

Smallpox

IMMEDIATELY REPORTABLE DISEASE

Per N.J.A.C. 8:57, healthcare providers and administrators shall immediately report **by telephone** confirmed and suspected cases of smallpox to the health officer of the jurisdiction where the ill or infected person lives, or if unknown, wherein the diagnosis is made. The health officer (or designee) **must immediately institute the control measures listed below in section 6, “Controlling Further Spread,”** regardless of weekend, holiday, or evening schedules. A directory of local health departments in New Jersey is available at <http://www.state.nj.us/health/lh/directory/lhdselectcounty.shtml>.

If the health officer is unavailable, the healthcare provider or administrator shall make the report to the Department by telephone to 609.826.5964, between 8:00 A.M. and 5:00 P.M. on non-holiday weekdays or to 609.392.2020 during all other days and hours.



1 THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Smallpox is caused by the *variola* virus, which belongs to the genus orthopoxvirus.

B. Clinical Description and Laboratory Diagnosis

Smallpox is a systemic viral disease that presents with a characteristic eruptive rash. The onset of smallpox is sudden, with a prodrome characterized by fever, malaise, headache, severe backache, prostration, and occasionally abdominal pain. After two to four days the temperature falls and a rash appears.

The rash progresses through successive stages of macules, papules, vesicles, pustules, and finally scabs that fall off at the end of the third or fourth week of illness; the lesions are at the same stage of development in any given area. The fever frequently rises as the rash progresses to the pustular stage. The lesions first appear on the face and subsequently on the body and extremities, are more abundant on the face and extremities than on the trunk (centrifugal distribution), and are abundant over prominences and extensor surfaces. In previously vaccinated persons, the illness may be significantly modified to the extent that systemic symptoms are absent to mild and the rash consists of only a few highly atypical lesions, which do not pass through the usual successive stages.

Two principal clinical-epidemiologic varieties of smallpox are recognized: *variola minor* (alastrim) with a case-fatality ratio of less than 1%, and *variola major* (classical smallpox) with a case-fatality ratio among the unvaccinated of 15% to 40%. Death occurs as early as the third or fourth day of development of rash but more usually during the second week. Approximately 3% of hospitalized *variola major* cases experience a fulminating disease characterized by a severe prodrome, prostration, and bleeding into the skin, mucous membranes, uterus, and genital tract, especially in pregnant women; such hemorrhagic cases are rapidly fatal. In some instances when the usual rash does not appear, disease has been confused with severe acute leukemia, meningococcemia, or idiopathic thrombocytopenic purpura.

In the highly lethal “flat” variety, observed in about 5% of cases, the focal lesions are slow to develop, and the vesicles contain very little fluid and tend to project only slightly above the

surrounding skin and are soft and velvety to the touch. In the few patients with this type who have survived, the lesions sometimes resolve without the usual pustulation and crusting.

Variola minor is associated with the rash similar to that observed in *variola major*; however, the patient generally experiences less severe systemic reactions. Smallpox is usually distinguished by the clear-cut prodromal illness, the centrifugal distribution of the rash, the appearance of all lesions more or less simultaneously, the similarity in appearance of all lesions in a given area, and its more deeply seated lesions. The disease most commonly confused with smallpox is chickenpox (including atypical presentations that occur rarely in adults and, after consultation with New Jersey Department of Health and Senior Services [NJDHSS] Infectious and Zoonotic Disease Program [IZDP], can be tested rapidly at NJDHSS Public Health and Environmental Laboratories [PHEL] to confirm *varicella* and rule out smallpox; see section 2B for rule-out testing available at NJDHSS PHEL).

