Acute, Generalized Vesicular or Pustular Rash Illness Testing Protocol in the United States

Introduction

This protocol has been developed to illustrate the types of laboratory testing to be undertaken in different situations involving patients with acute, generalized vesicular or pustular rash illness. The protocol is composed of four charts, each illustrating a different set of symptoms or circumstances. It has been designed to correlate with "Evaluating Patients for Smallpox: Acute, Generalized Vesicular or Pustular Rash Illness Protocol" (www.bt.cdc.gov/agent/smallpox/diagnosis/riskalgorithm). This is a pre-event algorithm, designed to address testing needs when no poxvirus emergency has been detected or declared. Changes to this algorithm may be required in an event. Any updates to the algorithm will be announced by the Laboratory Response Network.

Chart 1 lists the symptoms associated with acute, generalized vesicular or pustular rash illness and categorizes the risk of smallpox according to the patient's signs and symptoms.

Chart 2 presents a flow chart for laboratory testing of specimens from patients presenting with acute, generalized vesicular or pustular rash illness, following the assessment per the "Acute, Generalized Vesicular or Pustular Rash Illness" protocol (see above and chart 1 for abstraction of the protocol). A two-armed algorithm is presented to reduce the time to receive results and to ensure that testing of high-risk specimens is confined to laboratories with appropriate biosafety levels and expertise. The two arms of the testing algorithm are for 1) specimens from individuals with low- and moderate-risk symptoms and 2) specimens from individuals with high-risk symptoms.

Major points:

- a) high-risk specimens/cases require consultation with CDC
- b) low- or moderate-risk specimens/cases should be worked-up for more common causes of febrile exanthema. Due to the differences in run temperature between the Non-variola Orthopoxvirus PCR and the Orthopoxvirus PCR, the two assays cannot be performed simultaneously. If orthopoxvirus is suspected, then the Non-variola Orthopoxvirus PCR permits the laboratory to identify an orthopoxvirus and reassure that the specimen does not contain variola. The Orthopoxvirus generic PCR can be performed subsequently to provide additional confidence in the result.
- c) in the absence of endemic smallpox disease, the indiscriminate use of variola tests will lead to false positives.

Chart 3 presents a testing algorithm that should be used when a smallpox vaccine adverse event or monkeypox infection is suspected.

Chart 4 presents an orthopoxvirus testing algorithm for environmental samples.

The testing protocols are supported at Laboratory Response Network (LRN) reference laboratories. Details for performance and interpretation of each assay are specified in each LRN procedure.

Details on specimen collection can be found at the following websites:

Smallpox vaccine: www.bt.cdc.gov/agent/smallpox/vaccination/vaccinia-specimen-collection.asp

Smallpox: www.bt.cdc.gov/agent/smallpox/response-plan/files/guide-d.pdf

Monkeypox: www.cdc.gov/ncidod/monkeypox/diagspecimens.htm

ACUTE, GENERALIZED VESICULAR OR PUSTULAR RASH ILLNESS PROTOCOL Patient with Acute, Generalized Vesicular or Pustular Rash Illness **Institute Airborne & Contact Precautions Alert Infection Control on Admission Low Risk of Smallpox High Risk of Smallpox Moderate Risk of Smallpox** (see criteria be<u>low)</u> (see criteria below) (see criteria below) History and Exam Diagnosis Uncertain ID and/or Derm Consultation ID and/or Derm Consultation Highly Suggestive of Varicella VZV +/- Other Lab Testing as Indicated Local and State Health Depts

Non-Smallpox

Diagnosis Confirmed

Report Results to Infx Control

Risk of Smallpox High Risk of Smallpox 1. Febrile prodrome AND 2. Classic smallpox lesion AND 3. Lesions in same stage of development ND one other **MAJOR** smallpox criterion OR Febrile prodrome A Febrile prodrome / >4 MINOR smallpox criteria **Low Risk of Smallpox** No febrile prodrome **OR** Febrile prodrome AND <4 MINOR smallpox criteria

Test for VZV and Other

Varicella Testing

Optional

Chart 1

Ensure Adequacy of Specimen ID or Derm Consultant Re-evaluate Patient

No Diagnosis Made Appropriate Treatment for

Varicella/Other Conditions as Clinically Indicated

Response Team Advises on Management and Specimen Collection

Testing at CDC

NOT Smallpox Continue Diagnostic Testing

SMALLPOX

Contact Local/State Health Dept.

Cannot R/O Smallpox

Major Smallpox Criteria:

- Febrile prodrome
 - ->101F, 1-4 days prior to rash onset
- with headache, back ache, or abdominal pain
- Firm, deep-seated, well-circumscribed vesicles/pustules
- Lesions in the same stage of development in any one area of the body

Minor Smallpox Criteria:

- Centrifugal distribution of lesions
- First lesions in the pharynx, oral mucosa
- Patient appears "toxic"
- Slow evolution of rash
 - 1-2 days each stage: macule, papule, vesicle
- Lesions on the palms and soles

