

# Smallpox

(Also known as Variola)

**REPORT IMMEDIATELY**

## Section 1:

## ABOUT THE DISEASE

### A. Etiologic Agent

Smallpox is caused by the variola virus, a DNA virus and a member of the Poxviridae family (genus *Orthopoxvirus*).

### B. Clinical Description

Smallpox infection typically begins with a prodromal illness characterized by a high fever (102–104°F), malaise, headache, backache, and abdominal pain. This prodromal period typically lasts 2–4 days. During this time, those affected are usually too sick to carry on with normal activities. The prodromal period is followed by the development of lesions on the mucosa of the mouth and the pharynx, which often go unnoticed by the patient. Less than 24 hours after the development of mucosal lesions, patients develop a deep-seated rash. The rash usually begins on the face and spreads to involve the forearms, trunk, and legs. The rash follows a characteristic “centrifugal” pattern, with the highest concentration of lesions on the face and distal extremities, including the palms of the hands and soles of the feet. As the rash appears, the fever often falls and the person starts to feel better. The rash progresses slowly through successive stages of macules, papules, vesicles, pustules, and then crusted scabs, which fall off 3–4 weeks after rash onset. At any one time, most of a patient’s lesions are at the same stage, due to the slow and steady evolution of the rash. Patients sustain significant scarring after the crusted scabs fall off.

Two clinical forms of smallpox infection are recognized: variola major and variola minor. Variola major is the more severe form of smallpox. It has a case–fatality rate of 20–50% or more in unvaccinated populations, and it follows the classic presentation and progression. Hemorrhagic and malignant (or “flat-type”) smallpox are forms of severe smallpox which occur in under 5–10% of cases and are usually fatal. Variola minor, typically, is a less severe form of the illness, with a shorter duration and an overall case-fatality rate of less than 1%.

### C. Vectors and Reservoirs

Humans are the only known reservoir for the variola virus.

### D. Modes of Transmission

Transmission occurs primarily from person-to-person through the spread of droplets. Infrequent transmission through aerosols and direct contact with infectious lesions, clothing, or bedding has also been documented in the past.

### E. Incubation Period

The incubation period of smallpox to prodrome ranges from 7–19 days, but is most commonly 10–14 days (11 days average) with 2–4 additional days for rash onset.

### F. Period of Communicability or Infectious Period

The communicable period is generally three weeks, from the time of the development of the earliest lesions in the mouth or pharynx to the disappearance of all scabs. The first week of rash illness is the most infectious period.

## G. Epidemiology

The last naturally-acquired case of smallpox occurred in Somalia in 1977. Two additional laboratory-associated cases occurred in 1978. In 1980, global eradication of smallpox was certified by the World Health Organization (WHO). Currently, two WHO reference laboratories (the Centers for Disease Control and Prevention [CDC] in Atlanta, GA and the Institute of Virus Preparations in Moscow, Russia) hold variola virus stocks under strict security. All laboratory work with the smallpox virus is done under strict biosafety level 4 procedures.

## H. Bioterrorist Potential

Variola virus is listed by the CDC as a Category A bioterrorist agent. If acquired and properly disseminated, smallpox could cause a serious public health challenge in terms of casualties and the control of other repercussions.



### Section 2:

## REPORTING CRITERIA AND LABORATORY TESTING

### A. What to Report to the Massachusetts Department of Public Health (MDPH)

Report any of the following:

- ◆ Any suspect case of smallpox, defined as “moderate” or “high-risk” after utilizing the CDC rash illness protocol (found on the CDC website at [www.bt.cdc.gov/agent/smallpox/diagnosis](http://www.bt.cdc.gov/agent/smallpox/diagnosis));
- ◆ An outbreak of illness that is clinically compatible with smallpox; or
- ◆ Any suspected exposure to smallpox that may be the result of bioterrorism, such as a threatening package or possible dissemination device.

*Note: See Section 3C for information on how to report a case.*

### B. Laboratory Testing Services Available

The MDPH State Laboratory Institute (SLI) performs testing for smallpox by real-time detection polymerase chain reaction (RTD-PCR). Tests will be performed on specimens collected by the MDPH smallpox collection team after individual case review and approval by the MDPH Division of Epidemiology and Immunization staff (at [617] 983-6800 or [888] 658-2850). Appropriate specimens include vesicular “touch prep,” vesicle roof, vesicular swab, ocular swab or impression slide, and biopsy specimens. Swabs should be submitted in a dry tube without viral transport medium. All specimens will also be forwarded to the CDC for further testing and confirmation.