Smallpox (*Variola*): Clinical Features

Chickenpox (*Varicella*): Clinical Features

Major Distinguishing Features

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| <ul style="list-style-type: none"> • Febrile prodrome: temperature > 102°F and systemic symptoms (prostration, severe headache, backache, abdominal pain, or vomiting) one to four days before rash onset • Lesions are deep, firm, well-circumscribed pustules; may be confluent or umbilicated | <ul style="list-style-type: none"> • No or mild prodrome before rash onset • Lesions typically superficial vesicles |
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Other Distinguishing Features

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| <ul style="list-style-type: none"> • Rash concentrated on face and distal extremities (centrifugal) • Rash in same stage of evolution on any one part of the body • First lesions on oral mucosa/palate (enanthem), followed by examthem (rash) on face or forearm • Lesions on palms and soles (seen in > 50%) • Lesions may itch at scabbing stage | <ul style="list-style-type: none"> • Rash concentrated on trunk and proximal extremities (± face, scalp) • Rash appears in crops so lesions are in different stages of evolution (papules, vesicles, crusts) on any one part of the body • First lesions on trunk (occasionally face) • Lesions very uncommon on palms and soles • Lesions generally intensely itchy |
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- Lesions evolve from papule to pustule in days
- Lesions generally evolve from macules to papules to vesicles to crusts in < 24 hours
- Illness lasts 14 to 21 days
- Illness lasts four to seven days

Laboratory diagnosis is based on identification of virus by direct electron microscopy, immunohistochemistry, and polymerase chain reaction (PCR). Isolation of virus on live-cell cultures, followed by nucleic acid identification, or growth on chorioallantois, is confirmatory. Serologic testing is not recommended because antibody testing does not differentiate among orthopoxvirus species, and paired serum samples are required to distinguish recent infection from vaccination in the remote past. **Testing specifically for *variola* can be performed at level C or D laboratories only.**

C. Reservoirs

Prior to eradication, man was the only reservoir; now the only known virus is held in two secured laboratories.

D. Modes of Transmission

Smallpox is spread by close contact with respiratory discharges and skin lesions of patients or material that infected persons had recently contaminated; airborne spread of *variola* is infrequent.

Household, hospital, and school contacts are especially at risk. Spread to laundry workers by contaminated bedding and other linens has been frequently observed.

Inapparent infections have not been implicated, but unrecognized cases sometimes lead to extensive secondary spread. The secondary attack rate among unvaccinated populations is approximately 58% (range, 38% to 88% in eight studies).

E. Incubation Period

The incubation period for smallpox is seven to 19 days, commonly ten to 14 days to onset of illness and two to four days more to onset of rash.

F. Period of Communicability or Infectious Period

Smallpox patients are generally not infectious to others until the onset of rash (approximately seven to 17 days after exposure). However, because the exact date of rash onset may not be noted accurately and because of the infectious enanthem (lesions in the mouth and the posterior pharynx), which may precede cutaneous rash onset by one or two days, **case-patients should be considered potentially infectious from the date of onset of fever.** The period of highest transmission is during the first seven to ten days after onset of rash. However, a person is considered infectious until all scabs have separated. Risk of contracting disease increases during winter and early spring when aerosolized orthopox viruses survive longer at lower temperatures and lower levels of humidity.

G. Epidemiology

Smallpox was declared eradicated by the World Health Organization in 1979. The last known naturally occurring case was in 1977. In 1980, the World Health Assembly announced that smallpox had been eradicated and recommended that all countries cease vaccination. The last remaining samples of smallpox virus officially reside in two places: the Centers for Disease Control and Prevention (CDC) in the United States and the Research Institute for Viral Preparations in Moscow, Russia.

H. Bioterrorist Potential

Smallpox, because of its high case-fatality ratios and transmissibility, now represents one of the most serious bioterrorist threats to the civilian population. Introduction of *variola* virus into a nonimmune population could result in a major disaster unless controlled promptly. Despite the previous declaration of eradication in 1979, there is speculation that smallpox may have been obtained by rogue nations from the Soviets or that Soviet scientists may have sought work with rogue nations developing biological weaponry.

2 CASE DEFINITION

A. NJDHSS case definition and the CDC case definition are the same.

B. Case Classification

CONFIRMED

A clinically compatible illness (see above), AND

Isolation of smallpox (*variola*) virus from a clinical specimen (level D* laboratory only), OR

PCR identification of *variola* DNA in a clinical specimen (level D* laboratory only), OR

Negative-stain electron microscopy (EM) identification of *variola* virus in a clinical specimen (level D* laboratory or approved level C** laboratory).

