

# Rash Illness Evaluation

Department of Health and Human Services  
Centers for Disease Control and Prevention  
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Presented by Dr. Jane Seward, NIP, CDC

# Rash Illness Evaluation

- **Learning Objectives:**
  - Describe how to use the Diagnostic Algorithm
  - Discuss CDC's experience with the use of the Algorithm



## Need for a Diagnostic Algorithm?

- **No naturally acquired smallpox cases since 1977, however, concern about use of smallpox virus as a bioterrorist agent**
- **Recommencing smallpox vaccination in the United States is likely to heighten concerns about generalized vesicular or pustular rash illnesses**



There have been no naturally acquired cases of smallpox in the world since 1977, however, there are serious concerns about the use of smallpox virus as a bio-terrorist agent.

In the event of a bio-terrorist release of smallpox virus, effective public health control strategy requires early recognition of a smallpox case.

As most clinicians have not seen a case of smallpox, and therefore lack experience with making a smallpox diagnosis, and because other rash illnesses may be confused with smallpox, a diagnostic algorithm would be useful.

## Need for a Diagnostic Algorithm?

- **Public health control strategy requires early recognition of smallpox case**
- **Clinicians lack experience with smallpox diagnosis**
- **Other rash illnesses may be confused with smallpox**



There have been no naturally acquired cases of smallpox in the world since 1977, however, there are serious concerns about the use of smallpox virus as a bio-terrorist agent.

In the event of a bio-terrorist release of smallpox virus, effective public health control strategy requires early recognition of a smallpox case.

As most clinicians have not seen a case of smallpox, and therefore lack experience with making a smallpox diagnosis, and because other rash illnesses may be confused with smallpox, a diagnostic algorithm would be useful.

## Need for a Diagnostic Algorithm?

- ~1.0 million cases varicella (U.S.) this year and millions of cases of other rash illnesses
  - If 1/1000 varicella cases is misdiagnosed → 1000 false alarms
- Need strategy with high specificity to detect the first case of smallpox
- Need strategy to minimize laboratory testing for smallpox (risk of false positives)



We estimate that there will be approximately 1 million cases of varicella (or chickenpox) in the US this year and many more millions of cases of other rash illnesses. If for example, 1 out of every thousand varicella cases were suspected to be smallpox, there would be 1000 false alarms per year. The public health system cannot handle thousands of false alarms

We need a strategy with *high specificity* to accurately detect the first case of smallpox (should there ever be one).

This strategy will serve to minimize laboratory testing for smallpox, which would have the potential risk of producing a false positive lab test.

## Assumptions/Limitations

- **First case of smallpox may not be diagnosed until day 4-5 of rash**
- **First case of smallpox may not be diagnosed early if it presents atypically**
  - **Hemorrhagic**
  - **Flat/velvety**
  - **Highly modified**



Using this approach, we recognize and accept the fact that the first case of smallpox will not be diagnosed until day 4-5 of rash and also that the 1<sup>st</sup> case of smallpox will not be diagnosed early (as in the first 4-5 days), in fact, it is likely to be missed altogether, if it presents atypically such as a hemorrhagic, flat/velvety, or highly modified case

# Smallpox Disease

- **Incubation Period: 7-17 days**
- **Pre-eruptive Stage (Prodrome): fever and systemic complaints 1-4 days before rash onset**



Let's now review the signs and symptoms of smallpox disease:

The incubation period is 7-17 days.

The pre-eruptive stage, known as the prodrome, generally consists of fever and systemic complaints that occur 1 to 4 days before the rash.

After the prodrome begins the rash stage. The lesions start as macules then progress to papules then to vesicles and finally to pustules. After this point the pustules begin to crust and form scabs which separate and may leave deep scars, Let's review the rash stages to make sure that the terms are fully understood. A macule is a red, flat lesion on the skin that is not raised above the skin surface. A papule is a red, raised skin lesion (like a small pimple). A vesicle is a raised skin lesion that contains clear fluid and a pustule is a raised skin lesion that contains pus.

# Smallpox Disease

- **Rash stage**
  - **Macules**
  - **Papules**
  - **Vesicles**
  - **Pustules**
  - **Crusts (scabs)**
- **Scars**



Let's now review the signs and symptoms of smallpox disease:

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## Smallpox: Day 2 of Rash



The next few slides are photographs of an actual case of smallpox showing the progression of rash. Note that on the day 2, the rash is mild, is macular and papular and could easily be overlooked. If this were the first case, smallpox would not be considered at this stage.

## Smallpox: Day 4 of Rash



On day 4 the rash is more significant and has progressed to the papule stage with some vesicles. If there had been a febrile prodrome, we may be considering smallpox in the differential at this point.