**For additional information on testing or specimen submission, contact the SLI Virus Isolation Laboratory at (617) 983-6382. Please call the laboratory prior to specimen submission.**

Detailed instructions for smallpox-specific specimen collection can be found on the CDC website at [www.bt.cdc.gov/agent/smallpox/response-plan/files/guide-d.pdf](http://www.bt.cdc.gov/agent/smallpox/response-plan/files/guide-d.pdf). The CDC website also contains information on the clinical evaluation of patients for smallpox ([www.bt.cdc.gov/agent/smallpox/diagnosis/index.asp](http://www.bt.cdc.gov/agent/smallpox/diagnosis/index.asp)).



## Section 3:

**REPORTING RESPONSIBILITIES AND CASE INVESTIGATION****A. Purpose of Surveillance and Reporting**

- ◆ To identify and isolate smallpox cases as quickly as possible to prevent further disease spread; and
- ◆ To identify, vaccinate, and monitor contacts of cases and household contacts of contacts in order to prevent secondary cases.

**B. Laboratory and Health Care Provider Reporting Requirements**

Smallpox is reportable to the local board of health (LBOH). The MDPH requests that health care providers immediately report to the LBOH in the community where the case is diagnosed, all confirmed or suspect cases of smallpox, as defined by the reporting criteria in Section 2A. The MDPH will notify state and federal public health and law enforcement officials as well as local law enforcement and other LBOH that may be affected.

Laboratories performing examinations on any specimens derived from Massachusetts residents that yield evidence of smallpox infection shall report such evidence of infection, directly by phone, to the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850.

**C. Local Board of Health (LBOH) Reporting and Follow-up Responsibilities***Reporting Requirements*

MDPH regulations (*105 CMR 300.000*) stipulate that smallpox is reportable to the LBOH and that each LBOH must report any case of smallpox or suspect case of smallpox, as defined by the reporting criteria in Section 2A. Refer to the *Local Board of Health Timeline* at the end of this manual's *Introduction* section for information on prioritization and timeliness requirements of reporting and case investigation.

*Case Investigation*

**Case investigation of a suspect case of smallpox in Massachusetts will be directed by the MDPH, in collaboration with the CDC. If bioterrorism is suspected, the MDPH and other response authorities will work closely with the LBOH and will provide instructions/information on how to proceed. The occurrence of smallpox will be considered an event of national significance.**

1. If a LBOH learns of a suspect or confirmed case of smallpox, or any suspected exposure, it must call the MDPH immediately, any time of the day or night, at (617) 983-6800 or (888) 658-2850. The MDPH will notify state and federal public health and law enforcement officials, as well as local law enforcement and other LBOH that may be affected.
2. LBOH may be asked to assist in completing an official CDC *Smallpox Post-Event Surveillance Form* (found on the CDC website at [www.bt.cdc.gov/agent/smallpox/response-plan/files/guide-a-form-1.pdf](http://www.bt.cdc.gov/agent/smallpox/response-plan/files/guide-a-form-1.pdf)) by interviewing those who may be able to provide pertinent information. Other activities, done in conjunction with the Smallpox Response Team, may also need LBOH staff participation. Much of the information required on the form may be obtained from the health care provider or from the medical record. Note that circled items on the form indicate the minimum required fields. Every attempt should be made to at least complete the circled items. Use the following guidelines to assist in completing the form:

- a. Accurately report the case's demographic information in the "Case Information" section.
  - b. Include information on the reporting source, including the date first reported to public health.
  - c. Accurately complete sections on vaccination and medical history, clinical signs and symptoms, and clinical course of the illness, including whether or not the patient developed any complications from the infection.
  - d. Record all available laboratory information, including results of generic orthopox, variola, and vaccinia testing.
  - e. In the "Epidemiologic" section, record the transmission setting, if known.
  - f. Record the case's classification. (Official CDC case definitions are included on the form as well as in the *Additional Information* section of this chapter.)
3. You will receive instructions on how to submit forms and other information, as well as on other interventions.
  4. Institution of disease control measures is an integral part of case investigation. It is the responsibility of the LBOH to understand, and if necessary, institute the control guidelines listed in Section 4.