*CDC and US Army Medical Research Institute for Infectious Diseases (USAMRIID).

**PHEL, NJDHSS, and others that have required safety and containment facilities.

Initial confirmation of a smallpox outbreak requires testing in a level D laboratory (CDC and USAMRIID). Level C laboratories (e.g., NJDHSS PHEL) will assist with testing of clinical specimens following initial confirmation of an outbreak by CDC.

PROBABLE

A clinically compatible illness that is not laboratory confirmed, but has an epidemiological link to another confirmed or probable case.

POSSIBLE

A clinically compatible illness that is not laboratory confirmed and does not have an epidemiological link to a confirmed or probable case of smallpox, OR

A case that has an atypical presentation that is not laboratory confirmed but has an epidemiological link to a confirmed or probable case of smallpox. Atypical presentations of smallpox include (1) hemorrhagic lesions or (2) flat, velvety lesions not appearing as typical vesicles nor progressing to pustules.

NOTE: The case definitions above may require revision by public health personnel conducting the epidemiological investigation depending on the specifics of the epidemic.

3 LABORATORY TESTING SERVICES AVAILABLE

PHEL does not provide testing for *variola* virus. However, other tests can be run to rule out other illnesses with similar clinical features (e.g., *Varicella zoster*, *Herpes simplex*, *Vaccinia*).

Specimens can be sent to PHEL for referral to a Biosafety Level 4 facility after evaluation by the IZDP staff at 609.588.7500. Procedures for submitting specimens for suspected cases of smallpox may also be found on the CDC Web site at <http://www.cdc.gov/bt>.

4 PURPOSE OF SURVEILLANCE AND REPORTING AND REPORTING REQUIREMENTS

A. Purpose of Surveillance

- To identify potential sources of transmission in the United States and to stop transmission from such sources.
- To identify sources of transmission and geographical areas of risk outside the United States and to stop transmission from such sources.
- To identify cases as early as possible, establish the diagnosis and case classification, and prevent transmission to other persons.
- To identify cases and clusters of human illness that may be associated with a bioterrorist event.
- To identify contacts for tracing, vaccination, and surveillance.
- To impose isolation of confirmed, probable, and suspected cases.
- To monitor the clinical course and outcome of cases.
- To monitor the epidemiology of the outbreak for analysis and communications purposes.

B. Laboratory and Healthcare Provider Reporting Requirements

Any case of smallpox is considered an **INTERNATIONAL EMERGENCY**. NJDHSS requests that information about any suspect or known case of smallpox be **reported immediately** to the local health officer where diagnosed. If this is not possible, call NJDHSS IZDP at 609.588.7500 (business hours) or 609.392.2020 (nights and weekends).

C. Local Departments of Health Reporting and Follow-up Responsibilities

The New Jersey Administrative Code (NJAC 8:57-1.8) stipulates that each local health officer must report any case of smallpox (as defined by the reporting criteria in section 2A) immediately to NJDHSS IZDP at 609.588.7500 (business hours) or 609.392.2020 (nights and weekends).

5 CASE INVESTIGATION

A. The most important step a local health officer can take if he/she learns of a suspect or confirmed case of smallpox, or potential exposure to smallpox, is to call NJDHSS IZDP, any time of the day or night. The daytime telephone number is 609.588.7500. The emergency telephone number for nights and weekends is 609.392.2020.

B. NJDHSS IZDP will direct case investigations of smallpox in New Jersey residents in conjunction with CDC and other state and federal agencies. A confirmed case of smallpox will indicate a bioterrorist event until proven otherwise because naturally occurring *variola* was eradicated in 1977. The FBI and other response authorities will be involved, and the investigation will be done in close cooperation with the local health officer. Laboratory confirmation is important for a first case in a geographic area, leading to release of vaccine as part of a response. In a setting where multiple cases are identified, laboratory capacity may soon be overwhelmed. In such instances, priority for laboratory resources will include (1) testing of clinical or environmental specimens that will provide information about a potential source of exposure, facilitating law enforcement activities, and case detection; and (2) testing of clinical specimens from cases with an unclear presentation but who are suspected as cases following expert consultation.

