

Evaluating Patients With Acute Generalized Vesicular or Pustular Rash Illnesses



- This presentation discusses the evaluation of individuals with generalized vesicular or pustular rash illness for the likelihood of being smallpox.

Need for a Diagnostic Algorithm?

- No naturally acquired smallpox cases since 1977
- Concern about use of smallpox virus as a bioterrorist agent
- Heightened concerns about generalized vesicular or pustular rash illnesses
- Clinicians lack experience with smallpox diagnosis
- Public health control strategy requires early recognition of smallpox case



- There have been no naturally acquired cases of smallpox in the world since 1977; because of this, the likelihood of a rash illness being smallpox is extremely low
- However, there are serious concerns about the use of smallpox virus as a bioterrorist 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 easily be confused with smallpox in a pre-outbreak setting, a diagnostic algorithm would be useful to help guide evaluation.

Need for a Diagnostic Algorithm?

- ~1.0 million cases varicella (U.S.) this year (2003) 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)



- Estimated that there will be approximately 1 million cases of varicella (or chickenpox) in the US in 2003 and many more millions of cases of other rash illnesses. With this number of cases, if 1 out of every 1000 varicella cases were suspected to be smallpox, there would be 1000 false alarms per year. Most public health systems cannot easily deal with thousands of false alarms
- Strategy needed that has *high specificity* to accurately detect the first case of smallpox (should there ever be one).
- *High specificity* strategy will serve to minimize unnecessary laboratory testing for smallpox, that would have the potential risk of producing a false positive lab test.

Assumptions/Limitations

- Will miss the first case of smallpox until day 4-5 (by excluding maculo-papular rashes)
- Will miss an atypical case of smallpox (hemorrhagic, flat/velvety, or highly modified) if it is the first case



- Using this approach, must recognize and accept the fact that the first case of smallpox will not be recognized until day 4-5 of rash and therefore, not diagnosed as early as subsequent cases may be
- If the first case presents with one of the more rare, atypical clinical courses (hemorrhagic, flat/velvety, or highly modified case), it is likely to be missed altogether.
- However, the likelihood that the early case(s) will present with the typical presentation of smallpox that is used in the algorithm, is much greater than the likelihood that the early case(s) would be atypical in presentation.
- During eradication period, typical smallpox cases comprised 85% or more of the cases in most outbreaks

Justification

- System cannot handle thousands of false alarms
- Several days of delay in diagnosis will not have major impact:
 - Supportive treatment for smallpox
 - Appropriate contact/respiratory precautions will limit spread in hospital



- It is important to have a routine way of evaluating rash illness cases and ruling out smallpox
- The public health system cannot handle the thousands of false alarms that would be generated by the numerous rash illnesses that exist.
- We need a method to focus resources on the most suspicious cases.
- In the context of no smallpox disease currently anywhere in the world, several days of delay (for cases that do not meet the clinical case definition) while laboratory tests are done and other illnesses are ruled out will probably not have a major impact, as long as appropriate isolation precautions are taken.

Smallpox Disease

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



- Review several important characteristics of smallpox:
- 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.

Smallpox Disease

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



- The rash technically begins in the mouth (enanthem), but usually the first rash noticed is the one that appears on the body (exanthem) about 24 hours following the lesions in the mouth.
- Lesions start as macules then progress to papules then to vesicles and finally to pustules. The pustules crust and form scabs which separate and may leave deep scars.
- Each stage of the lesions lasts about 1-2 days before progressing to the next stage.

Smallpox Surveillance Clinical Case Definition

An illness with acute onset of fever \geq 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.



- The Smallpox Surveillance Clinical Case Definition is an illness with acute onset of fever \geq 101° F (38.3° F) followed by a rash characterized by firm, deep-seated vesicles or pustules in the same stage of development without other apparent cause.

Clinical Determination of Smallpox Risk: Major Criteria

- Prodrome (1-4 days before rash onset):
 - Fever $\geq 101^{\circ}\text{F}$ (38.3°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).



•Clinical features of smallpox were used to create major and minor criteria for rash risk classification in a pre-outbreak setting.

•We classify the patient for risk or likelihood of being smallpox according to combinations of these criteria. It is necessary to be aware of these clinical features of smallpox when evaluating other rash illnesses that may look like smallpox.

•The 3 major criteria for smallpox correspond to the 3 essential components of the clinical case definition:

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

•includes fever of $\geq 101\text{F}$ (38.3C) 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. They have a “shotty” feel, like rolling a pea around under the skin