## Section 4:

# CONTROLLING FURTHER SPREAD

## CDC Smallpox Response Plan and Guidelines

The CDC *Smallpox Response Plan and Guidelines* is a working document that is frequently revised and updated to reflect input from state and local health officials. The plan would be implemented whenever a smallpox emergency occurs. Federal officials will implement all or portions of the CDC *Smallpox Response Plan and Guidelines* under the "Criteria for Implementation" that are outlined within the document.

The document is organized into multiple sections outlining the criteria for smallpox response plan implementation; notification procedures for suspect cases; CDC, state, and local responsibilities and activities (including some that should take place prior to a smallpox emergency); and CDC vaccine and personnel mobilization. The plan also provides guidelines and annexes to assist federal, state, and local health officials in implementing the specific activities that are essential for the management of a smallpox emergency. The CDC *Smallpox Response Plan and Guidelines* can be found online at [www.bt.cdc.gov/agent/smallpox/response-plan/index.asp#exec](http://www.bt.cdc.gov/agent/smallpox/response-plan/index.asp#exec).

### A. Isolation and Quarantine Requirements (105 CMR 300.200)

#### *Minimum Period of Isolation of Patient*

In conjunction with public health authorities, place case(s) on highest level of isolation to prevent direct contact, droplet contact, and airborne exposure until lesions have dried and crusts have separated.

#### *Minimum Period of Quarantine of Contacts*

Afebrile contacts shall be placed under fever surveillance (quarantine) for 18 days from the last contact or 14 days from successful vaccination (whichever comes first), with monitoring and recording of temperature occurring twice daily (morning and evening). Febrile contacts with or without rash shall be considered the same as a case and shall be handled in the same fashion (isolation). If no rash develops after five days and the fever is diagnosed as being caused by recent vaccination or some other non-smallpox etiology, the contact may be released from isolation to home but

with continued fever surveillance for 18 days following their last contact with a case or 14 days following successful vaccination (whichever comes first).

## B. Protection of Contacts of a Case

The following information is derived from the CDC *Smallpox Response Plan and Guidelines, Draft Guide A: Smallpox Surveillance and Case Reporting; Contact Identification, Tracing, Vaccination, and Surveillance; and Epidemiologic Investigation*. This document is available on the CDC website at [www.bt.cdc.gov/agent/smallpox/response-plan/files/guide-a.doc](http://www.bt.cdc.gov/agent/smallpox/response-plan/files/guide-a.doc).

Vaccinating and monitoring contacts of cases and family contacts of contacts will help to protect those at greatest risk for contracting the disease as well as form a buffer of immune individuals to prevent the spread of disease. Large-scale vaccination in potentially exposed communities may become necessary, although it is crucial that cases be identified and isolated. Large-scale vaccination might also be applied to unaffected communities to protect against further spread of smallpox and additional releases as well as to build the public's confidence in its protection and ability to return to normal activities.

For the purposes of smallpox surveillance and case investigation, a "contact" is defined as follows:

Contact: A person who has been exposed to the risk of infection.

Primary contact: A person with contact with a confirmed, probable, or suspect case of smallpox during the infectious period. Primary contacts include both household and non-household contacts. Risk of smallpox transmission is increased with increased duration of face-to-face contact of less than two meters ( $\leq 6.5$  feet).

Priority categories for contacts, from highest priority to lowest, are as follows:

1. Case's household family members and others spending three or more hours in the household since the case's onset of fever.
2. Non-household members with contact 2 meters or less ( $\leq 6.5$  feet) with case with rash for 3 or more hours.
3. Non-household members with contact 2 meters or less ( $\leq 6.5$  feet) with case with rash for fewer than 3 hours.
4. Non-household members with any contact with case with rash for three or more hours.
5. Non-household members with any contact with case with rash for fewer than three hours.

Household contact: A person who lives or works in the same household as the case.

Non-household contact: A person who does not live or work in the case's household.

Secondary contact: A household member of a primary contact, a non-household contact, and a person who works in the household of a primary contact.