C. Following immediate notification of NJDHSS, the local health officer may be asked to assist in investigating cases that live within his/her jurisdiction.

D. Communicable Disease Reporting and Surveillance System

The mandatory fields in CDRSS include: disease, last name, county, municipality, gender, race, ethnicity, case status, report status.

The following table can be used as a quick reference guide to determine which CDRSS fields need to be completed for accurate and complete reporting of smallpox cases. The “CDRSS Screen” column includes the tabs which appear along the top of the CDRSS screen. The

“Required Information” column provides detailed explanations of what data should be entered.

CDRSS Screen	Entry Considerations
Patient Info	Enter the disease name (“SMALLPOX”), patient demographic information, illness onset date, and the date the case was reported to the local health department (LHD). There are no subgroups for smallpox.
Addresses	Enter any alternate address (e.g., a work site). Use the Comments section in this screen to record any pertinent information about the alternate address. Entering an alternate address will allow other disease investigators access to the case if the alternate address falls within their jurisdiction.
Clinical Status	Enter any treatment that the patient received and record the names of the medical facilities and physician(s) involved in the patient’s care. If the patient received care from two or more hospitals, be sure that all are entered so the case can be accessed by all infection control professionals (ICPs) covering these facilities. If immunization status is known, it should also be entered here. If the patient is alive, select “NO” in the Mortality section. If the patient died, select “YES” in the Mortality section with the date of death.
Signs/Symptoms	Check appropriate boxes for signs and symptoms and indicate their onset. Make every effort to get complete information by interviewing the physician, family members, ICP, or others who might have knowledge of the patient’s illness. Also, information regarding the resolution of signs and symptoms should be entered.
Risk Factors	Enter complete information about risk factors as known. Since this disease has been eradicated, any suspect case of smallpox will be investigated thoroughly on a case by case basis to identify the source and related risk factors. This investigation will be directed by representatives of the federal government.
Laboratory Eval	Laboratory testing is not commercially available for smallpox. Results of testing performed at CDC or USAMRIID should be entered in the Comments section.
Contact Tracing	Contact tracing (identification of contacts as described below) is the most urgent task when investigating smallpox cases. Information regarding contacts is to be recorded, as possible and as directed on a case by case basis.

CDRSS Screen	Entry Considerations
<p>Case Comments</p>	<p>Enter general comments (i.e., information that is not discretely captured by a specific topic screen or drop-down menu) in the Comments section. NOTE: Select pieces of information entered in the Comments section CANNOT be automatically exported when generating reports. Therefore, whenever possible, record information about the case in the fields that have been designated to capture this information; information included in these fields CAN be automatically exported when generating reports.</p>
<p>Epidemiology</p>	<p>Record name of and contact information for case investigators from other agencies (e.g., CDC, out-of-state health departments). Document communication between investigators in the Comments section.</p>
<p>Case Classification Report Status</p>	<p>Case status options are: “REPORT UNDER INVESTIGATION (RUI),” “CONFIRMED,” “PROBABLE,” “POSSIBLE,” and “NOT A CASE.”</p> <p>All cases entered by laboratories (including LabCorp electronic submissions) should be assigned a case status of “REPORT UNDER INVESTIGATION (RUI).”</p> <p>Cases still under investigation by the LHD should be assigned a case status of “REPORT UNDER INVESTIGATION (RUI).”</p> <p>Upon completion of the investigation, the LHD should assign a case status on the basis of the case definition. “CONFIRMED,” “PROBABLE,” “POSSIBLE” and “NOT A CASE” are appropriate options for classifying a case of smallpox (see section 2A).</p> <p>Report status options are: “PENDING,” “LHD OPEN,” “LHD REVIEW,” “LHD CLOSED,” “DELETE,” “REOPENED,” “DHSS OPEN,” “DHSS REVIEW,” and “DHSS APPROVED.”</p> <p>Cases reported by laboratories (including LabCorp electronic submissions) should be assigned a report status of “PENDING.”</p> <p>Once the LHD begins investigating a case, the report status should be changed to “LHD OPEN.”</p> <p>The “LHD REVIEW” option can be used if the LHD has a person who reviews the case before it is closed (e.g., health officer or director of nursing).</p> <p>Once the LHD investigation is complete and all the data are entered into CDRSS, the LHD should change the report status to “LHD CLOSED.”</p> <p>“LHD CLOSED” cases will be reviewed by DHSS and be</p>