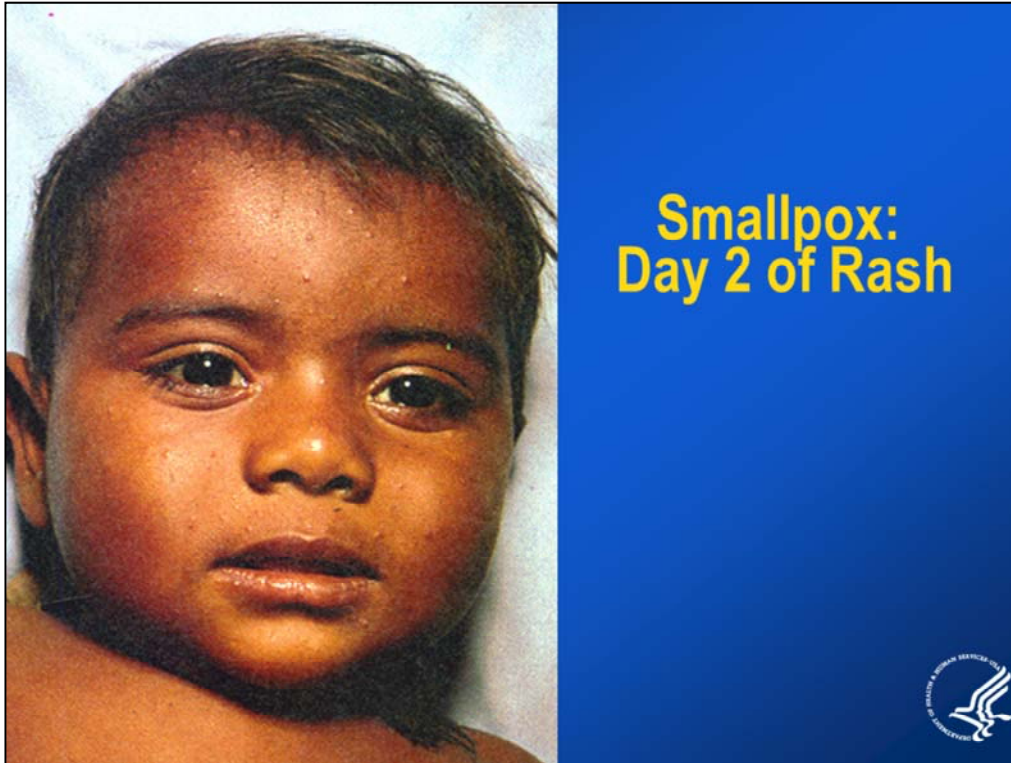
3. All the lesions are in same stage of development (on any one part of the body). This means that all lesions on the arm or all lesions on the trunk would be all vesicles, all pustular, or all crusting—not a mixture of different skin lesions

Clinical Determination of Smallpox Risk: Minor Criteria

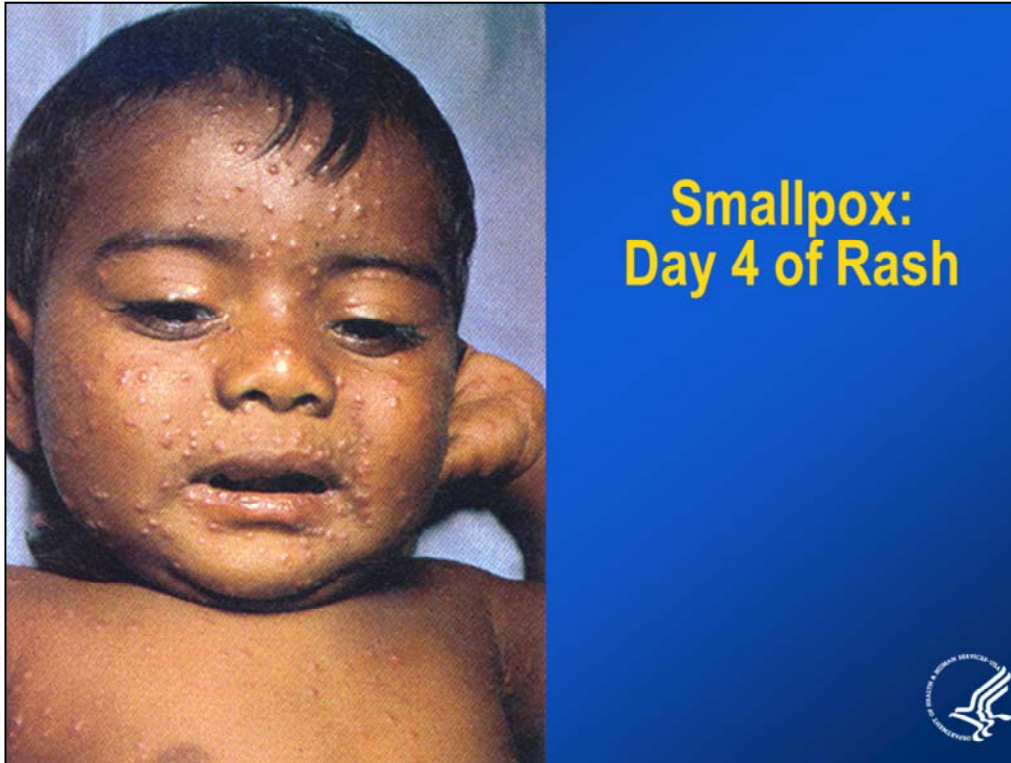
- Centrifugal (distal) distribution
- First lesions: oral mucosa, face, or forearms
- Patient toxic or moribund
- Slow evolution (each stage 1-2 days)
- Lesions on palms and soles