# Smallpox Rash

## Vesicles



Day 4 and 5

## Pustules



Days 7-11



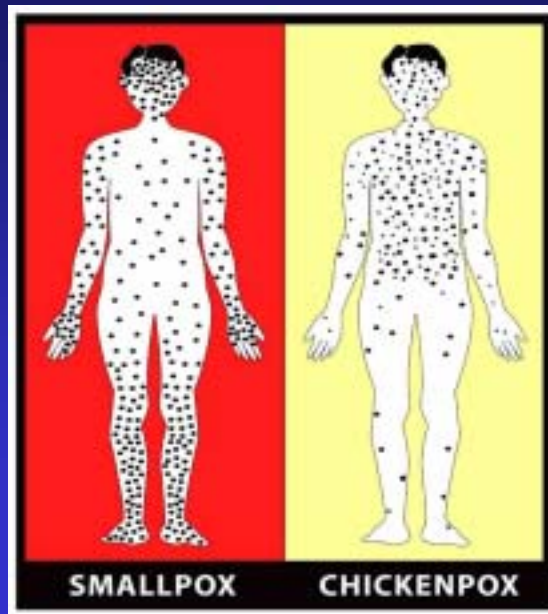
On day 4 and 5, the rash is now vesicular. At this stage, there is an accumulation of fluid in the vesicles; Over the next 24-48 hours, the clear fluid becomes cloudy and begins to thicken leading to pustules which reach their maximum size by day 11. Note that in smallpox, the lesions are all in the same stage of development on that part of the body. That is, you would not expect to find both vesicles and pustules on the face but you may see pustules on the face and vesicles on the trunk.

## Classic Smallpox Lesions: Pustules



Here is another photograph of smallpox pustular lesions that clearly demonstrates their deep seated nature. One can imagine just from the photo that these lesions, if pressed on, would feel hard and pea-like and could be rolled around under the skin.

# Rash Distribution



The typical pattern of smallpox rash distribution is demonstrated in this cartoon. Note that the lesions are concentrated distally on the head and the extremities in contrast with the central distribution (more lesions on the trunk) that is typically seen in varicella.

## Differential Diagnosis

**Varicella is the disease  
most likely to be  
confused with smallpox**



varicella is the disease most likely to be confused with smallpox

## Differentiating Features: Varicella

- **No or mild prodrome**
- **No history of varicella or varicella vaccination**
- **Superficial lesions “dew drop on a rose petal”**
- **Lesions appear in crops**



It is important then to recognize the differentiating features of varicella. With varicella, there is generally no, or a mild, prodrome period. However, adults get much sicker with varicella than children do and they may have a febrile prodrome. There is likely to be no history of varicella or varicella vaccination. The skin lesions in varicella are superficial, that is they are located on the skin surface. They are classically described as “dew drop on a rose petal”. They typically appear in crops meaning that new lesions appear over several days. This leads to the next important differentiating feature.

## Differentiating Features: Varicella

- Lesions in **DIFFERENT** stages of development
- **Rapid** evolution of lesions
- **Centripetal (central)** distribution
- Lesions rarely on palms or soles
- Patient rarely toxic or moribund



Lesions are typically in *different* stages of development. Thus, on any one part of the body, there may be macules, papules, vesicles and crusted lesions. There tends to be a more rapid evolution of lesions (they may progress from macule to vesicle and even crust within 24 hours) and unlike smallpox, there is a centripetal (central) distribution of the lesions. Lesions appear rarely on the palms or soles of the feet and the

Patient with chickenpox is rarely toxic or moribund. Again, adults are more likely to be the exception to this rule than children. A severe case of varicella may also have so many lesions that distribution may not be a useful differentiating feature



# Varicella



These photos show varicella rashes. The upper right photo shows the classic varicella, “dew drop on a rose petal” type lesions. The child in the lower photo has pustular and vesicular lesions.

## Varicella Adult Case



These 2 photographs are of varicella infection in an adult. Varicella Lesions can be extensive in adults but if we could examine the lesions closely, we would see that they are in different stages of development and that they are superficial.

## Varicella: Infected Lesions



Varicella infected lesions may confuse the diagnosis.

# Differential Diagnosis

- Disseminated herpes zoster
- Impetigo
- Drug eruptions
- Contact dermatitis
- Erythema multiforme



Other rash illnesses that should be in the differential diagnosis in a febrile rash illness are:

Disseminated herpes zoster

Impetigo

Drug eruptions

Contact dermatitis

Erythema multiforme

# Differential Diagnosis

- **Enteroviral infections (especially Hand, Foot and Mouth)**
- **Disseminated herpes simplex**
- **Scabies, insect bites**
- **Molluscum contagiosum (in immunocompromised)**



Other rash illnesses that should be in the differential diagnosis in a febrile rash illness are:

Enteroviral infections (especially, hand, foot and mouth disease)

Disseminated herpes simplex

Scabies, insect bites

Molluscum contagiosum (in immunocompromised patients)

# Differential Diagnosis

- Rare dermatological conditions
- Acne
- Secondary syphilis
- Rickettsial diseases
- Smallpox vaccine-related rashes



The poster lists the most common diagnoses that are likely to be confused with smallpox. Other dermatological conditions, acne, secondary syphilis and rickettsial diseases may also be rare causes of confusion. If we start a smallpox vaccination program in the United States, then generalized vaccinia may raise suspicions of smallpox but a recent history of smallpox vaccination should assist in this differentiation.