CDRSS Screen	Entry Considerations
	<p>assigned one of the DHSS-specific report status categories. If additional information is needed on a particular case, the report status will be changed to “REOPENED” and the LHD will be notified by e-mail. Cases that are “DHSS APPROVED” cannot be edited by LHD staff (see Section C below).</p> <p>If a case is inappropriately entered (e.g., a case of <i>Varicella</i> was erroneously entered as a case of smallpox) the case should be assigned a report status of “DELETE.” A report status of “DELETE” should NOT be used if a reported case of smallpox simply does not meet case definition. Rather, it should be assigned the appropriate case status, as described above.</p>

E. Other Reporting and Investigation Issues

1. Once a local health department completes its investigation and assigns a report status of “LHD CLOSED,” NJDHSS will review the case, and when complete change the report status to “DHSS Approved.” At this time, the case will be locked for editing. If additional information is received after a case has been placed in “DHSS APPROVED,” a local health department will need to contact NJDHSS to reopen the case. This should only be done if the additional information changes the case status of the report.
2. **Contact identification** is the most urgent task when investigating smallpox cases. A *contact* is defined as a person who has had contact with a suspected, probable, or confirmed case of smallpox. A contact’s risk of contracting smallpox increases with close contact (six feet or less), increasing length of exposure to a case-patient, and the stage and severity of the case-patient’s illness (i.e., contact’s risk depends on case-patient’s onset of rash and/or cough). Thus, *close contact* is defined as any face-to-face contact (≤ 6 feet, able to reach out and touch) with a smallpox case-patient. Duration of contact should be quantified, if possible. Vaccinate close contacts as soon as possible following exposure, but preferably within three to four days to prevent or modify disease. This was the successful strategy used for the global eradication of smallpox.
3. Institution of disease-control measures is an integral part of case investigation. It is the local health officer’s responsibility to understand, and, if necessary, institute in conjunction with NJDHSS and CDC the control guidelines listed in section 6, “Controlling Further Spread.”

6 CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements

1. Minimum Period of Isolation of Patient

Strict isolation precautions must be instituted until all scabs have separated.

NOTE: Infection can be transmitted by air currents, and virus can be carried on various materials contaminated by the patient, especially on clothing and linen.

2. Minimum Period of Quarantine of Contacts

- All persons living in the same house with the smallpox patient, as well as face-to-face contacts, should be vaccinated promptly with known potent vaccine and placed under daily surveillance for 21 days after last contact with the smallpox patient.
- Quarantine should be substituted for surveillance of intimate contacts whose cooperation is uncertain.
- At the first sign of fever or other illness, the individual should be isolated.
- Any case contact who has not been vaccinated (as determined by the absence of a vaccination scar) and who refuses vaccination should be placed under quarantine for the period when disease might appear (i.e., from seven days after the first contact to 19 days after the last exposure to a case).