### *Contact Tracing*

Contact tracing should include the following steps:

1. Trace each contact whose name, address, and/or telephone number is known.
2. Use work and school contact numbers, telephone directories, voting lists, neighborhood interviews, site visits, "hangouts," etc., to trace contacts when contact information is unknown or incomplete. If contacts cannot

be found through these mechanisms, other sources for notification of potential contacts (such as media announcements) may have to be considered.

3. Locate and interview each primary contact to confirm contact with the suspect, probable, or confirmed smallpox case, the presence or absence of symptoms in the contact (fever and/or rash), and to identify additional contacts that may not have been listed by the case.
4. Identify household contacts of each primary contact of the smallpox case (secondary contacts).
5. Arrange for immediate vaccination of each primary contact and their household contacts (secondary contacts). Either vaccinate contacts in the household (if this is feasible with the vaccine supply, security issues, and resources), or provide a vaccination ticket with identifying information and designate a vaccination facility for the contact(s) to attend as soon as possible. It is extremely important for smallpox outbreak control to prioritize the vaccination of contacts. In the past, when vaccination was done in the household, the task was given priority over transportation of a case to an isolation facility.
6. If the primary contact is symptomatic with fever or rash, arrangements should be made for prompt vaccination and transportation of the contact to a Type C facility (capable of isolating contagious individuals) or other designated evaluation site for medical evaluation to rule out smallpox. Contacts with symptoms should be counseled, interviewed, and reported as suspect cases using the appropriate smallpox surveillance (case reporting) form, and their contacts should be identified, interviewed, and vaccinated as soon as possible.
7. If the primary contact does not have a fever or rash, vaccinate or arrange for prompt vaccination, and place the contact under surveillance (quarantine) so that if the contact develops a fever or rash, he/she is immediately isolated and evaluated and does not expose other persons to smallpox (see #8 below).
8. If a household member cannot be vaccinated because of contraindications, the household member should be instructed to avoid physical contact with the primary contact until the incubation period of the disease has passed (18 days) or all vaccinated persons in the household are non-infectious for vaccinia virus (after the scab at the vaccine site has separated, 14–21 days after vaccination).
9. Each household contact should be provided with a vaccination ticket and instructed to attend a designated vaccination clinic site as soon as possible.
10. If any contacts have left the state, the contact tracers should notify the supervisor responsible for out-of-state contacts. The supervisor will then notify the appropriate authorities.

Numerous forms and work sheets have been created to facilitate the activities above. These are available on the CDC website at [www.bt.cdc.gov/agent/smallpox/exposure](http://www.bt.cdc.gov/agent/smallpox/exposure).

#### *Surveillance (Monitoring) of Health Status and Vaccine “Take” of Contacts*

Surveillance of contacts of a case of smallpox will be conducted for early signs of smallpox disease (fever on two consecutive days and/or rash) and for vaccine “take.” Contacts will be provided with a health department phone number to call if they develop any of the severe vaccine adverse reactions shown on the *Vaccine Information Statement*. Ideally, and if resources are available, primary contacts who do not have fever or rash at the time of interview should remain under active surveillance for 21 days after their last contact with the smallpox case or 14 days following successful vaccination.

### **C. Managing Special Situations**

If smallpox were to reoccur in the U.S. or elsewhere, the most likely circumstances of reintroduction are generally accepted to be:

- ◆ An unintentional infection in a laboratory. Currently there are only two WHO-approved smallpox virus research and repository laboratories: the CDC in Atlanta, Georgia and the Institute of Virus Preparations in Moscow, Russia. There is speculation, however, that stockpiles of variola virus may exist elsewhere.
- ◆ A bioterrorist attack involving deliberate infection of a person.
- ◆ A bioterrorist attack involving intentional release of smallpox virus into the environment.

**If a bioterrorist event is suspected, the MDPH and other response authorities will work closely with the LBOH and will provide instructions/information on how to proceed.**

## D. Preventive Measures

### *Environmental Measures*

If a patient presents to an emergency department, clinic, or doctor's office with an acute generalized vesicular or pustular rash illness, care should be taken to decrease the risk of disease transmission. Patients should not be left in common waiting areas. The patient should be assessed to determine whether there is a high, medium, or low risk of smallpox, using the interactive CDC algorithm and the major and minor criteria found on the CDC website at [www.bt.cdc.gov/agent/smallpox/diagnosis/riskalgorithm/index.asp](http://www.bt.cdc.gov/agent/smallpox/diagnosis/riskalgorithm/index.asp).

