

A Smallpox False Alarm

To the Editor: We report a case in which a man presented with a papulovesicular rash with centrifugal distribution ([Figure 1](#)) that had been preceded by four days of headache, backache, fever, nausea, and vomiting. Because the rash started on the face, evolved slowly, and was in the same stage of development on any one part of the body, smallpox was considered in the differential diagnosis. Urgent consultation was obtained, and health departments and the Centers for Disease Control and Prevention (CDC) were contacted. Limited specimens sent to the hospital laboratory tested positive for varicella–zoster virus (VZV) IgG, negative for VZV on direct fluorescent-antibody staining, and negative for the human immunodeficiency virus on serologic analysis. Digital photographs were e-mailed to the CDC. Specimens were collected according to CDC guidelines¹ and sent to the CDC. A culture performed at the CDC was positive for herpes simplex virus (HSV) type 2.

Once smallpox was considered, limited laboratory tests to rule out VZV were performed. If direct fluorescence antibody tests for HSV had been performed, we could have avoided sending specimens to the CDC. Our hospital has instituted a protocol for the rapid evaluation of patients presenting with illnesses involving fever and rash that includes smallpox in the differential diagnosis. Persons presenting with a rash that is consistent with classic smallpox will be evaluated in conjunction with health departments, as occurred in this case. In persons presenting with a suspicious rash that is deemed to represent a low or moderate risk in the algorithm for evaluation of smallpox,^{2,3} direct fluorescence antibody testing for HSV and VZV will be performed, as well as a test for syphilis. These tests and the need for a digital camera should be considered at other hospitals.

The collection and shipping of specimens were more complex than we had anticipated. Not all items listed by the CDC¹ as necessary for the collection of specimens are generally available in hospitals, so it is worth reviewing this list ahead of time. Collecting the appropriate specimens took about 90 minutes. By the time that was done, there was very little time left to get the specimens to the commercial carrier. Hospitals should review shipping policies for biologic specimens. Commercial carriers that accept biologic specimens may do so only at certain stations. Detailed paperwork must be completed and sent with the specimen. The collection, packaging, and transport of specimens to the commercial carrier can take a great deal of time. Twenty-five hours elapsed from the time that health departments were contacted to the time negative results that ruled out smallpox were received. Had this event not occurred during normal business hours, the process could have taken even longer. These problems should be taken into consideration in emergency response plans.

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This letter was published at www.nejm.org on December 19, 2002.

The New England Journal of Medicine
Volume 348:467-468

January 30, 2003

Number 5

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 2. Evaluating patients for smallpox. Atlanta: Centers for Disease Control and Prevention, 2002. (Accessed January 10, 2003, at <http://www.bt.cdc.gov/agent/smallpox/diagnosis/pdf/spox-poster-full.pdf>.)
 3. Worksheet: evaluating patients for smallpox. Atlanta: Centers for Disease Control and Prevention, 2002. (Accessed January 10, 2003, at <http://www.bt.cdc.gov/agent/smallpox/diagnosis/pdf/spox-patient-eval-wksheet.pdf>.)
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The CDC offers the following reply: The case study presented by Hanrahan et al. offers an excellent example of the type of partnership that is required between health care providers and local, state, and federal public health personnel in smallpox-response efforts. As predicted by the algorithm for the evaluation of febrile rash,^{1,2} smallpox was not the final diagnosis in this case because only one or two major criteria were met and the patient was thus classified as being at low risk for smallpox. Nevertheless, testing for smallpox was performed in order to provide reassurance to a health care community that is not yet familiar with the use of the algorithm for the assessment of risk of smallpox in patients with febrile rash illnesses. This case demonstrates the clinical usefulness of digital cameras, and it shows that public health laboratories have a need for rapid diagnostic tests for the full range of diseases included in the differential diagnosis of smallpox. The appropriate diagnosis would have been made hours earlier in this case if a test for HSV had been readily available. It is this level of preparedness that the CDC is committed to achieving.

To provide rapid local testing for infectious causes of illnesses involving rashes that could be confused with smallpox, both direct fluorescence antibody and polymerase-chain-reaction (PCR) testing for varicella have been made available at all laboratories of the Laboratory Response Network for Bioterrorism (LRN). PCR testing capabilities for HSV, such as those used by the CDC in this case, may also be useful. LRN laboratories can currently evaluate clinical specimens for vaccinia, a step that may become necessary in certain cases of smallpox-vaccine-related adverse events. In addition, a subgroup of LRN laboratories with appropriate technical, biosafety, and biosecurity measures will have diagnostic laboratory tests to screen for smallpox. As Hanrahan et al. demonstrate, transportation of specimens introduces a delay in obtaining laboratory confirmation. To minimize such delays, guidelines for the collection and shipping of specimens should be reviewed (they can be found at <http://www.cdc.gov/smallpox>). When indicated, aircraft are available 24 hours a day, 7 days a week, to move specimens to reference laboratories or physicians who can assist in the evaluation of patients.

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The New England Journal of Medicine

Volume 348:467-468

January 30, 2003

Number 5

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