# Goal: Rash Illness Algorithm

- **Systematic approach to evaluation of cases of febrile vesicular or pustular rash illness**
- **Classify cases of vesicular/pustular rash illness into risk categories (likelihood of being smallpox) according to major and minor criteria developed for smallpox according to the clinical features of the disease**



The goal of the rash illness algorithm is to provide a systematic approach to evaluation of cases of febrile vesicular or pustular rash illness. The algorithm uses clinical features of smallpox to establish major and minor criteria and uses these criteria to classify cases of vesicular/pustular rash illness into risk categories (likelihood of being smallpox)

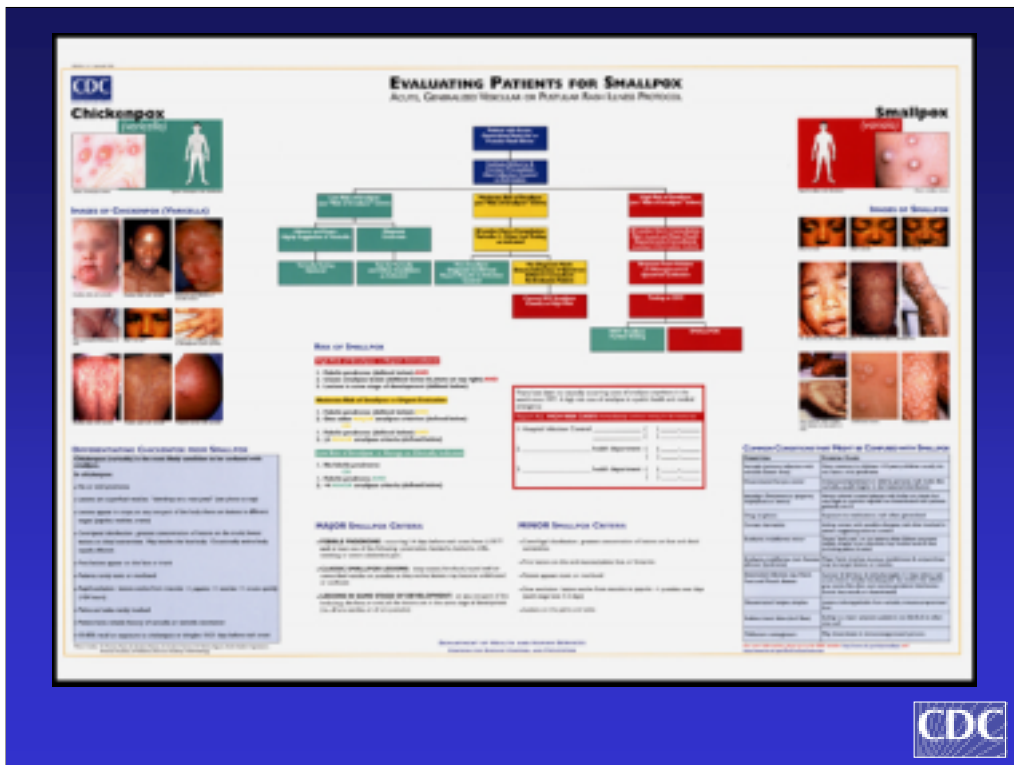
# Investigation Tools

- Available through state health departments and at [www.cdc.gov/smallpox](http://www.cdc.gov/smallpox)
  - Rash algorithm poster
    - Health care providers link to view and print poster
  - Protocol (written guide for use of poster)
    - File can be downloaded and printed



The following case investigation tools are available to assist in evaluating a suspected smallpox case: the rash algorithm poster is available through state health departments. It can also be viewed and ordered from the CDC website and a black and white version can be printed from the website. An accompanying protocol can also be downloaded and printed.





The poster looks like this. It is available in 2 sizes, a wall size of 2ft by 3ft and a smaller size 11 x 17 inches. The poster shows images of smallpox (in this corner) and chickenpox (in this corner); lists features that differentiate chickenpox from smallpox and common conditions that might be confused with smallpox. Finally, it presents a method for classifying cases according to their risk of smallpox using major and minor criteria for smallpox.

# Investigation Tools

- **Case investigation worksheet for investigation of febrile vesicular or pustular rash illnesses**
  - **Questions on prodromal symptoms, clinical progression of illness, history of varicella, vaccinations for smallpox and varicella, exposures, lab testing**
  - **Worksheet can be downloaded and printed from [www.cdc.gov/smallpox](http://www.cdc.gov/smallpox)**



A worksheet for collecting standard information on the case being evaluated is also available through state health departments and can be downloaded and printed from the CDC website.

