VDH VIRGINIA DEPARTMENT OF HEALTH

Virginia Department of Health
Smallpox: Overview for Healthcare Providers

Organism	Variola virus (DNA virus); genus *Orthopoxvirus*, family *Poxviridae*, subfamily *Chordopoxvirinae.* Smallpox eradicated globally in 1979, bioweapon potential.
Reporting to Public Health	Suspected or confirmed cases of smallpox require immediate notification to the local health department (LHD). See https://www.vdh.virginia.gov/health-department-locator/
Infectious Dose	1 virus particle
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 droplets (thought to be rare)
Communicability	• Contagious from the time the first lesion appears 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 public health purposes, consider potentially infectious from fever or rash onset. • 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 for Variola Major (ordinary smallpox) • 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	• Prodrome: Acute onset of fever, malaise, rigors, vomiting, headache, and backache lasting 2–4 days. All smallpox patients have a febrile prodrome. • 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, mpox, generalized vaccinia, disseminated herpes zoster, disseminated herpes simplex, erythema multiforme, contact dermatitis, enteroviral infections, molluscum contagiosum, secondary syphilis, atypical measles. Refer to CDC's Acute, Generalized Vesicular or Pustular Rash Protocol for evaluating patients for smallpox. Differentiating Smallpox from Chickenpox: • High fever precedes smallpox lesions. With chickenpox, children typically do not have a prodrome; adults might have a mild prodrome of fever/malaise. • Smallpox lesions present at same stage of development within any 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 your LHD 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. • DCLS conducts presumptive testing 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, but there are currently two FDA-approved medications for treating children and adults • Tecovirimat (TPOXX®) has been shown to be effective in treating animals with related poxviruses. Administered orally or intravenously. • Brincidofovir (TEMBEXA) has been shown to be effective in treating animals with diseases similar to smallpox. Administered orally. • Cidofovir is not FDA-approved for treating smallpox but might be considered during an outbreak
Postexposure Prophylaxis	Administering smallpox vaccine within 3–4 days after exposure to variola virus can prevent or attenuate disease. Per CDC, the ACAM2000 vaccine is preferred for people with competent immune systems; for severely immunocompromised people, the JYNNEOS vaccine can be considered.
Vaccine	Currently, two FDA-licensed smallpox vaccines are available: JYNNEOS and ACAM2000. Both are made from vaccinia virus, not variola virus, so it is not possible for vaccine providers or recipients to develop smallpox. Recipients 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. • JYNNEOS (also known as Imvamune or Imvanex) is a live attenuated, replication-deficient, vaccine against smallpox. It can be used to prevent smallpox in people aged 18 years and older, including people who have HIV disease or atopic dermatitis. JYNNEOS is administered as a subcutaneous injection. The vaccine series consists of two doses spaced 4 weeks apart. • ACAM2000 is made from replication-competent vaccinia virus and provides high-level immunity for 3–5 years and then wanes. Pericarditis or myocarditis may occur in an estimated 5.7 per 1000 vaccinees. ACAM2000 is administered via the percutaneous route using the multiple puncture technique and a bifurcated needle. It is important that the vaccine site be covered well with gauze until it scabs over, the scab has completely fallen off, and new tissue has replaced it. If another person contacts the bare vaccine site while it's healing, vaccinia virus could spread. • Per CDC, routine smallpox vaccination is not recommended for providers who administer ACAM2000, but it should be offered to them. • Vaccination is indicated for people at high risk for smallpox infection (e.g., people who work with smallpox or related viruses in laboratories, certain providers, and smallpox response team members). It is not available to the public but would be if a bioterrorism event occurred.
Infection Control	• Follow strict Standard, Contact, and Airborne precautions and use appropriate personal protective equipment 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