

**WEBCAST TRANSCRIPT****Transcript of "Rash Illness Evaluation"**

**Presented by Dr. Jane Seward, 6 December 2002, on the satellite broadcast of "CDC Bioterrorism Update: Smallpox Preparedness"**

(Associated graphics can be found at

[www.bt.cdc.gov/agent/smallpox/training/webcast/dec2002/files/rash-illness-eval.ppt](http://www.bt.cdc.gov/agent/smallpox/training/webcast/dec2002/files/rash-illness-eval.ppt) and [www.bt.cdc.gov/agent/smallpox/training/webcast/dec2002/files/rash-illness-eval.pdf](http://www.bt.cdc.gov/agent/smallpox/training/webcast/dec2002/files/rash-illness-eval.pdf).)

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(Slides 1 and 2 are title and objectives, respectively)

**SEWARD:**

Today I am going to discuss evaluation of cases of febrile vesicular or pustular rash illness. This is important because if a case of smallpox were ever to occur again in the United States, on the one hand, we would want to diagnose the case as early as possible so that appropriate public health actions could be implemented. On the other hand, we want to minimize lab testing for smallpox virus for suspected smallpox cases unless they meet the clinical case definition because of the very real danger of obtaining a false positive lab test. The predictive value of a positive lab test for smallpox is extremely low when the prevalence of smallpox is zero.

**Slide 3**

Is there a need for a diagnostic algorithm? 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. Recommencing smallpox vaccination in the United States is likely to heighten concerns about febrile vesicular and pustular rash illnesses.

**Slide 4**

In the event of a bio-terrorist release of smallpox virus, effective public health control strategy requires early recognition of a smallpox case. Most clinicians have never seen a case of smallpox and therefore lack experience with making a smallpox diagnosis. Because other rash illnesses may be confused with smallpox, a diagnostic algorithm or a standard approach to evaluating rash illness cases would be useful.

**Slide 5**

We estimate that there will be approximately 1 million cases of varicella (or chickenpox) in the U.S. 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. This strategy will serve to minimize laboratory testing for smallpox, which will reduce the risk of producing a false positive lab test.

**Slide 6**

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

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### **Slide 7**

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.

### **Slide 8**

Although the rash starts as an enanthem in the mouth, frequently the first rash noticed is in the exanthem. The 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. 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. We will see examples of these types of lesions in the following photographs of smallpox cases.

### **Slide 9**

The next few photographs of a smallpox case show the progression of the 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.

### **Slide 10**

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

### **Slide 11**

On day 4 and 5, the rash is now vesicular. At this stage, there is an accumulation of fluid in the vesicles. During 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.

### **Slide 12**

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

### **Slide 13**

The typical pattern of smallpox rash distribution is demonstrated in this drawing. 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.

### **Slide 14**

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

### **Slide 15**

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 "a 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.

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### **Slide 16**

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. The lesions evolve more rapidly than smallpox lesions; typically they progress from macule to vesicle and even crust within 24 hours, and unlike smallpox, there is a centripetal (central) distribution of the rash. Lesions appear rarely on the palms of the hands or soles of the feet and the patient with varicella 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 and there may be lesions on the palms and soles.

### **Slide 17**

These photographs show varicella rashes. The lesions are superficial and are in different stages of development. The upper right photo shows the classic varicella, "dew drop on a rose petal" type lesions. The child in the lower photograph has pustular and vesicular lesions.

### **Slide 18**

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.

### **Slide 19**

Varicella infected lesions may confuse the diagnosis. During the smallpox eradication era, varicella cases among adults, especially those with infected lesions were the most difficult to differentiate from smallpox cases.

### **Slide 20**

Apart from varicella, other conditions to consider in the differential diagnosis in a patient with fever and a vesicular or pustular rash are: disseminated herpes zoster; impetigo; drug eruptions; contact dermatitis; and erythema multiforme.

### **Slide 21**

Other rash illnesses included on the rash algorithm poster that should be considered in the differential diagnosis include: enteroviral infections (especially, hand, foot and mouth disease); disseminated herpes simplex virus infections; scabies and insect bites; and molluscum contagiosum (in immunocompromised patients). The rash algorithm poster that you will see on the screen shortly lists these diagnoses as well as clinical clues for every condition.