## WORKSHEET: EVALUATING PATIENTS FOR SMALLPOX

Identification Number	_____
Please Complete Form	_____
Date of Contact with Case	_____
Special Use (optional)	_____

### PATIENT INFORMATION

<p>Name: _____</p> <p>DOB: <input type="text"/> / <input type="text"/> / <input type="text"/></p> <p>Date of Birth: <input type="text"/> / <input type="text"/> / <input type="text"/> Age: <input type="text"/> Sex: <input type="checkbox"/> Male <input type="checkbox"/> Female</p> <p>Telephone: _____</p> <p>Name: _____ Other: _____</p> <p>Address: _____</p> <p>City: _____ State: _____ Zip: _____</p> <p>Race: <input type="checkbox"/> White <input type="checkbox"/> Black <input type="checkbox"/> Asian <input type="checkbox"/> Other Ethnicity: <input type="checkbox"/> Hispanic <input type="checkbox"/> Non-Hispanic Country of Birth: _____</p>	<p>Where is the patient now? <input type="checkbox"/> Home <input type="checkbox"/> Doctor's Office</p> <p><input type="checkbox"/> Emergency Room or medical center (please specify)</p> <p><input type="checkbox"/> Hospital or prison, continue below</p> <p><input type="checkbox"/> Other (specify): _____</p> <p>Hospital Name: _____</p> <p>City/State: _____</p> <p>Admission Date: <input type="text"/> / <input type="text"/> / <input type="text"/> Discharge Date: <input type="text"/> / <input type="text"/> / <input type="text"/></p> <p>Hospital Telephone Number: <input type="text"/> / <input type="text"/> / <input type="text"/></p>
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### PROVIDER INFORMATION

<p>Name: _____</p> <p>Patient Population Specialty: _____</p> <p>Telephone: _____</p> <p>Type: <input type="checkbox"/> Adult <input type="checkbox"/> Pediatric <input type="checkbox"/> Both</p> <p>Type: <input type="checkbox"/> _____</p> <p>E-mail Address: _____</p>	<p>Name: _____</p> <p>Patient Population Specialty: _____</p> <p>Telephone: _____</p> <p>Type: <input type="checkbox"/> Adult <input type="checkbox"/> Pediatric <input type="checkbox"/> Both</p> <p>Type: <input type="checkbox"/> _____</p> <p>E-mail Address: _____</p>
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### CLINICAL INFORMATION

<p><b>PROBABLE/CONFIRMED/CLINICAL CASES REPORTED BY SOURCE</b></p> <p>Did the patient have a fever and other illness 1-4 days before rash onset? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown</p> <p>Date of probable onset: <input type="text"/> / <input type="text"/> / <input type="text"/></p> <p>If Yes, on what date did the patient first have a fever? <input type="text"/> / <input type="text"/> / <input type="text"/></p> <p>What was the highest temperature? <input type="text"/> °F or <input type="text"/> °C</p> <p>On what date: <input type="text"/> / <input type="text"/> / <input type="text"/></p> <p>Check all features of the prodrome that apply:</p> <table border="0"> <tr> <td><input type="checkbox"/> Headache (1-7 days)</td> <td><input type="checkbox"/> Muscular pain</td> </tr> <tr> <td><input type="checkbox"/> Headache</td> <td><input type="checkbox"/> Sore throat</td> </tr> <tr> <td><input type="checkbox"/> Nausea</td> <td><input type="checkbox"/> Other (specify): _____</td> </tr> </table>	<input type="checkbox"/> Headache (1-7 days)	<input type="checkbox"/> Muscular pain	<input type="checkbox"/> Headache	<input type="checkbox"/> Sore throat	<input type="checkbox"/> Nausea	<input type="checkbox"/> Other (specify): _____	<p>What kind of lesions does the patient have now? (check all that apply)</p> <table border="0"> <tr> <td><input type="checkbox"/> Macules (flat, reddish spots)</td> <td><input type="checkbox"/> Papules (slightly raised with core)</td> </tr> <tr> <td><input type="checkbox"/> Papules (solid bumps)</td> <td><input type="checkbox"/> Crusts</td> </tr> <tr> <td><input type="checkbox"/> Vesicles (fluid-filled blisters)</td> <td><input type="checkbox"/> Other: _____</td> </tr> </table> <p>If more than one kind of lesion, which kind of lesion is now the most common? _____</p> <p>Are the lesions now:</p> <table border="0"> <tr> <td><input type="checkbox"/> Superficial (on top of the skin)</td> <td><input type="checkbox"/> Papules (slightly raised with core)</td> </tr> <tr> <td><input type="checkbox"/> Deep (that penetrated deeply in the skin)</td> <td><input type="checkbox"/> Neither (specify): _____</td> </tr> </table> <p>How many lesions are present? (in total) _____</p> <p>If no precise count is available, please estimate: <input type="checkbox"/> &lt; 10 <input type="checkbox"/> 10-100 <input type="checkbox"/> &gt; 100</p>	<input type="checkbox"/> Macules (flat, reddish spots)	<input type="checkbox"/> Papules (slightly raised with core)	<input type="checkbox"/> Papules (solid bumps)	<input type="checkbox"/> Crusts	<input type="checkbox"/> Vesicles (fluid-filled blisters)	<input type="checkbox"/> Other: _____	<input type="checkbox"/> Superficial (on top of the skin)	<input type="checkbox"/> Papules (slightly raised with core)	<input type="checkbox"/> Deep (that penetrated deeply in the skin)	<input type="checkbox"/> Neither (specify): _____
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The worksheet looks like this. When CDC receives a call on a febrile rash illness case, we direct the caller to this form and suggest that they use it to gather relevant information on the case.