B. Protection of Contacts of a Case

- While a patient is being transported from the emergency department or clinic to an inpatient room, the patient should wear a surgical mask. A sheet should be used to cover the skin as much as possible, and efforts should be made to limit patient movement and manipulations of the linen to minimize aerosolization.
- Minimize the number of persons who enter the patient's room, as well as the traffic in and out of the room, as much as possible.
- All hospital staff (including transport personnel) and visitors (limited to immediate family ONLY) must don contact and airborne personal protection equipment prior to entering a suspected or confirmed smallpox patient's room (i.e., disposable gloves, gowns, and a surgical mask or properly fit-tested respirator, N-95 or higher; see NJ Guidelines for the Management of a Suspect Case of Smallpox in Medical Care Settings, <http://nj.gov/health/er/documents/smpxguidelines.pdf>, for more information).
- Preferably no staff without at least one prior vaccination for smallpox should be allowed in the patient's room.
- Ensure that all staff and visitors entering the room are instructed in the meaning of contact and airborne precautions.
- Dedicated equipment (e.g., blood pressure cuffs and stethoscopes) should be left in the room when possible. No personal equipment (e.g., stethoscopes) should be used on the suspect patient and then taken out of the room for use on other patients until decontaminated.
- A disinfectant labeled "tuberculocidal" is recommended for use on diagnostic equipment used on the patient.
- Use disposable items whenever possible.
- Arrange to have food brought into the room in disposable containers.
- Disinfect and/or sterilize nondisposable medical devices according to the manufacturer's specifications. **No extraordinary efforts are necessary.** Articles contaminated with excessive blood or body fluids (i.e., lesions or respiratory secretions)

- should be handled as regulated medical waste. All other nonsharps waste can be handled as regular waste. Ideally, all laundry and linens (e.g., bedding, towels) should be handled by the vaccinated staff caring for the patient. Laundry and linen can be put in impervious bags in the patient's room. Any staff wearing gloves can transport the bagged linen according to the hospital's standard laundry protocol.
- Immunization of contacts: All contacts of a laboratory-confirmed smallpox case, both intimate and casual, should be promptly vaccinated, employing a known potent vaccine. Epidemiological studies have shown that an increased level of protection against smallpox persists for ≤ 5 years after primary vaccination and substantial but waning immunity can persist for ≥ 10 years. Antibody levels after revaccination can remain high for a longer period, conferring a greater period of immunity than occurs after primary vaccination alone. Although it is assumed that adults older than 30 years in the United States have little or no immunity to smallpox, there is evidence that vaccination during infancy results in long-term reduction in mortality.
 - NJDHSS will immediately obtain assistance from national and international authorities for detailed investigation and for implementation of necessary control measures.
 - Vaccine will be made available from national stockpiles or the World Health Organization emergency reserve.
 - The number of people to be vaccinated will depend on the specific circumstances surrounding the event, but in past outbreaks, vaccination of a few hundred to a few thousand persons has successfully stopped spread. The local health department will be responsible for making vaccination clinics available, with coordination accountability at the LINCS site.
 - At this time, when there is no known smallpox illness, mass vaccination of entire communities is considered neither necessary nor desirable to control an outbreak.
 - Investigation of contacts and source of infection
 - Prompt investigation to determine the source of infection is of the greatest importance.
 - The diagnosis in some outbreaks was not made until the third or fourth generation of cases.
 - Because inapparent cases of smallpox are rare and do not appear to transmit infection, the chain of infection can almost always be determined.
 - Persons with supposed chickenpox or those who have recently experienced pustular or hemorrhagic disease (especially fatal cases) should be considered as possible sources of infection.

C. Managing Special Situations

One suspected case of smallpox is considered an **INTERNATIONAL EMERGENCY**. Therefore, NJDHSS and other response authorities will work closely with local boards of health to provide instructions and information on how to proceed.

7 OUTBREAK SITUATIONS

See section 5, which includes contact identification. Identification of a true case of smallpox would indicate an act of bioterrorism. Therefore, one suspect case would initiate an intensive investigation involving numerous partners at the federal, state, and local levels, especially law enforcement.

Additional Information

Technical information about smallpox is available from CDC at <http://www.bt.cdc.gov/agent/smallpox>.

The formal CDC surveillance case definition for smallpox is the same as the criteria outlined in section 2A of this chapter. CDC case definitions are used by state health departments and CDC to maintain uniform standards for national reporting. For reporting to NJDHSS, always use the criteria outlined in section 2A.

For more information on state emergency preparedness activities and plans related to smallpox, visit <http://nj.gov/health/er/smallpox.shtml>.

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