# Smallpox: Overview for Healthcare Providers

<table>
<thead>
<tr>
<th><strong>Organism</strong></th>
<th>Variola virus; genus <em>Orthopoxvirus</em>, family <em>Poxviridae</em>, subfamily <em>Chordopoxvirinae</em></th>
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</thead>
<tbody>
<tr>
<td><strong>Reporting to Public Health</strong></td>
<td>Suspected or confirmed cases of smallpox require immediate notification to the local health department (LHD). See <a href="http://www.vdh.virginia.gov/local-health-districts/">http://www.vdh.virginia.gov/local-health-districts/</a>.</td>
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<tr>
<td><strong>Infectious Dose</strong></td>
<td>1 virus particle</td>
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| **Route of Infection** | Variola virus can spread from person to person through:  
- Respiratory droplets that are released when an infected person coughs or sneezes (requires close contact or <6 feet)  
- Direct contact with lesions  
- Contact with contaminated material such as clothing or bedding (less common)  
- Airborne transmission via fine-particle aerosol droplet (thought to be rare) |
| **Communicability** | Contagious from the time the first oropharyngeal lesions appear until the last scab separates from the body (~3 weeks), with the most infectious period being the 1st week of rash as oropharyngeal lesions release virus into saliva.  
- For surveillance, investigation, and containment purposes, consider potentially infectious from onset of fever or rash.  
- Secondary attack rate is estimated to be 38–88% among susceptible household contacts. |
| **Risk factors** | Susceptibility among unvaccinated people is universal |
| **Case-fatality Rate** | Historically, case-fatality rate has averaged 30% among unimmunized populations.  
- There are more severe, though less common, clinical forms with >95% case-fatality rate: flat-type (~5% of cases) associated with severe toxemia and flat, velvety, confluent lesions; hemorrhagic-type (~5% of cases) associated with severe toxemia and hemorrhagic rash. |
| **Incubation Period** | Usually 10–14 days (range 7–19 days) |
| **Clinical Description (variola major, ordinary type)** | Stage 1 (prodrome/preruptive stage): Acute onset of fever, malaise, rigors, vomiting, headache, and backache lasting 2–4 days; 15% have delirium. All smallpox patients have a febrile prodrome.  
- Stage 2 (eruptive stage): Maculopapular rash (2–4 days after prodrome) on oral mucosa, face, forearms and palms, spreading to trunk, legs and soles → deeply-embedded firm, round papules (day 2 of rash) → vesicles (day 3–4 of rash) → pustules (day 5–12 of rash) → crusty scab (day 13–18 of rash). |
| **Differential Diagnosis (eruptive stage)** | Chickenpox, monkeypox, generalized vaccinia, disseminated herpes zoster, disseminated herpes simplex, erythema multiforme, contact dermatitis, enteroviruses, molluscum contagiosum, secondary syphilis, atypical measles. CDC developed an algorithm for acute, generalized vesicular or pustular rash illness and evaluating patients for smallpox ([https://www.cdc.gov/smallpox/clinicians/algorithm-protocol.html](https://www.cdc.gov/smallpox/clinicians/algorithm-protocol.html))  
Differentiating Smallpox from Chickenpox:  
- Prodrome of high fever precedes smallpox lesions. With chickenpox, children typically do not have a prodrome, but adults might have a mild prodrome of fever and malaise.  
- Smallpox lesions present at same stage of development within any 1 anatomical region; chickenpox lesions appear in different stages.  
- Smallpox lesions tend to be concentrated on face and distal extremities (centrifugal distribution). Chickenpox lesions tend to be more concentrated on trunk (centripetal distribution). |
• Smallpox lesions typically occur on palms and soles. Chickenpox lesions rarely involve the palms and soles.
• Smallpox lesions are deeply embedded in the dermis. Chickenpox lesions are superficial.
• Smallpox lesions evolve from macules to papules to vesicles to pustules over several days (1–2 days/stage). Chickenpox lesions evolve from macules to papules to vesicles to crusts rapidly (<24 hours).

**Specimen Collection and Laboratory Testing**

- If smallpox is suspected, notify the [LHD](https://www.vdh.virginia.gov/) immediately to discuss the case and laboratory testing. Specimens may be sent to the Division of Consolidated Laboratory Services (DCLS) after testing has been approved by VDH.
- Virus can be detected in vesicular or pustular fluid by various test methods. Only PCR can definitively diagnose infection. All other testing methods (electron microscopy, immunohistochemistry, culture) screen for orthopoxviruses.
- DCLS conducts screening and CDC conducts confirmatory testing.
- Do not attempt specimen collection without prior vaccination and proper personal protective equipment. For questions about specimen collection and handling, the DCLS Emergency Officer can be reached 24/7 at 804-335-4617.

**Treatment**

- Medical care is generally supportive. Tecovirimat, the only FDA-approved treatment for smallpox, and other antivirals that are under investigation have been shown to be effective against related poxviruses in animals and in vitro studies. The effectiveness of these therapeutics in treating smallpox in humans is unknown.
- Vaccinia human immunoglobulin intravenous (VIGIV), available only through CDC, is licensed to treat certain vaccine adverse effects. It has no role in the treatment of smallpox.

**Postexposure Prophylaxis**

- Administering smallpox vaccine within 3–4 days after exposure to variola virus can prevent or attenuate disease.

**Vaccine**

- Smallpox vaccine is made from live vaccinia virus; the vaccine does not contain the variola virus that causes smallpox.
- The only smallpox vaccine licensed and used in the United States is ACAM2000® which provides high-level immunity for 3–5 years and then wanes. Pericarditis or myocarditis may occur in an estimated 5.7 per 1000 vaccinees.
- Vaccine is primarily for people at high risk for smallpox infection (e.g., people who work with smallpox or related viruses in laboratories, certain health care providers, and smallpox response team members). It is not available to the general public; however, a CDC stockpile has enough vaccine for the entire country if a bioterrorism event occurred.
- Those receiving vaccine need to be carefully evaluated for contraindications (e.g., skin conditions, weakened immune systems). Post-vaccination care is essential to prevent autoinoculation or transmission to others.

**Infection Control**

- Follow strict Standard, Contact, and Airborne precautions and use appropriate personal protective equipment (PPE) until scabs have separated (3–4 weeks). Isolate patients in airborne infection isolation rooms equipped with high-efficiency particulate air filtration. Keep doors closed.
- Consult with health department and hospital infection control as soon as possible.
- Healthcare workers providing direct patient care, personnel performing environmental control tasks, and personnel handling laundry or waste should be vaccinated (if available); administer post-exposure vaccine to susceptible persons within 4 days after exposure.
- Vaccinated workers should cover the vaccination site with gauze and semi-permeable dressing until scab separates (≥21 days) and observe hand hygiene. Use N95 or higher respiratory protection for susceptible and successfully vaccinated individuals.
- Decontaminate surfaces with an EPA-registered disinfectant approved to inactivate vaccinia virus and follow the manufacturer’s directions.
- Follow waste management guidelines and regulations for Category A infectious substances.