1. If in a doctor's office or clinic, the patient should be placed immediately in a private room with the door kept shut.
2. When admitted or while being held for observation, the facility should institute appropriate airborne isolation and contact precautions and should alert the infection control department. The patient should be placed in a private room at negative pressure to the rest of the facility (airborne infection isolation). The door should be kept closed at all times, except when staff or the patient must enter or exit.
3. Staff and visitors, regardless of vaccination status, should wear properly fitted respirators (N95 or higher level of protection), gloves, and gowns.
4. The patient should wear a surgical mask whenever he/she must be outside of the negative pressure isolation room and must be gowned or wrapped in a sheet so that the rash is fully covered.

### *Personal Preventive Measures/Education*

#### **Vaccine**

The Smallpox vaccine, a live-virus vaccine made from vaccinia virus, is highly effective at inducing immunity against smallpox when administered effectively prior to exposure. If administered within three days after exposure to smallpox virus, it may prevent disease or decrease the severity of disease and the risk of death. Smallpox vaccine production ceased in the early 1980s, and current supplies of smallpox vaccine are limited. However, recent studies have demonstrated that vaccines stored in the 1960s and 1970s still have excellent potency, even when diluted (1:5). New cell-culture-grown smallpox vaccines will become available soon.

Although smallpox vaccine is considered safe when used as indicated, post-vaccination adverse events can occur. These adverse events and their rates, as determined in a 1968 ten-state survey, include: 1) inadvertent inoculation (vaccine virus infection at a site other than the vaccination site, 529.2/million primary vaccinations); 2) generalized vaccinia (relatively mild, disseminated disease caused by the vaccine virus, 241.5/million primary vaccinations);

3) eczema vaccinatum (superinfection of eczema by the vaccine virus, 38.5/million vaccinations); 4) progressive vaccinia (severe disseminated disease, 1.5/million primary vaccinations); and 5) post-vaccinial encephalitis (12.3/million primary vaccinations). Death also occurred in about one per million primary vaccinations, usually as a result of progressive vaccinia, post-vaccinial encephalitis, or severe eczema vaccinatum. In recent vaccination efforts in the U.S. and among U.S. military personnel, self-limited myocarditis and myopericarditis have been described in a small proportion of vaccines. This was a previously recognized, but not fully appreciated, adverse event associated with vaccination.

Several groups have been identified as being at higher risk for developing post-vaccination complications. These persons are advised not to receive smallpox vaccination unless they have been exposed or are at high risk of exposure to smallpox virus. These include: 1) persons with atopic dermatitis or eczema (including a history of atopic dermatitis or eczema); 2) persons with acute, active, or exfoliative skin conditions; 3) persons with altered immune states (e.g., HIV, AIDS, leukemia, lymphoma, immunosuppressive drugs); 4) pregnant and breast-feeding women; 5) children younger than age one year; and 6) persons who have a serious allergy to any component of the vaccine. During an outbreak, additional public health guidance will be circulated on priority groups for vaccination.

Vaccinia immune globulin (VIG) is used to treat certain vaccine adverse reactions and is available through the CDC. Supplies of VIG may be limited in a post-event setting.

**A Smallpox Public Health Fact Sheet is available from the MDPH Division of Epidemiology and Immunization or on the MDPH website at [www.mass.gov/dph](http://www.mass.gov/dph). Click on the “Publications and Statistics” link, and select the “Public Health Fact Sheets” section under “Communicable Disease Control.”**



## ADDITIONAL INFORMATION

The following is the formal CDC surveillance case definition for smallpox. It is provided for your information only and should not affect the investigation and reporting of a case that fulfills the criteria in Section 2A of this chapter. (The CDC and the MDPH use the CDC case definitions to maintain uniform standards for national reporting.) For reporting to the MDPH, always use the criteria outlined in Section 2A.