### **Slide 22**

Other rare dermatological conditions, acne, secondary syphilis, rickettsial diseases and diseases like monkeypox that are unlikely to be seen in the United States may also be rare causes of confusion. If we start a smallpox vaccination program in the United States, then generalized vaccine related rashes may raise suspicions of smallpox.

### **Slide 23**

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).

### **Slide 24**

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

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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.

### **Slide 25**

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.

### **Slide 26**

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.

### **Slide 27**

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.

### **Slide 28**

The Smallpox Surveillance Clinical Case Definition is an illness with acute onset of fever > 101 degrees Fahrenheit followed by a rash characterized by firm, deep-seated vesicles or pustules in the same stage of development without other apparent cause.

### **Slide 29**

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 >101 degrees F (38.3 degrees 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 vesicles or 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 pustules, or all crusted lesions—not a mixture of different skin lesions.

### **Slide 30**

We created five minor criteria that are characteristic of smallpox cases: 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 lasts for 1-2 days so it takes more than a week to reach the height of the pustular stage; and 5) there are lesions on the palms of the hands and/or the soles of the feet.

### **Slide 31**

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.

### **Slide 32**

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

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presentation of the patient and assess if the illness is high, moderate or low risk for smallpox according to the major and minor criteria.

### **Slide 33**

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?

### **Slide 34**

The clinician's response to a high risk case should be to request an Infectious Diseases and/or dermatology consultation to confirm the high risk status. If the high risk status is confirmed, then alert the local or state 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, it fits the clinical case definition and therefore should be considered a probable case of smallpox until smallpox virus laboratory results are completed. For such a case, **DO NOT PERFORM OTHER LAB TESTING TO RULE OUT OTHER DIAGNOSES.**

### **Slide 35**

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.

### **Slide 36**

The response for a moderate risk case is to request 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 health lab or through a private lab. Rapid lab tests for varicella zoster virus 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 within an hour. A skin biopsy may be useful and can also be performed and read by pathologist rapidly. Obtain digital photos if possible. Re-evaluate risk level at least daily as risk level to determine if risk level has changed.

### **Slide 37**

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.

### **Slide 38**

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

### **Slide 39**

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 (or as soon as it meets the clinical case definition) without generating a high number of false alarms. With no cases of smallpox disease (or zero prevalence), 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. We need to recognize the first case of smallpox early without disrupting the health care and public health systems and without increasing public anxiety.

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### **Slide 40**

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. Seventeen 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. Four cases were considered moderate risk and the other 19 cases were low risk.

### **Slide 41**

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

### **Slide 42**

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.

### **Slide 43**

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.

### **Slide 44**

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.

### **Slide 45**

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.

### **Slide 46**

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.



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### **Slide 47**

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.

### **Slide 48**

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.

### **Slide 49**

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.

### **Slide 50**

Support for local health departments and private physicians who are evaluating a case of rash illness suspected to be smallpox 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.

The Centers for Disease Control and Prevention has on-call-staff available 24 hour a day, 7 days a week, every day of the year to assist state health departments. The on call staff have smallpox disease experts available for consultation. CDC can also provide laboratory support as requested.

### **Slide 51**

A final reminder, as already mentioned, The smallpox algorithm poster is available through state health departments and can be viewed and printed from the CDC website and can be ordered through the CDC on line ordering system.

### **Slide 52**

CDC has developed a written protocol to accompany the poster and a worksheet that can be used for investigation of febrile vesicular pustular rash illnesses suspected to be smallpox. They are also available through state health departments and can be downloaded and printed from the CDC smallpox website.

### **SEWARD:**

In summary, the diagnostic algorithm is an important tool for evaluating cases of febrile vesicular or pustular rash illness suspected to be smallpox. Understanding the clinical features of smallpox disease and smallpox look alike illnesses, especially varicella, is important for evaluating these cases so that their risk of being smallpox can be assessed in a systematic way and an appropriate clinical and public health response can occur.

END

For more information, visit [www.cdc.gov/smallpox](http://www.cdc.gov/smallpox), or call the CDC public response hotline at (888) 246-2675 (English), (888) 246-2857 (Español), or (866) 874-2646 (TTY)

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