for details), to vaccination should collect specimens. Initial investigation will be conducted immediately upon notification by the LAC Public Health Smallpox Response Team.

¹ <https://www.cdc.gov/smallpox/clinicians/vaccination-contraindications1.html>



Note: Ideally, only successfully vaccinated individuals wearing barrier protection should be involved in collecting specimens from suspected smallpox cases. If unvaccinated individuals must be used for this purpose, they must wear fit-tested N95 masks and not have contraindications for vaccination, as they would require immediate vaccination if the diagnosis of smallpox is confirmed.

CASE:

1. Place case immediately into airborne, contact and standard isolation precautions; maintain isolation for the duration of disease until all scabs have separated from skin lesions. Refer to LAC Smallpox Response Plan for details.
2. Interview case (if in person, interviewer must be wearing coverall or impervious gown, gloves, eye protection, and N95 respirator or PAPR) to obtain:
 - Detailed name and contact information for all persons with whom the case had face-to-face contact (within 6 feet) since onset of fever until time of interview
 - Places visited by the case since onset of fever including health care provider offices, clinics, and emergency departments, work, school, and regular, as well as occasional activities. (If case is unable to answer questions because of age or illness, obtain information from case's close family members and friends.) Refer to LAC Smallpox Response Plan for details.

CONTACTS:

1. List and prioritize all contacts for urgency of vaccination based on duration and intimacy of exposure, and prior immunization history for smallpox.
2. Locate and interview each contact to confirm exposure to the case and to determine the presence or absence of symptoms in the contact.
3. Make arrangements for the immediate vaccination of asymptomatic contacts and contact's household. (If household members cannot be vaccinated due to contraindications, insure that they avoid

exposure to the contact until the end of the contact's surveillance period).

4. If contact is symptomatic with fever or rash, make immediate arrangements (with appropriate safety precautions to prevent transmission of possible disease to others) for transportation of contact to an LAC designated facility for evaluation of smallpox.
5. If contact does not have fever or rash, place contact under surveillance so that if he/she develops fever or rash, he/she can be immediately isolated. Asymptomatic contacts must be kept under surveillance for 19 days after their last exposure to the case, or until 14 days after successful vaccination (whichever comes first). Refer to LAC Smallpox Response Plan for details.

CARRIERS: Not applicable.

PREVENTION-EDUCATION

Stress the importance of immunizing all contacts to the case as soon as possible. In a smallpox emergency, all contraindications to vaccination would be reconsidered in light of the risk of smallpox exposure.

Educate all cases and contacts regarding the transmission and communicability of smallpox and the actions required to prevent further transmission including precautions for the handling of case's clothing, bedding, linens, and eating utensils.

Provide information on decontamination of household surfaces. Refer to LAC Smallpox Response Plan for details.

OUTBREAK DEFINITION

A single case of smallpox is a public health emergency and warrants an immediate investigation, in consultation with ACDC.

DIAGNOSTIC PROCEDURES

1. **Culture:** Culture of vesicular or pustular fluid or scabs is available through the CDC. Contact the LAC Public Health Laboratory for specific procedures prior to any attempt to obtain specimens from patients with suspected smallpox.



2. **Serologic Testing:** Acute and convalescent serologic testing is available through the CDC. 7-10 cc of blood should be drawn into a red/gray (marbled), gold, or red topped serum separator tube. Contact the LAC Public Health Laboratory prior to collection of serologic specimens from patients with suspected smallpox.
3. **Electron Microscopy:** Because of the distinct appearance of poxviruses, electron microscopy can be helpful in the rapid diagnosis of smallpox. This test is available through the CDC. Contact the Public Health Laboratory for information regarding this test.

SMALLPOX VACCINE (VACCINIA VIRUS)

The smallpox vaccine is made from a virus called vaccinia, which is a poxvirus similar to smallpox, but less harmful. They do not contain variola virus, the causative agent of smallpox. In 2007, the Food and Drug Administration (FDA) licensed a new smallpox vaccine, ACAM2000, to replace the previously licensed vaccine (Dryvax).

The U.S. government has stockpile of smallpox vaccine that would be provided to persons identified at risk for infection in the event of a smallpox exposure or release.

SMALLPOX VACCINE (VACCINIA VIRUS) ADVERSE EVENTS MONITORING

Timely recognition of and response to smallpox vaccine adverse events are important in protecting the public from unnecessary risk and to maintain confidence during an immunization effort.

Adverse events that are serious or unexpected may require expert consultation or IND (investigational new drug) therapeutics.

Healthcare workers should report any unexpected or serious event occurring after smallpox vaccination as well as adverse events occurring in persons following close contact with a vaccine recipient to the Vaccine Adverse Event Reporting System (VAERS). An adverse event is any clinically significant medical event that occurs following administration of a vaccine. Refer to [Side Effects of Smallpox Vaccination](#)² on CDC website for details.

² <https://www.cdc.gov/smallpox/vaccine-basics/vaccination-effects.html>