11/14/2007 Page 2 of 5

LABORATORY TESTING FOR ACUTE, GENERALIZED VESICULAR OR PUSTULAR RASH ILLNESS IN THE UNITED STATES

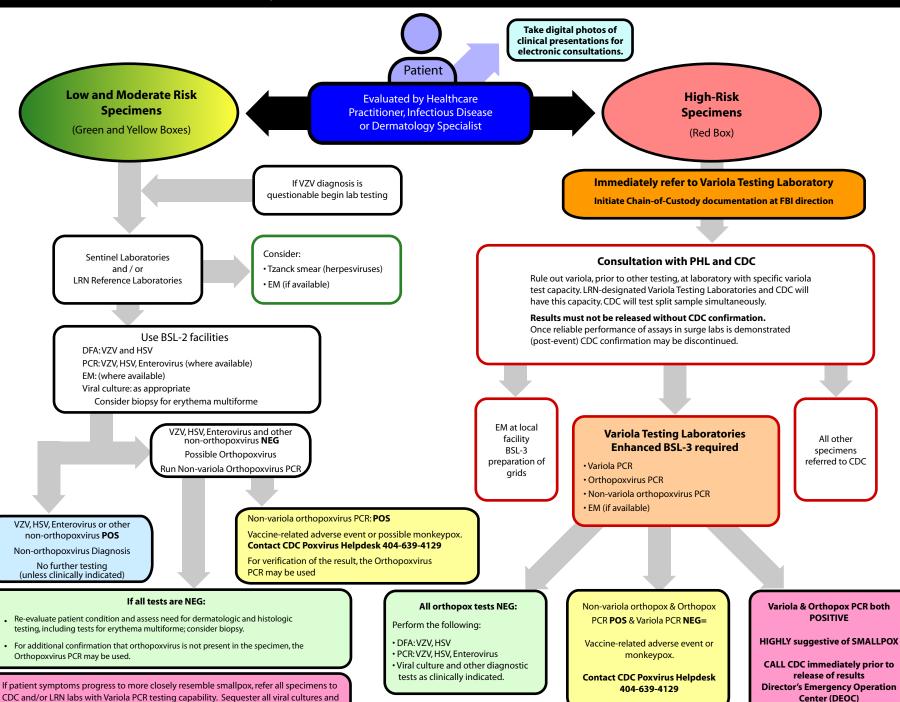


Chart 2 11/14/2007 Page 3 of 5

770-488-7100

specimens. Contact PHL for transport of specimens.

LABORATORY TESTING FOR SUSPECTED SMALLPOX VACCINE (VACCINIA) ADVERSE EVENTS OR MONKEYPOX IN THE UNITED STATES

Take digital photos of clinical presentations for electronic Acceptable specimens: consultations. Vesicular "touch prep" Vesicle roof **Patient** Vesicular swab Ocular swab or impression slide Patient with Suspected Vaccine-Related Adverse Event or Monkeypox** Biopsy specimens All Sentinel Laboratory and Reference LRN Labs (with PCR capability) LRN with no Orthopoxvirus PCR capacity Non-variola Orthopoxvirus PCR Orthopoxvirus PCR Refer only EM – (if available) **Note:** A non-variola orthopoxvirus PCR POS and orthopoxvirus PCR NEG should not be generated. **Test Results** If that occurs, consult CDC Poxvirus Helpdesk 404-639-4129 Non-variola orthopoxvirus PCR: POS Non-variola orthopoxvirus PCR: **NEG** Non-variola orthopoxvirus PCR: **NEG** Orthopoxvirus PCR: POS Orthopoxvirus PCR: NEG Orthopoxvirus PCR: POS EM (optional): POS for poxvirus EM (optional): **NEG** for poxvirus EM: POS or NEG for poxvirus Vaccine-related adverse event or Re-evaluate patient condition and Orthopoxvirus identified - possible assess need for dermatologic and monkeypox. histologic testing, including tests for Refer immediately to CDC for **Evaluate exposure history and** erythema multiforme; consider biopsy. confirmatory testing contact CDC to submit specimen for **Call the Director's Emergency** confirmatory tests. Perform: DFA: VZV, HSV **Operation Center (DEOC) Contact CDC Poxvirus Helpdesk** PCR: VZV, HSV, Enterovirus 770-488-7100 404-639-4129 Viral culture and other diagnostic tests as clinically indicated *Note: Could also represent differential sensitivities of the assays ** includes any non-variola orthopoxvirus, such as vaccinia, monkeypox and cowpox.

Chart 3 11/14/2007 Page 4 of 5

LABORATORY TESTING FOR ENVIRONMENTAL SAMPLES IN THE UNITED STATES

Environmental Samples Initiate Chain-of-Custody **Law Enforcement Credible Threat Assessment** documentation (Explosives, radiation, hazardous chemicals and toxins ruled out) **Sentinel Laboratory LRN Reference Laboratory** Refer only Orthopoxvirus PCR Non-variola orthopoxvirus PCR • EM – (with CDC consultation only) **Note:** A non-variola orthopoxvirus PCR POS and orthopoxvirus PCR NEG should not be generated. **Test Results** If that occurs, contact CDC Poxvirus Helpdesk. 404-639-4129 Orthopoxvirus PCR: **NEG** Orthopoxvirus PCR: POS Orthopoxvirus PCR: POS Non-variola orthopoxvirus PCR: NEG Non-variola orthopoxvirus PCR: POS Non-variola orthopoxvirus PCR: **NEG** EM: NEG for poxvirus EM: POS or NEG for poxvirus EM: POS or NEG for poxvirus Orthopoxvirus ruled out. Orthopoxvirus material identified -Orthopoxvirus material identified -Assess need for further testing with law most likely non-variola possible variola. enforcement. Report negative results to Refer immediately to CDC for other groups investigating specimens. Refer to CDC for confirmatory testing. confirmatory testing. **Contact CDC Poxvirus Helpdesk** 404-639-4129 Call the Director's Emergency **Operation Center (DEOC)** 770-488-7100