EVALUATING PATIENTS FOR SMALLPOX
ACUTE, GENERALIZED VESICULAR OR PUSTULAR RASH ILLNESS PROTOCOL

RISK OF SMALLPOX

**High Risk of Smallpox → Report Immediately**
1. Febrile prodrome (defined below) AND
2. Classic smallpox lesion (defined below & photo at top right) AND
3. Lesions in same stage of development (defined below)

**Moderate Risk of Smallpox → Urgent Evaluation**
1. Febrile prodrome (defined below) AND
2. One other **MAJOR** smallpox criterion (defined below) OR
3. Febrile prodrome (defined below) AND
   2. ≥4 **MINOR** smallpox criteria (defined below)

**Low Risk of Smallpox → Manage as Clinically Indicated**
1. No febrile prodrome OR
2. Febrile prodrome AND
3. <4 **MINOR** smallpox criteria (defined below)

**MAJOR SMALLPOX CRITERIA**
- **FEBRILE PRODROME:** occurring 1-4 days before rash onset: fever ≥101°F and at least one of the following: prostration, headache, backache, chills, vomiting or severe abdominal pain
- **CLASSIC SMALLPOX LESIONS:** deep-seated, firm/hard, round well-circumscribed vesicles or pustules; as they evolve, lesions may become umbilicated or confluent
- **LESIONS IN SAME STAGE OF DEVELOPMENT:** on any one part of the body (e.g., the face, or arm) all the lesions are in the same stage of development (i.e., all are vesicles, or all are pustules)

**MINOR SMALLPOX CRITERIA**
- Centrifugal distribution: greatest concentration of lesions on face and distal extremities
- First lesions on the oral mucosa/palate, face, or forearms
- Patient appears toxic or moribund
- Slow evolution: lesions evolve from macules to papules → pustules over days (each stage lasts 1-2 days)
- Lesions on the palms and soles

For more information, please go to the CDC website [www.cdc.gov/smallpox](http://www.cdc.gov/smallpox)
**Evaluating Patients for Smallpox**

Acute, Generalized Vesicular or Pustular Rash Illness Protocol

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### Chickenpox (Varicella)

- Classic chickenpox lesions
- Typical chickenpox rash distribution

#### Images of Chickenpox (Varicella)

- Healthy child with varicella
- Healthy adult with varicella
- Bacterial superinfection of varicella lesions
- Note centripetal distribution of rash
- Day 3 of rash
- Lesions are in different stages of development (back of hand)
- Healthy adult with varicella
- Healthy adult with varicella
- Pregnant woman with varicella

### Smallpox

- Typical smallpox rash distribution
- Classic smallpox lesions

#### Images of Smallpox

- Day 3 of rash
- Day 5 of rash
- Day 7 of rash
- On any one part of the body, all lesions are in the same stage of development
- Umbilicated lesions
- Most patients with smallpox have lesions on the palms or soles
- Confluent lesions

### Differentiating Chickenpox from Smallpox

Chickenpox (varicella) is the most likely condition to be confused with smallpox.

- In chickenpox:
  - No or mild prodrome
  - Lesions are superficial vesicles; “dewdrop on a rose petal” (see photo at top)
  - Lesions appear in crops: on any one part of the body there are lesions in different stages (papules, vesicles, crusts)
  - Centripetal distribution: greatest concentration of lesions on the trunk, fewest lesions on distal extremities. May involve the face/scalp. Occasionally entire body equally affected.
  - First lesions appear on the face or trunk
  - Patients rarely toxic or moribund
  - Rapid evolution: lesions evolve from macules → papules → vesicles → crusts quickly (<24 hours)
  - Palms and soles rarely involved
  - Patient lacks reliable history of varicella or varicella vaccination
  - 50-80% recall an exposure to chickenpox or shingles 10-21 days before rash onset

### Common Conditions That Might Be Confused with Smallpox

<table>
<thead>
<tr>
<th>Condition</th>
<th>Clinical Clues</th>
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<tbody>
<tr>
<td>Varicella (primary infection with varicella-zoster virus)</td>
<td>Most common in children &lt;10 years; children usually do not have a viral prodrome</td>
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<tr>
<td>Disseminated herpes zoster</td>
<td>Immuno compromised or elderly persons; rash looks like varicella, usually begins in dermatomal distribution</td>
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<tr>
<td>Impetigo (Streptococcus pyogenes, Staphylococcus aureus)</td>
<td>Honey-colored crusted plaques with bullae are classic but may begin as vesicles; regional not disseminated rash; patients generally not ill</td>
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<tr>
<td>Drug eruptions</td>
<td>Exposure to medications; rash often generalized</td>
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<td>Contact dermatitis</td>
<td>Itching; contact with possible allergens; rash often localized in pattern suggesting external contact</td>
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<tr>
<td>Erythema multiforme minor</td>
<td>Target, “bull’s eye,” or iris lesions; often follows recurrent herpes simplex virus infections; may involve hands &amp; feet (including palms &amp; soles)</td>
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<tr>
<td>Erythema multiforme (incl. Stevens-Johnson Syndrome)</td>
<td>Major form involves mucous membranes &amp; conjunctivae; may be target lesions or vesicles</td>
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<tr>
<td>Enteroviral infection esp. Hand, Foot and Mouth disease</td>
<td>Summer &amp; fall; fever &amp; mild pharyngitis 1-2 days before rash onset; lesions initially maculopapular but evolve into whitish-grey tender, flat oval vesicles; peripheral distribution (hands, feet, mouth, or disseminated)</td>
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<tr>
<td>Disseminated herpes simplex</td>
<td>Lesions indistinguishable from varicella; immunocompromised host</td>
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<td>Scabies; insect bites (incl. fleas)</td>
<td>Itching is a major symptom; patient is not febrile &amp; is otherwise well</td>
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<td>Molluscum contagiosum</td>
<td>May disseminate in immunosuppressed persons</td>
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