*Note: The most up-to-date CDC case definitions are available on the CDC website at [www.cdc.gov/epo/dphsi/casedef/case\\_definitions.htm](http://www.cdc.gov/epo/dphsi/casedef/case_definitions.htm).*

### Smallpox Clinical Case Definition

An illness with acute onset of fever  $\geq 101^{\circ}\text{F}$  ( $38.3^{\circ}\text{C}$ ), followed by a rash characterized by firm, deep seated vesicles or pustules in the same stage of development without other apparent cause.

### Laboratory Criteria for Confirmation\*

- ◆ Polymerase chain reaction (PCR) identification of variola DNA in a clinical specimen; or
- ◆ Isolation of smallpox (variola) virus from a clinical specimen (WHO Smallpox Reference Laboratory or laboratory with appropriate reference capabilities) with variola PCR confirmation.

\* Laboratory diagnostic testing for variola virus should be conducted in a CDC Laboratory Response Network (LRN) laboratory utilizing LRN-approved PCR tests and protocols for variola virus. Initial confirmation of a smallpox outbreak requires additional testing at the CDC.

*Note: Generic orthopox PCR and negative stain electron microscopy (EM) identification of a pox virus in a clinical specimen are suggestive of an orthopox virus infection but are not diagnostic for smallpox.*

## Case Classification

Since smallpox no longer exists as a naturally occurring disease, a single laboratory confirmed case of smallpox would be considered an outbreak. Once an outbreak of smallpox has been confirmed, the following case classifications should be used:

<b>Probable</b>	A case that meets the clinical case definition or a case that does not meet the clinical case definition but is clinically consistent with smallpox and has an epidemiological link to a confirmed case of smallpox. Examples of clinical presentations of smallpox that would not meet the ordinary type (pre-event) clinical case definition are: a) hemorrhagic type, b) flat type, and c) variola sine eruption.
<b>Confirmed</b>	A case of smallpox that is laboratory confirmed, or a case that meets the clinical case definition that is epidemiologically linked to a laboratory-confirmed case.
<b>Suspect</b>	A case with a febrile rash illness with fever preceding development of rash by 1–4 days.



## REFERENCES

American Academy of Pediatrics. [Smallpox (Variola).] In: Pickering L.K., ed. *Red Book: 2003 Report of the Committee on Infectious Diseases, 26<sup>th</sup> Edition*. Elk Grove Village, IL, American Academy of Pediatrics; 2003: 554–558.

Heymann, D., ed. *Control of Communicable Diseases Manual, 18<sup>th</sup> Edition*. Washington, DC, American Public Health Association, 2004.

MDPH. *Regulation 105 CMR 300.000: Reportable Diseases, Surveillance, and Isolation and Quarantine Requirements*. MDPH, Promulgated November 4, 2005.

“Smallpox Response Plan and Guidelines (Version 3.0)” Centers for Disease Control and Prevention. November 26, 2002. <[www.bt.cdc.gov/agent/smallpox/response-plan/index.asp#exec](http://www.bt.cdc.gov/agent/smallpox/response-plan/index.asp#exec)>.

“Smallpox Resources for Health Officials.” Centers for Disease Control and Prevention. June 28, 2004. <[www.bt.cdc.gov/agent/smallpox/healthofficials.asp](http://www.bt.cdc.gov/agent/smallpox/healthofficials.asp)>.

# Smallpox

**REPORT IMMEDIATELY**

(Also known as Variola)



## LBOH Action Steps

*This form does not need to be submitted to the MDPH with the case report form. It is for LBOH use and is meant as a quick-reference guide to smallpox case investigation activities.*

LBOH staff should follow these steps when smallpox is suspected in the community. For more detailed information, including disease epidemiology, reporting, case investigation and follow-up, refer to the preceding chapter.

*Note: Case investigation of smallpox in Massachusetts residents will be directed by the MDPH Division of Epidemiology and Immunization. If a bioterrorist event is suspected, the MDPH and other response authorities will work closely with LBOH and will provide instructions/information on how to proceed.*

- Immediately notify MDPH Division of Epidemiology and Immunization, at (617) 983-6800 or (888) 658-2850, to report all confirmed or suspect case(s) of smallpox.
- Obtain laboratory confirmation.
- Identify other potentially exposed persons.
- Fill out the case report form (attach laboratory results).
- Work with MDPH to institute isolation and quarantine requirements (*105 CMR 300.200*), as they apply to a particular case.
- Send the completed case report form (with laboratory results) to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS).