Smallpox Case Definitions

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.

Case definition

Smallpox clinical case definition

An illness with acute onset of fever >101°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.

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