# Smallpox Surveillance Clinical Case Definition

**An illness with acute onset of fever  $\geq 101^{\circ}$  F followed by a rash characterized by firm, deep-seated vesicles or pustules in the same stage of development without other apparent cause**



The Smallpox Surveillance Clinical Case Definition is an illness with acute onset of fever  $\geq 101^{\circ}$  F followed by a rash characterized by firm, deep-seated vesicles or pustules in the same stage of development without other apparent cause

# Smallpox: Major Criteria

- **Prodrome (1-4 days before rash onset)**
  - **Fever  $\geq 101^{\circ}\text{F}$  ( $38.3^{\circ}\text{C}$ ) and**
  - **>1 symptom: prostration, headache, backache, chills, vomiting, abdominal pain**
- **Classic smallpox lesions**
  - **Firm, round, deep-seated pustules**
- **All lesions in same stage of development (on one part of the body)**



There are 3 major criteria for the clinical diagnosis of smallpox that correspond to the 3 essential components of the clinical case definition:

1. A prodrome that begins 1-4 days before rash onset

And includes fever  $\geq 101^{\circ}\text{F}$  ( $38.3^{\circ}\text{C}$ ) and

At least one of the following symptoms: prostration, headache, backache, chills, vomiting, abdominal pain

2. Presence of classic smallpox lesions: firm, round, deep-seated pustules. As previously mentioned, they have a “shotty” feel, like rolling a pea around under the skin

3. All the lesions are in same stage of development (on one part of the body). This means that all lesions on the arm or all lesions on the trunk would be all vesicles, all pustular, or all crusting—not a mixture of different skin lesions

# Smallpox: Minor Criteria

- Centrifugal (distal) distribution
- First lesions: oral mucosa, face, or forearms
- Patient toxic or moribund
- Slow evolution (each stage 1-2 days)
- Lesions on palms and soles



Five signs make up the smallpox minor criteria:

The lesions have a centrifugal (distal) distribution

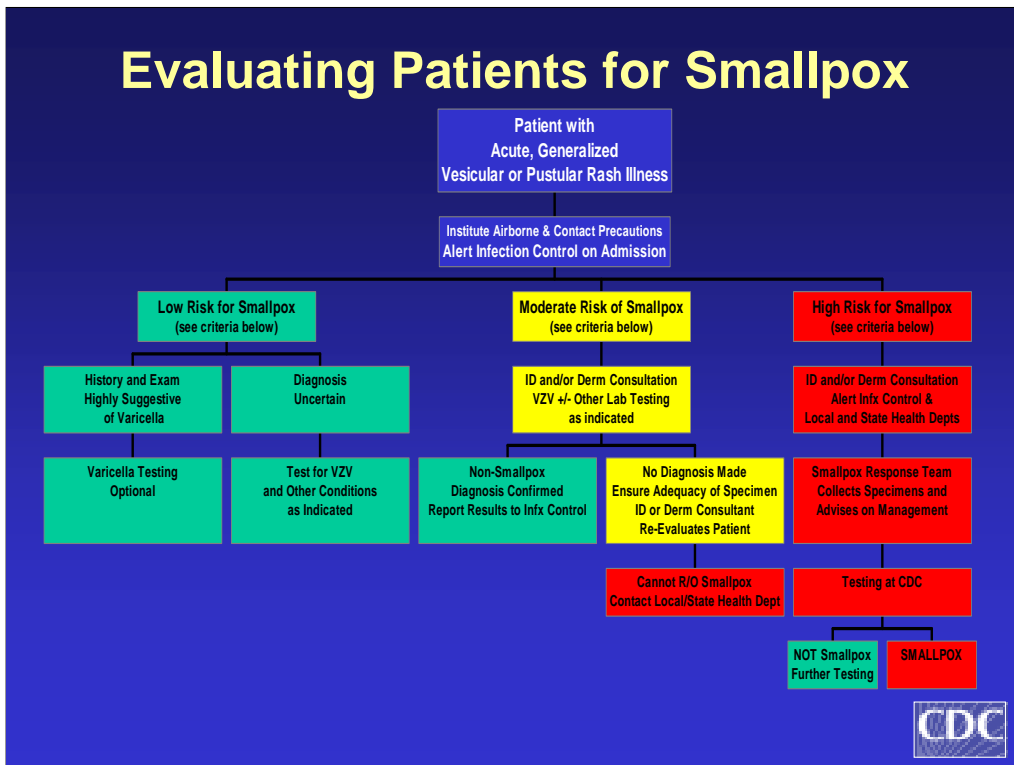
The first lesions appear on the oral mucosa, face, or forearms

The patient appears toxic or moribund (typically a patient is so sick that they are bed ridden)

The rash has a slow evolution (each stage 1-2 days)

There are lesions on the palms and soles

# Evaluating Patients for Smallpox



The major and minor criteria are combined to classify cases of rash illness as seen in this poster. Depending on the major and minor criteria present, the case is classified as high risk (red boxes), moderate risk (yellow boxes) or low risk (green boxes) for smallpox. The poster and protocol suggest evaluation steps and public health actions based on the level of assessed risk.

## **Immediate Action for Patient with Generalized Vesicular or Pustular Rash Illness**

- **Airborne and contact precautions instituted**
- **Infection control team alerted**
- **Assess illness for smallpox risk**



Firstly, if a patient presents at an emergency room or a hospital with a fever and an acute, generalized vesicular or pustular rash illness, airborne and contact precautions should be immediately instituted and the infection control team alerted if the patient is admitted. This is standard practice for a case of varicella or measles. In a doctor's office, they should be isolated in a room with the door closed. Review the clinical presentation of the patient and assess if the illness is high, moderate or low risk for smallpox according to the major and minor criteria.



## High Risk: All 3 Major Criteria

- **Prodrome (1-4 days before rash onset)**
- **Classic smallpox lesions**
- **All lesions in same stage of development (on one part of the body)**



Any patient presenting with all 3 major criteria is classified as high risk for smallpox. Again, these criteria are:

Prodrome , 1-4 days before rash onset.

Classic smallpox lesions (firm and deep seated)

And all lesions in same stage of development (that means all vesicles, all pustules, all scabbing etc) on one part of the body. Examine several different areas of the patient to assess this criterion. For example, on the face, are all lesions of the same type? On the trunk?

# Response: High Risk Case

- **Infectious diseases (and possibly dermatology) consult to confirm high risk status**
- **Alert health department**
- **Digital photos**
- **Alert CDC rash-illness response team**
  - specimen collection
  - management advice
  - laboratory testing at CDC



The clinician's response to a high risk case should be to request an Infectious Diseases and/or dermatology consultation to confirm high risk status.

If high risk status is confirmed, then alert the health department and obtain digital photos if possible. After concurrence, the state health department will alert CDC to arrange for specimen collection and testing at CDC and to discuss management advice until the case is confirmed. State health departments are developing state smallpox response plans that would be initiated once a case of smallpox is laboratory confirmed. If a case is high risk, **DO NOT PERFORM OTHER LAB TESTING TO RULE OUT OTHER DIAGNOSES**

## Moderate Risk

- **Prodrome AND 1 other major criteria**

**OR**

- **Prodrome AND  $\geq$ 4 MINOR smallpox criteria**



Moderate risk for smallpox would be a patient presenting with a vesicular or pustular rash and reporting a prodrome *and* one other major criteria or prodrome and at least 4 minor smallpox criteria

## Response: Moderate Risk Case

- **Infectious diseases (and possibly dermatology) consult**
- **Laboratory testing for varicella and other diseases**
- **Skin biopsy**
- **Digital photos**
- **Re-evaluate risk level at least daily**



The response for a moderate risk case is to request an infectious diseases +/- dermatology consultation to confirm the risk status

Lab testing for varicella and other rash diseases should be conducted as appropriate at the hospital, local or state level health department or through a private lab. Rapid lab tests for VZV are the DFA test where results can be available within an hour or PCR which takes 4-8 hours. A Tzanck smear can often be performed locally which will confirm an alpha herpes virus infection. A skin biopsy may be useful and can also be performed and read by a pathologist rapidly. Obtain digital photos if possible

Re-evaluate risk level at least daily as risk level to determine if risk level has changed

## Low Risk

- No febrile prodrome

OR

- Febrile prodrome AND <4 MINOR smallpox criteria



Low risk for smallpox would be a patient presenting with a vesicular or pustular rash and reporting no febrile prodrome prior to rash eruption or reports a prodrome, and less than four minor smallpox criteria.

# Response: Low Risk Case

- **Patient management and laboratory testing as clinically indicated**



The response for a low-risk patient is management and lab testing as clinically indicated.