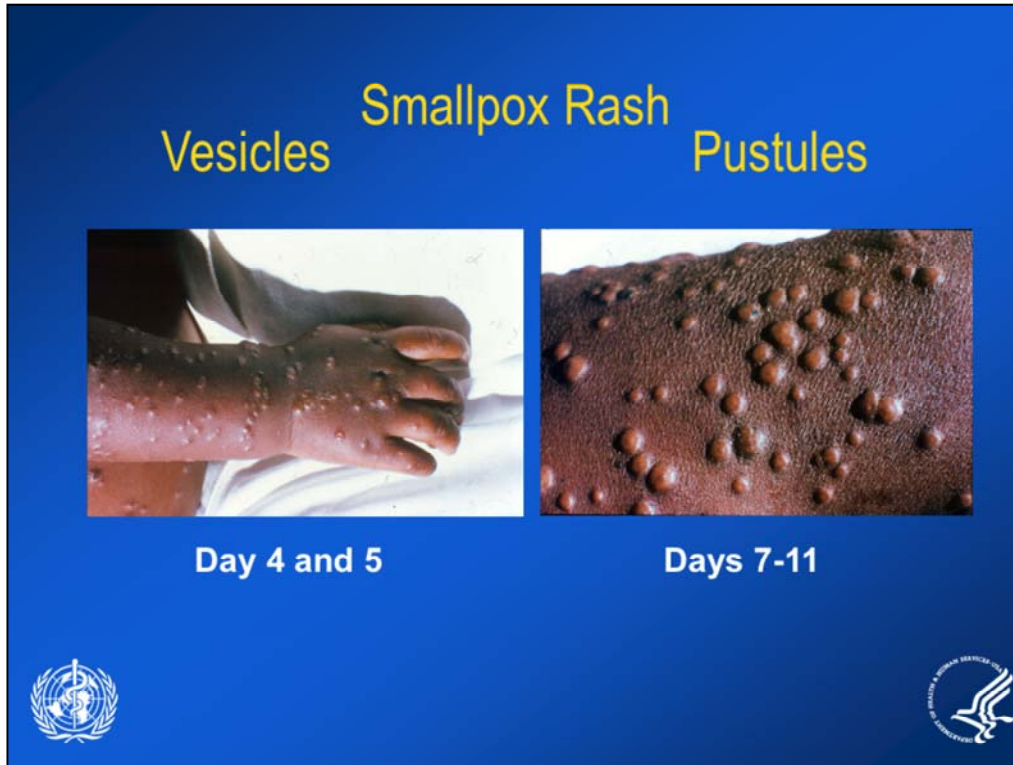
- Five signs make up the smallpox minor criteria:
 1. The lesions have a centrifugal (distal) distribution
 2. The first lesions appear on the oral mucosa, face, or forearms
 3. The patient appears toxic or moribund (typically a patient is so sick that they are bed ridden)
 4. The rash has a slow evolution (each stage 1-2 days)
 5. There are lesions on the palms and soles
- Taken together, these major and minor criteria are useful for differentiating smallpox from other rash illnesses.



- Let's review photographs of a typical case of smallpox and focus on the progression of the rash.
- Note that on the day 2, the rash is mild, is macular or papular and could easily be overlooked.
- If this were the first presenting case, smallpox would probably not be considered at this stage.



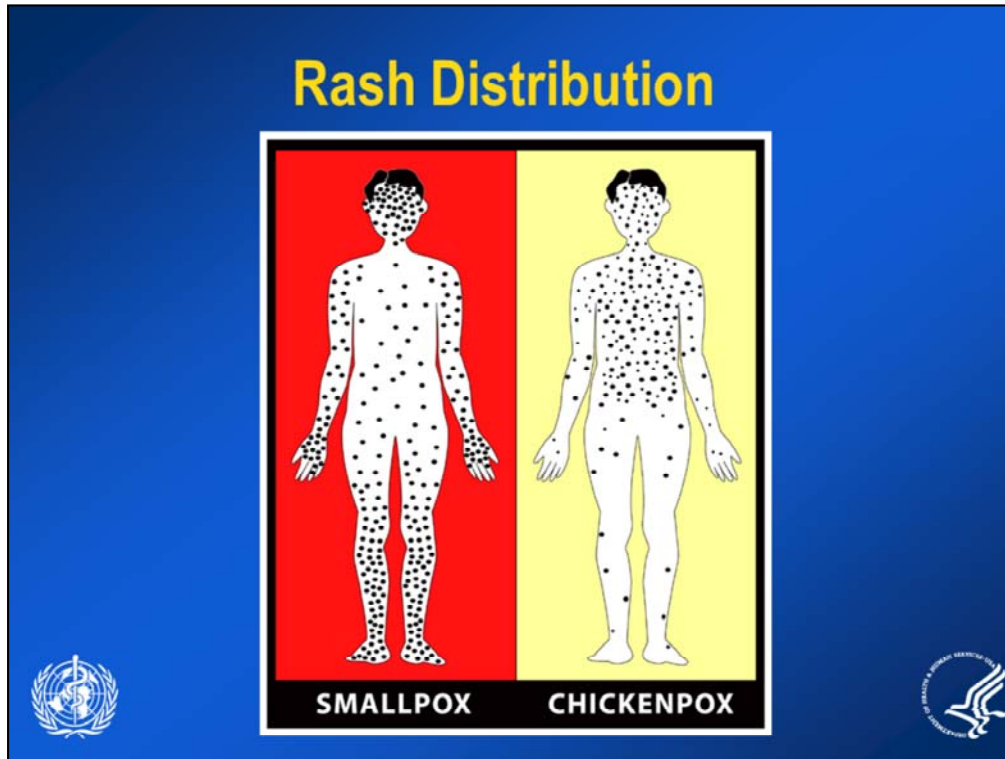
- On day 4 the rash is more significant and has fully progressed to the papule stage with the beginnings of progression to vesicles.
- If there had been a febrile prodrome, we may be considering smallpox in the differential at this point.



- On day 4 and 5, the rash is now vesicular.
- 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 both photos, the lesions are all in the same stage of development



- 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 firm and pea-like and could be rolled around under the skin.



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

Varicella is the most likely illness
to be confused with smallpox.



- By far the most common rash illness likely to be confused with smallpox is varicella (chickenpox).

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.



- Because of the potential for confusion between smallpox and varicella, it is important to recognize the differentiating features of varicella.
- With varicella, there is generally no, or just a mild, prodrome period. 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 which leads to the next important differentiating feature.

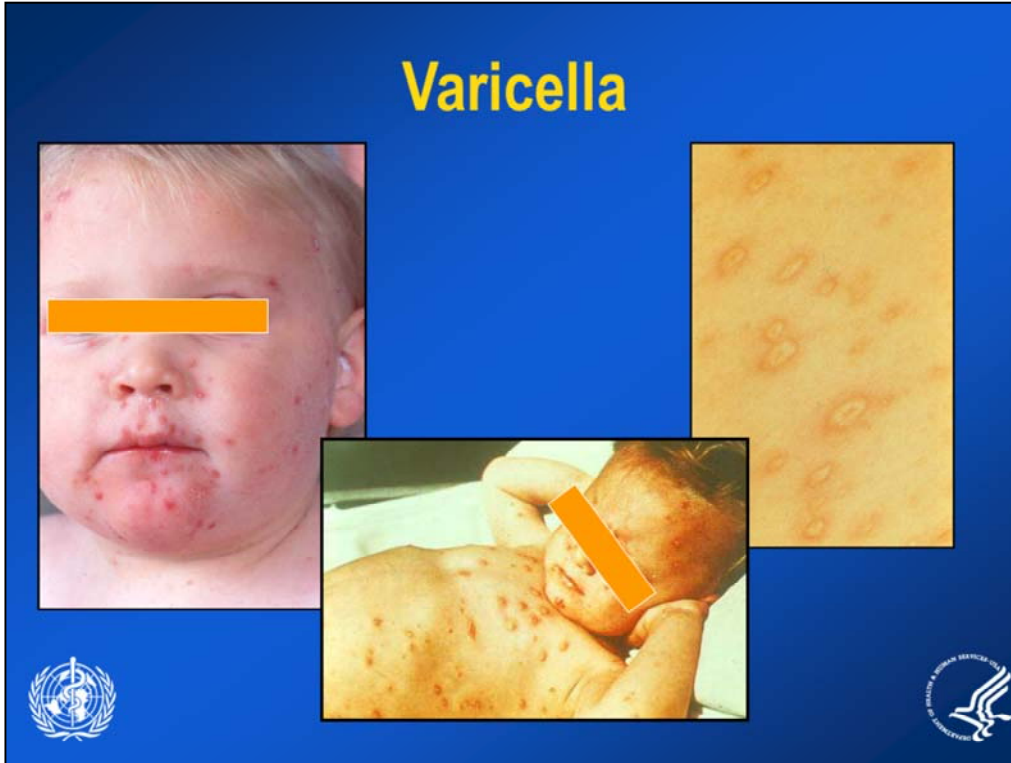
Differentiating Features: Varicella

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



- One of the most important differentiating features of varicella is that lesions are typically in *different* stages of development (not the same stage like in smallpox).
- 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 rarely appear on the palms of the hands or soles of the feet.
- Most patients with chickenpox are rarely toxic or moribund. However, adults can become quite ill and 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



- 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 both 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 lesions that are secondarily infected with bacteria may confuse the diagnosis as this may increase the size and “deepness” of the lesions.
- In the smallpox eradication era, varicella cases that had secondarily infected lesions, especially in adults, were the most difficult cases to distinguish from smallpox.



- To summarize, the most important differentiating features between smallpox and varicella are the appearance, evolution, and distribution of the rash.
- Although there may be some overlap in the appearance of the lesions, particularly early after rash onset, classic smallpox looks quite different than varicella.
- In this and the next few slides, we will examine additional photographs to highlight differences between smallpox and varicella.

- Here is a person with smallpox.
- The lesions are very well circumscribed, and similar in size.
- The lesions are larger than varicella lesions.
- Also, all the lesions visible in this picture are in the same stage of evolution (uniformity).



- Note in this slide how patients with smallpox have lesions on the palms of their hands. They are also found on the soles of the feet.
- Patients with chickenpox rarely have lesions in these areas.

Distribution of Rash Chickenpox



- Picture of a child with varicella.
- Notice the concentration of lesions is greatest on the abdomen (with less unaffected skin between lesions), and become a little less dense on the arms and legs.

Distribution of Rash Smallpox



- Picture of a child with smallpox.
- The lesions are most concentrated on the arms, legs, and face, with fewer lesions on the abdomen and chest

Distribution of Rash Smallpox



- There are also fewer lesions on the back when compared to the ones on the extremities.

Differential Diagnosis

Condition	Clinical Clues
Varicella (primary infection with varicella-zoster virus)	<ul style="list-style-type: none"> •Most common in children <10 years •Children usually do not have a viral prodrome
Disseminated herpes zoster	<ul style="list-style-type: none"> •Prior history of chickenpox •Immunocompromised hosts
Impetigo (<i>Streptococcus pyogenes</i> , <i>Staphylococcus aureus</i>)	<ul style="list-style-type: none"> •Honey-colored crusted plaques with bullae •May begin as vesicles •Regional not disseminated
Drug eruptions and contact dermatitis	<ul style="list-style-type: none"> •Exposure to medications •Contact with possible allergens
Erythema multiforme (incl. Stevens Johnson Sd)	<ul style="list-style-type: none"> •Major form involves mucous membranes and conjunctivae



- Next several slides discuss other conditions that might be confused with smallpox.
- There are many other causes of generalized rash illnesses, from common etiologies like insect bites, scabies, and contact dermatitis to less common conditions such as disseminated herpes simplex, or erythema multiforme.
- In addition, there are exceedingly rare causes, such as rickettsial pox and monkey pox.
- This chart also discusses clinical and or patient history clues of the conditions that can help distinguish them from smallpox
- [discuss clinical clues for each condition]

Differential Diagnosis

Condition	Clinical Clues
Enteroviruses incl. Hand, Foot and Mouth disease	<ul style="list-style-type: none">•Summer and fall•Fever and mild pharyngitis at same time•Small vesicles on hands, feet and mouth or disseminated
Disseminated herpes simplex	<ul style="list-style-type: none">•Lesions indistinguishable from varicella•Immunocompromised host
Scabies ; insect bites (incl. fleas)	<ul style="list-style-type: none">•Pruritis•In scabies, look for burrows•Vesicles and nodules also occur•Flea bites are pruritic•Patient usually unaware of flea exposure



- Enteroviruses diseases are more prominent in the summer and fall, present with a fever and mild pharyngitis at the same time, vesicles are generally small
- Disseminated herpes simplex has lesions indistinguishable from varicella on visual examination, but generally only occur in neonates or in individuals with some underlying immune compromised state
- Insect bites are generally pruritic and scabies shows the typical burrows

Differential Diagnosis

Condition	Clinical Clues
Molluscum contagiosum	<ul style="list-style-type: none"> •Healthy afebrile children •HIV+ individuals
Bullous Pemphigoid	<ul style="list-style-type: none"> •Bullous lesions •Positive Nikolski sign
Secondary syphilis	<ul style="list-style-type: none"> •Rash can mimic many diseases •Rash may involve palms and soles •95% maculo-papular, may be pustular •Sexually active persons
Vaccinia	<ul style="list-style-type: none"> • Recent vaccination or contact with a vaccinee



- Molluscum contagiosum can be seen in healthy, afebrile children but is more likely to be disseminated in adults with HIV
- Bullous pemphigoid will have a positive Nikolski sign and consistent path on biopsy of lesions
- Secondary syphilis may involve the palms and soles but most lesions are maculo-papular
- Now that vaccinia vaccination (smallpox vaccine) is being done more frequently than in the recent past because of bioterrorism preparedness, vesicular rashes may present as a result. These may be seen in persons recently vaccinated or in individuals with contact transmission of vaccinia from a recent vaccinee. This differential diagnosis should also be considered and evaluated when clinically appropriate.

Bullous Pemphigoid

- Bullous lesions
- Positive Nikolski sign.

Secondary syphilis

- Rash can mimic many diseases
- Rash may involve palms and soles

- 95% maculo-papular, may be pustular
- Sexually active persons

Differential Diagnosis Herpes Zoster



- This is a picture of Herpes zoster, or shingles
- This illness usually presents with a localized painful rash in one or two dermatomes on one side of the body.
- In immunocompromised persons, however, it can become disseminated and can present with a generalized vesicular rash. People with this condition have a history of previous varicella infection.

Differential Diagnosis Drug Eruptions

- History of medications:
 - Prescription
 - Over the Counter
 - Prior Reactions



- Drug eruptions can also present with a variety of generalized rashes, and may have concurrent symptoms, such as fever.
- For this reason, it is important to take a detailed history of all medications the patient is currently taking (or recently took) including prescription and over the counter medications.

Differential Diagnosis Drug Reaction



- Drug reactions can cause rashes which range from macular-papular, to the vesicular eruption seen here.

Differential Diagnosis Hand Foot and Mouth Disease



- Hand foot and mouth disease is an enteroviral disease that most commonly occurs in the summer or fall.
- Ulcerative lesions can be seen in the mouth, and tender vesicular or pustular lesions on the hands and feet, including the palms and soles.
- This distribution sometimes raises concerns about smallpox. However, the individual lesions are easy to distinguish from the hard pustules of smallpox and the lesions resolve in about a week.

Differential Diagnosis Molluscum Contagiosum



- Molluscum contagiosum is a common viral infection of the skin and mucous membranes caused by a poxvirus.
- Lesions can become disseminated. When the lesions are disseminated, the rash could be confused with smallpox; particularly in an HIV-infected patient with concurrent illnesses.
- Molluscum contagiosum can also occurs in healthy children who are perfectly well and afebrile but lesions are usually fewer and not disseminated.

Differential Diagnosis Secondary Syphilis



- Secondary syphilis can produce almost any type of generalized rash, including pustules.
- The rash may appear anywhere on the body, and may involve the palms and soles.
- It should be considered in a sexually active person with a generalized rash and ruled out with appropriate testing.

Differential Diagnosis HSV2



Disseminated HSV2 lesions on face/scalp



Disseminated HSV2 lesions on palms



- This individual had a rash from a disseminated Herpes simplex virus 2 infection.
- The lesions on the face and forehead that were superficial and scabbed over.
- There are also lesions that look like blisters that were present on the palms.
- The palm lesions were more deep-seated because of the thicker layers of skin in that area.

Clinical Determination of the Risk of Smallpox Variations on Smallpox

Hemorrhagic smallpox: Misdiagnosed as meningococemia?



Flat-type smallpox: Difficult diagnosis



- Although we have focused on differentiating smallpox from conditions that can present with generalized vesicular or pustular rashes, a small percentage of smallpox cases present atypically, with hemorrhagic or flat type lesions
- These variants of smallpox are called hemorrhagic and flat-type respectively.
- Both variants are highly infectious and have a high mortality rate
- Hemorrhagic smallpox can be mistaken for meningococemia.

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.



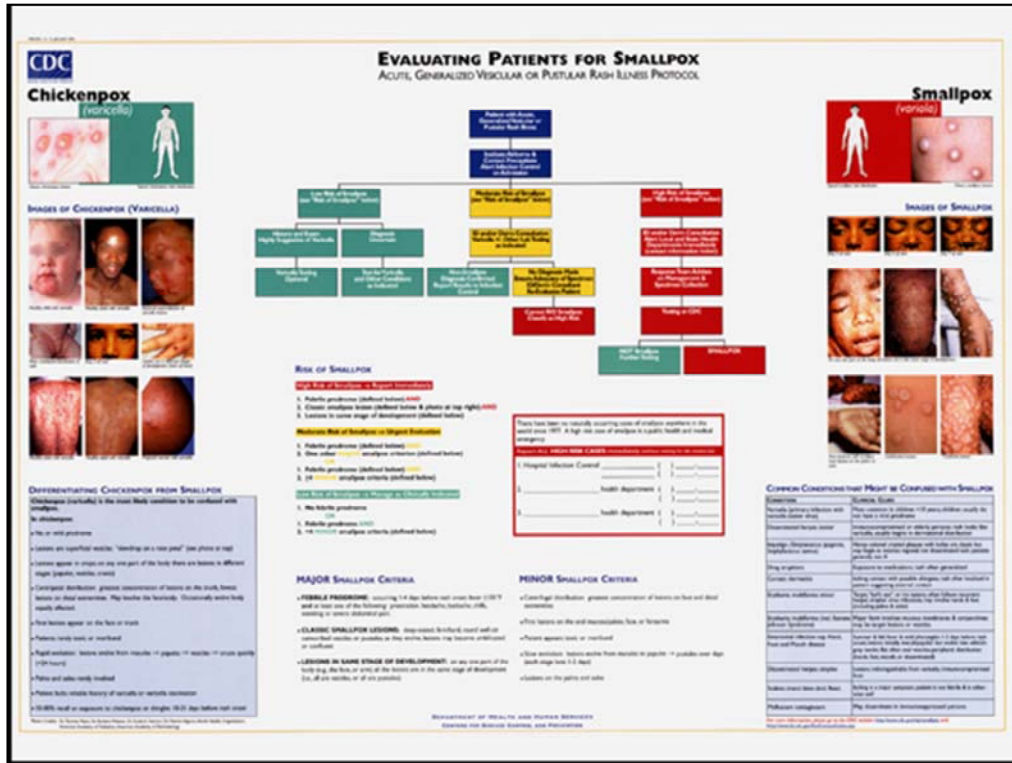
- The goal of the rash illness algorithm is to provide a systematic approach to evaluation of cases of febrile vesicular or pustular rash illness.
- The algorithm uses the main clinical features of smallpox to establish major and minor criteria and uses these criteria to classify cases of vesicular/pustular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

Investigation Tools

- Available at www.cdc.gov/smallpox:
 - Rash algorithm poster:
 - Health care providers link to view and print poster.
 - Worksheet (case investigation)



- The following case investigation tools that will be discussed are available to assist in evaluating a suspected smallpox case:
- Available on the CDC smallpox website.



- The rash algorithm poster is shown here.
- 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 the right corner) and chickenpox (in the left corner); lists features that differentiate chickenpox from smallpox, and common conditions that might be confused with smallpox.
- The poster presents a method for classifying cases according to their risk for being smallpox using major and minor criteria for the disease.

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.



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

02/25/2002 10:30am

WORKSHEET: EVALUATING PATIENTS FOR SMALLPOX

Identification Number _____
 Person Completing Form _____
 Date of Contact with Case _____
 Today's Date (m/d/y) _____

PATIENT INFORMATION

Name: _____
LAST FIRST MIDDLE INITIAL

Date of Birth: ____/____/____ Age: ____ Sex: Male Female

Telephone: _____
Home _____ Other _____

Address: _____
CITY STATE ZIP

Race: White Black Asian Other Ethnicity: Hispanic Non-Hispanic Country of Birth: _____

Where is the patient now? Home Doctor's Office
 Emergency Room (if checked, continue below)
 Hospital (if checked, continue below)
 Other (specify) _____

Hospital Name _____
 City/State _____
 Admission Date ____/____/____ Discharge Date ____/____/____
 Hospital Telephone Number (____) _____

PROVIDER INFORMATION

Name: _____

Patient Population Specialty: _____
 Adult Peds Both

Telephone: _____
Type (____) _____

E-mail Address: _____

Name: _____

Patient Population Specialty: _____
 Adult Peds Both

Telephone: _____
Type (____) _____

E-mail Address: _____

CLINICAL INFORMATION

PRODROME / SYMPTOMS 1-4 DAYS BEFORE RASH ONSET

Did the patient have a fever and other illness 1-4 days before rash onset? Yes No Unknown

Date of prodrome onset ____/____/200____

If Yes, on what date did the patient first have a fever? ____/____/____

What was the highest temperature? _____°F or _____°C

On what date: ____/____/____

Check all features of the prodrome that apply:

<input type="checkbox"/> No/Mild prodrome (<1 day)	<input type="checkbox"/> Abdominal pain
<input type="checkbox"/> Headache	<input type="checkbox"/> Sore throat*
<input type="checkbox"/> Backache	<input type="checkbox"/> Other (specify) _____

What kind of lesions does the patient have now? (check all that apply)

<input type="checkbox"/> Macules (flat, reddish spots)	<input type="checkbox"/> Pustules (blisters filled with pus)
<input type="checkbox"/> Papules (solid bumps)	<input type="checkbox"/> Crusts
<input type="checkbox"/> Vesicles (fluid-filled blisters)	<input type="checkbox"/> Other _____

If more than one kind of lesion, which kind of lesion is now the most common? _____

Are the lesions now:

<input type="checkbox"/> Superficial (on top of the skin)
<input type="checkbox"/> Deep (feet embedded deeply in the skin)
<input type="checkbox"/> Neither (describe) _____

How many lesions are present? (in total) _____

If no precise count is available, please estimate:
 <20

- The worksheet is shown here.
- This sheet is used to help gather the relevant information for the case that is being evaluated.

Smallpox: Major Criteria

- Prodrome (1-4 days before rash onset):
 - Fever $\geq 101^{\circ}\text{F}$ (38.3°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).



• From the history and physical examination of the patient, the evaluator should determine how many major and minor criteria are present

• Review of the major criteria:

Prodrome that includes fever $\geq 101^{\circ}\text{F}$ (38.3°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.

3. All the lesions are in same stage of development (on one part of the body).

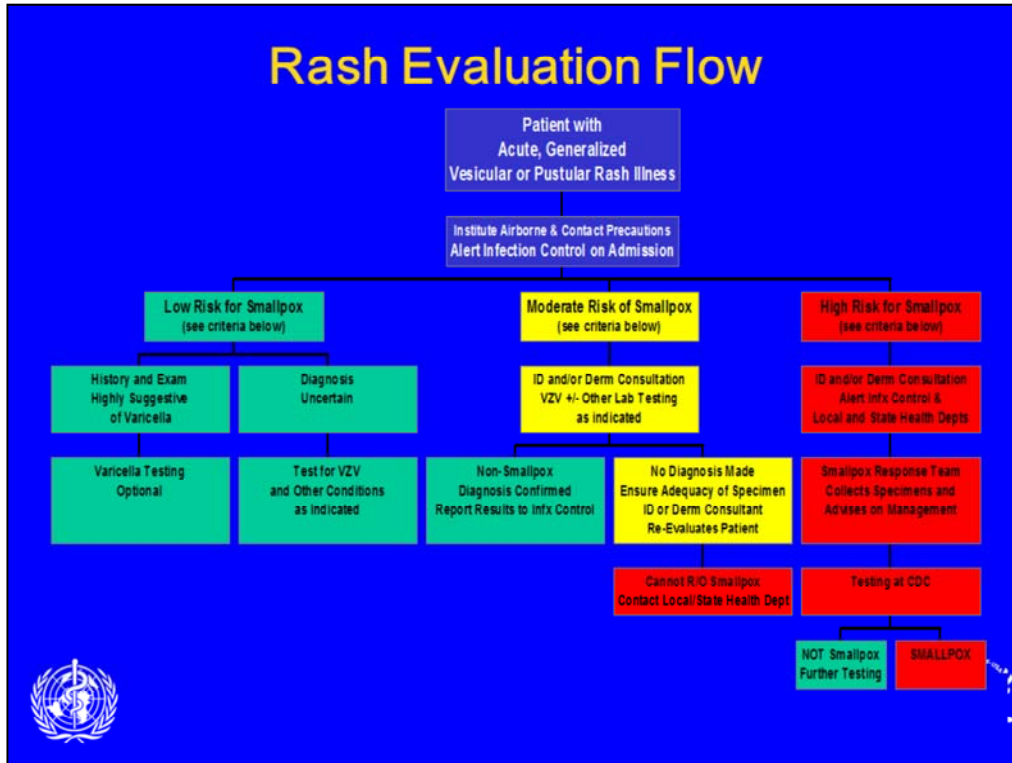
Smallpox: Minor Criteria

- 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.



•The minor criteria are:

- 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



- These major and minor criteria are combined to classify cases of rash illness into low, medium, and high risk suspicion for smallpox.
- These classifications are on the poster that was shown earlier and is available on the CDC website <http://www.bt.cdc.gov/agent/smallpox/diagnosis/index.asp>.
- The classification that the patient falls in also guides the additional evaluation and diagnostic steps that should be taken.

Immediate Action for Patient with Generalized Vesicular or Pustular Rash Illness

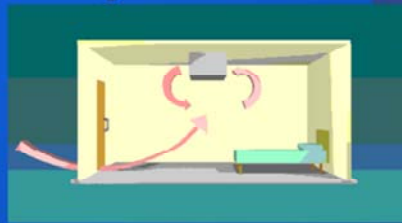
- Airborne and contact precautions instituted
- Infection control team alerted
- Assess illness for smallpox risk



- All patients that present to a hospital with a fever and an acute, generalized vesicular or pustular rash illness should be placed under airborne and contact precautions. This is standard practice for a case of varicella or measles.
- The hospital infection control team should be alerted if the patient is admitted.
- In a doctor's office, these patients 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.

Safety Precautions

- Respiratory and contact precautions
- Isolation Rooms
- Gloves
- Hand Washing

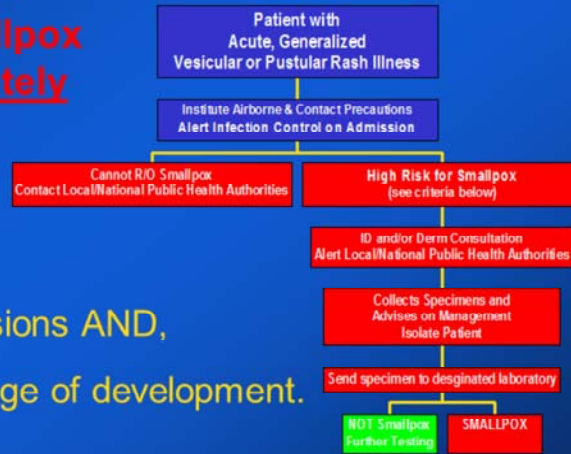


- Whether or not you think the person you are evaluating has smallpox, it is important to institute appropriate precautions to prevent spread of an infectious agent.
- Always wear gloves when touching a patient with a rash illness, and institute respiratory precautions if there is any concern about an infectious agent that can have airborne spread, as occurs with both varicella and smallpox.

Clinical Determination of the Risk of Smallpox

High Risk of Smallpox
→ report immediately

- Prodrome AND,
- Classic smallpox lesions AND,
- Lesions in same stage of development.



- Any patient presenting with all 3 major criteria is classified as high risk for smallpox and should be reported to public health officials and hospital officials immediately.
- Immediate action should be taken to make sure that contact precautions and respiratory isolation are in place.

Response: High Risk Case

- Infectious diseases (and possibly dermatology) consult to confirm high risk status
- Obtain digital photos
- Alert public health officials that high risk status confirmed:
 - specimen collection
 - management advice
 - laboratory testing at facility with appropriate testing capabilities

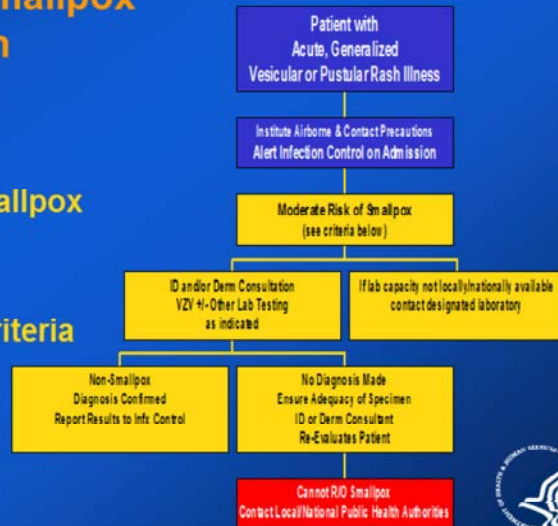


- The clinician’s response to a high risk case should be to notify the appropriate authorities and also request an Infectious Diseases and/or dermatology consultation to confirm the high risk status.
- If high risk status is confirmed by a specialist, then inform public health officials and obtain digital photos, if possible.
- Health officials can assist with confirming high-risk status and arranging for specimen collection and testing at the appropriate laboratory.
- Health officials can also assist with management advice until the case is confirmed.
- If a case is high risk, **DO NOT PERFORM OTHER LAB TESTING TO RULE OUT OTHER DIAGNOSES** until the diagnosis of smallpox is ruled-out.

