



Smallpox Case Definitions

As described in "Guide A" of the "Smallpox Response Plan and Guidelines"
(www.bt.cdc.gov/agent/smallpox/response-plan)

Introduction

Surveillance for a disease that does not currently exist anywhere in the world presents unique challenges. The goal of pre-outbreak (pre-event) smallpox surveillance is to recognize the first case of smallpox, should it ever occur, without generating excessive numbers of false alarms, unnecessarily disrupting the health care and public health systems, or increasing public anxiety. In the absence of known smallpox disease, the predictive value of a positive smallpox diagnostic test is extremely low; therefore, testing to rule out smallpox should be limited to cases that fit the clinical case definition in order to lower the risk of obtaining a false-positive test result. It is neither feasible nor desirable, in the pre-event scenario, to perform laboratory testing for suspected cases that do not meet the clinical case definition.

Thus, in the absence of smallpox disease in the world, the suggested approach to surveillance relies on a highly specific clinical case definition, which is focused on identifying the classic case presentation (ordinary type) of smallpox. Before eradication, classic (ordinary type) smallpox generally accounted for approximately 90% of smallpox cases in previously unvaccinated individuals and 70% of cases that occurred in previously vaccinated individuals who were no longer fully protected by vaccination.

Because the likelihood of reintroduction of smallpox is extremely low, and acknowledging that there are many other causes of vesicular and pustular rash illnesses, healthcare providers evaluating such cases should also familiarize themselves with diseases that can be confused with smallpox (e.g., varicella, herpes simplex, drug reactions, erythema multiforme), as well as the clinical manifestations of smallpox disease. In this way, in the unlikely event of a smallpox case, the disease will be clearly and quickly recognized.

Several resources to assist a clinician in the evaluation of a febrile, rash-illness patient for the likelihood of smallpox can be found on the "Smallpox Diagnosis and Evaluation" page (www.bt.cdc.gov/agent/smallpox/diagnosis).

These resources include:

1. The algorithm "Evaluating Patients for Smallpox," presented in poster format that provides a standard method for evaluating patients with acute, severe vesicular or pustular rash illness. The purpose of the protocol is to provide a systematic approach for evaluating patients with generalized rash illnesses and to direct an appropriate clinical and public health response, including diagnostic testing: www.bt.cdc.gov/agent/smallpox/diagnosis/evalposter.asp.
2. An online interactive risk evaluation algorithm (based on the poster algorithm above) that can be filled in to quickly determine the likelihood of clinical smallpox: www.bt.cdc.gov/agent/smallpox/diagnosis/riskalgorithm.
3. A downloadable standard worksheet that can be used to collect the clinical information to classify the risk of smallpox using the CDC criteria outlined in the poster ("Evaluating Patients for Smallpox"): www.bt.cdc.gov/agent/smallpox/diagnosis/pdf/spox-patient-eval-wksheet.pdf.

ANY SUSPECTED SMALLPOX CASE SHOULD BE IMMEDIATELY REPORTED TO LOCAL PUBLIC HEALTH OFFICIALS.

Smallpox Clinical Case Definition, Case Classifications and Clinical Types

(continued from previous page)

Case definition

Smallpox clinical case definition

An illness with acute onset of fever $\geq 101^{\circ}\text{F}$ (38.3°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 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 not diagnostic for smallpox.*

The importance of case confirmation using laboratory diagnostic tests differs depending on the epidemiological situation. Because of the low predictive value of a positive lab test result in the absence of a known smallpox outbreak, in the pre-outbreak (pre-event) setting, laboratory testing should be reserved for cases that meet the clinical case definition and are thus classified as being a potential high risk for smallpox according to the rash algorithm poster (www.bt.cdc.gov/agent/smallpox/diagnosis/evalposter.asp).

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:

Confirmed case: 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.

Probable case: 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 eruptione. See "Guide A: Smallpox Surveillance and Case Reporting; Contact Identification, Tracing, Vaccination, and Surveillance; and Epidemiologic Investigation" (www.bt.cdc.gov/agent/smallpox/response-plan/files/guide-a.pdf) for full descriptions of atypical smallpox presentations.

Suspect case: A case with a febrile rash illness with fever preceding development of rash by 1-4 days.

Additional information on post-outbreak (post-event) response and smallpox case classification and reporting can be found in the "CDC Smallpox Response Plan and Guidelines" (www.bt.cdc.gov/agent/smallpox/response-plan).

For more information, visit www.cdc.gov/smallpox, or call the CDC public response hotline at (888) 246-2675 (English), (888) 246-2857 (español), or (866) 874-2646 (TTY)

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