# Smallpox Pre-event Surveillance

- **Goal: to recognize the first case of smallpox early without:**
  - **Generating large number of false alarms through conducting lab testing for smallpox cases that do not fit the case definition**
  - **Disrupting the health care and public health systems**
  - **Increasing public anxiety**



In an era of no smallpox cases in the world, the goal of smallpox surveillance is to recognize the first case of smallpox early in the course of illness without

Generating a high number of false alarms. With no cases of smallpox disease, the predictive value of a positive lab test is essentially zero. If we test cases of rash illness that do not fit the case definition for smallpox, we will sooner or later get a false positive lab result. We need to minimize that risk given the extremely serious consequences of such a result

Without disrupting the health care and public health systems and

Without increasing public anxiety

## CDC Rash Illness Response Team Experience with Use of Algorithm

- **23 calls to CDC January 1 – November 30, 2002**
  - **14 states and New York City**
  - **17 adults and 6 children**
  - **Smallpox risk classification:**
    - **High risk = 0. No indications for variola virus testing**
    - **Moderate risk = 4**
    - **Low risk = 19**



Now I will review CDC's rash illness response team's experience using the algorithm

There have been 23 rash illness calls for suspected smallpox cases to CDC since January 2002 that have been evaluated using this diagnostic algorithm

The calls were received from 14 states and New York City

17 cases were adults and 6 were children. There have been no cases classified as high risk and therefore there have been no indications for smallpox virus testing. 4 cases were considered moderate risk and the other 19 cases were low risk.



## CDC Rash Response Team Experience with Use of Algorithm

- **>50% of the cases including 2 deaths have been varicella**
- **12 diagnoses confirmed by lab and/or pathology; 11 clinically diagnosed**
- **Other diagnoses:**
  - **drug reaction**
  - **erythema multiforme**
  - **disseminated herpes zoster**
  - **disseminated HSV2**
  - **contact dermatitis**
  - **other dermatological disorders**



More than half of the reported cases have been varicella infections including 2 cases that resulted in death (including 1 low-risk case).

12 of the diagnoses were confirmed by lab and/or pathology; the other 11 were clinically diagnosed.

Apart from varicella, other diagnoses included drug reaction, erythema multiforme, disseminated herpes zoster, disseminated Herpes simplex virus, and other dermatological conditions

# Experience with Implementation of Rash Algorithm

- Rule in Varicella Zoster Virus (VZV)!!
- Algorithm has limited variola testing by standard approach to evaluation



The CDC experience with implementation of the rash algorithm is that the clinician should rule *in* varicella zoster virus as this is the most common condition that has raised suspicions for smallpox.

Very importantly, this algorithm has limited testing for smallpox virus by providing a standard approach to evaluation of suspected smallpox cases.

# Differential Diagnosis: Lessons from the Past

CONDITION	Variola Major Eng./Wales, 1946-48	Variola Minor Somalia, 1977-79
Chickenpox	41	20
Acne	10	0
Erythema Multiforme	7	
Allergic Dermatitis/Urticaria	7	1
Drug Rash	6	1
Vaccinia	5	1
<b>TOTAL</b>	<b>97</b>	<b>29</b>



Our experience with evaluating cases of suspected smallpox is similar to experience from earlier this century from the United Kingdom and Somalia. The majority of suspected cases in these series were chickenpox; other diagnoses included those described on the poster and those we that have been reported to CDC this year. Note that vaccinia is included in these series. As we commence smallpox vaccination in the United States, we will need to consider vaccine complications in the differential of generalized febrile vesicular pustular rashes and enquire about recent smallpox vaccination or contact with a vaccinee.

## **Generalized Rashes following Smallpox Vaccination: Generalized Vaccinia**

- **Uncommon, rate = 240 per million primary vaccinees from 10 state survey**
- **Occurs 6 to 9 days following vaccination**
- **Lesions usually small and superficial, mature more rapidly than smallpox lesions and more likely to be confused with modified smallpox**
- **Rash distribution is indiscriminate (follows no set pattern)**
- **History of recent vaccinia vaccination**



Smallpox vaccination may result in complications in either the vaccinee and/or close contacts. Two of these complications present as generalized rashes where fever may also be present. Generalized vaccinia is a benign, self limiting condition that, in a 10 state survey conducted in the late 1960s, was reported to occur at a rate of approximately 240 cases per million primary vaccinees. The generalized rash occurs 6 to 9 days after vaccination; the lesions are smaller and more superficial than classic smallpox lesions; they mature more rapidly and they are more likely to be confused with modified smallpox. The distribution of the lesions follows no set pattern and is not typically greater on the face and distal extremities as is characteristic of smallpox. A history of recent smallpox vaccination will help raise suspicion of this complication.