Clinical Determination of the Risk of Smallpox

Moderate Risk of Smallpox → urgent evaluation

- Febrile prodrome
AND
- One other MAJOR smallpox criterion
OR
- ≥4 MINOR smallpox criteria



•For a person to be considered a moderate risk for smallpox, they must have had a febrile prodrome and either one other major criterion or febrile prodrome and at least 4 minor criteria.

•These patients should also be isolated and be evaluated urgently to determine the cause of the illness.

•Persons classified as high or moderate risk should be seen in consultation with a specialist in infectious diseases and/or dermatology whenever possible to re-affirm the patient meets the classification for the risk category assigned to them. These specialist generally have extensive experience in evaluating rashes associated with infectious disease and/or other causes.

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



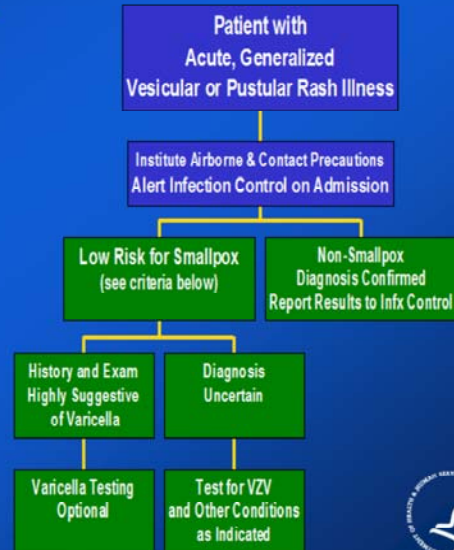
- The response for a moderate risk case includes

- Obtaining an infectious diseases and possibly 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 that can provide results 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 to determine if risk level has changed (i.e. if person has moved into high or low risk category as rash illness progresses and testing results for other etiologies becomes available)
 - Lab testing for smallpox would be indicated if the person's risk level was elevated to high during their daily re-evaluation, or if all testing was negative for different etiologies and a clinical diagnosis of smallpox was strongly considered on the basis of history and the clinical picture being consistent with an atypical presentation for smallpox
- Local public health authorities should be made aware that a moderate risk rash patient is being evaluated for other etiologies of the rash illness.

Clinical Determination of the Risk of Smallpox

Low Risk of Smallpox → manage as clinically indicated

- No/mild febrile prodrome
- OR
- Febrile prodrome
- AND
- < 4 MINOR smallpox criteria (no major criteria)



- Any person who did not have a febrile prodrome is considered low risk for smallpox, as are persons who had a febrile prodrome and less than 4 minor criteria.
- These patients should be managed as clinically indicated and fully evaluated for other causes of the rash illness.

Response: Low Risk Case

- Patient management and laboratory testing as clinically indicated



•The response for a low-risk patient is appropriate infection control and treatment management with lab testing for diagnosis of other, non-smallpox etiologies as clinically indicated.

Smallpox Pre-event Surveillance

- **Goal → to recognize the first case of smallpox early without:**
 - **Generating high 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 rash illnesses that do not fit the case definition for smallpox are tested for this disease, sooner or later a false positive lab result would occur.

• Because of the extremely serious consequences of a false-positive result (chain reaction), we need to minimize that risk.

• False alarms would:

- Disrupt the health care and public health systems and
- Increase public anxiety

Smallpox 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
Syphilis	3	4
Drug Rash	6	1
Vaccinia	5	1
Other diagnoses	18	3
TOTAL	97	29



- This slide shows the many other conditions that were initially diagnosed as smallpox during past outbreaks of variola major and minor
- Chickenpox (varicella) was the most common disease confused with smallpox

CDC Rash Illness Response Team Experience with Use of Algorithm

- 25 calls to CDC January 1 – December, 2002
- Smallpox risk classification:
 - High risk = 0
 - Moderate risk = 4
 - Low risk = 21



- In the US, the CDC rash illness response team has been utilizing this febrile rash illness algorithm to assess patients reported to CDC since January 1, 2002
- Between January and December, 2002, evaluated 25 calls
 - None met criteria as high risk cases
 - 4 were classified as moderate risk
 - The rest were determined to be low risk for smallpox

CDC Rash Response Team Experience with Use of Algorithm

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



- Over 50% of the cases were confirmed as varicella
- 14 of the 25 cases had the diagnosis confirmed by laboratory of pathology testing; 11 were diagnosed clinically
- Laboratory confirmed diagnosis or clinical designations for the remaining, non-varicella cases are shown here.

Experience with Implementation of Rash Algorithm

- Rule in VZV!!
- Algorithm has limited variola testing by standard approach to evaluation



- The CDC experience with implementation of the rash algorithm shows that many times the clinician should work to rule *in* varicella zoster virus
- Of our moderate risk rash illness calls (4 calls), 75% have been chickenpox
- Of our low risk calls (21), nearly 70% of have also turned out to be chickenpox
- Very importantly, this algorithm has resulted in limited testing for variola virus by providing a standard approach to evaluation