## **Generalized Rashes following Smallpox Vaccination: Eczema Vaccinatum**

- **Rare but life-threatening complication of smallpox vaccination**
- **May occur in vaccinee or in a close contact**
- **5 – 19 days following vaccination**
- **40 per million primary vaccinees (10 state survey)**



Eczema vaccinatum is a rare but more serious and life threatening complication of smallpox vaccination that may occur in the vaccinee or in a close contact 5 to 19 days following vaccination. From the 10 state survey, the rate of eczema vaccinatum was 40 cases per million primary vaccinees.

## **Generalized Rashes following Smallpox Vaccination: Eczema Vaccinatum**

- **10-20 cases in contacts per million primary vaccinees (Neff, JAMA, 2002)**
- **Distribution is not centrifugal; lesions usually commence in abnormal areas of skin and then spread**
- **History of vaccination or contact with a vaccinee**



In addition, 10 to 20 cases occurred in contacts of every million primary vaccinees. The rash commences in abnormal areas of skin and then spreads all over the body but does not follow the centrifugal (or distal) pattern of smallpox. When evaluating cases of febrile vesicular or pustular rash illness, the patient should be asked if they received smallpox vaccine recently or if they have been in close contact with someone who was vaccinated.

## Laboratory and Pathology Support for Rash Illness Evaluation

- Assess availability of laboratory and/or pathology testing locally (hospital and private labs) especially Tzanck smear and skin biopsy
- Contact State health department for other testing:
  - VZV rapid tests/pathology
    - DFA
    - PCR
    - Tzanck smear (alphaherpes virus infection)



For cases that are not high risk for smallpox, laboratory capacity is needed to diagnose conditions that may be confused with smallpox especially moderate risk cases which may cause more concern. Lab and pathology capacities at the local level may include Tzanck smear, skin biopsy and less commonly, DFA for varicella. Capacity to perform rapid varicella zoster virus diagnostics (DFA or PCR) is now available in every state health lab.

## Laboratory and Pathology Support for Rash Illness Evaluation

- **Electron microscopy**
  - Pox virus
  - Herpes virus
  - Other viruses
- **HSV1 and HSV2**
  - Tzanck smear
  - PCR and culture



Other tests that may be useful are electron microscopy (looking for a pox virus, a herpes virus or other viruses) which may be available in academic medical centers, and tests for Herpes simplex virus infections.



## Laboratory and Pathology Support for Rash Illness Evaluation

- **Vaccinia PCR (if vaccinated)**
- **Other tests as clinically indicated:**
  - **Syphilis, enterovirus, rickettsia, staph, strep, molluscum contagiosum, scabies**



Testing for vaccinia should be considered if there is a history of recent smallpox vaccination or close contact with a vaccinee. Other tests should be performed as clinically indicated.

# Rash Illness Evaluation Technical Support

- **State health departments**
  - 24 hour emergency phone number
  - Laboratory and pathology testing – VZV, other
  - Infectious disease, dermatology experts
- **Centers for Disease Control and Prevention**
  - 24 hour on call staff to assist state health departments with rash illness calls
  - Smallpox disease experts available
  - Laboratory and pathology support as requested



Support for local health departments and private physicians who are evaluating a case of rash illness suspected to be smallpox cases is provided by state health departments via their 24 hour emergency phone number; by providing rapid laboratory testing for varicella and other rash illnesses; and by providing infectious disease and dermatology expertise support.

Centers for Disease Control has available a 24 hour rash-illness on-call-staff to assist state health departments. The on call staff has smallpox disease experts available for consultation. CDC can also provide laboratory support as requested.

# Smallpox Algorithm Poster

- Available in 2 sizes:
  - 11 x 17 inch poster
  - 24 x 36 inch wall poster
- Available through state health departments and at [www.cdc.gov/smallpox](http://www.cdc.gov/smallpox)
  - Health care providers link to view and print poster
- Order through CDC on line ordering system at [www.cdc.gov/smallpox/publications](http://www.cdc.gov/smallpox/publications)
  - 2 per order of 11 x 17 poster
  - 1 per order of 24 x 36 poster



The smallpox algorithm poster is available through state health departments and can be viewed on the CDC website

# Smallpox Protocol and Worksheet

- Use for investigation of febrile vesicular or pustular rash illnesses suspected to be smallpox
- Available through state health departments and at [www.cdc.gov/smallpox](http://www.cdc.gov/smallpox)
- Files can be downloaded and printed



CDC had developed a smallpox worksheet that can be used for investigation of febrile vesicular pustular rash illnesses suspected to be smallpox. It is available through state health departments and at [www.cdc.gov/nip/smallpox](http://www.cdc.gov/nip/smallpox)

## For More Information

- **CDC Smallpox website**  
[www.cdc.gov/smallpox](http://www.cdc.gov/smallpox)
- **National Immunization Program website**  
[www.cdc.gov/nip](http://www.cdc.gov/nip)

