

Virginia Department of Health
Monkeypox: Guidance for Healthcare Professionals
Key Medical and Public Health Interventions

Monkeypox is a zoonotic disease caused by the monkeypox virus of the genus *Orthopoxvirus*. Monkeypox virus is genetically distinct from other orthopoxviruses, including variola virus (the cause of smallpox) and vaccinia virus (the virus used in the smallpox vaccine). Previously endemic only to central and West Africa, the first reported U.S. outbreak of human monkeypox occurred in 2003. During the U.S. outbreak, most people with confirmed monkeypox reported exposure to native prairie dogs that had contact with imported African rodents, which are a likely reservoir for monkeypox virus.

Monkeypox is usually transmitted to humans from the bite of an infected animal or from direct contact with lesions or body fluids from an infected animal. Less frequently, monkeypox can be transmitted from person-to-person by respiratory droplets during prolonged face-to-face contact. Monkeypox also may be transmitted from person-to-person by direct contact with body fluids of an infected person or with virus-contaminated objects, such as bedding and clothing. Airborne transmission cannot be excluded, especially among persons presenting with cough. During the 2003 U.S. outbreak of monkeypox, no human cases were attributed exclusively to person-to-person transmission.

1. Clinical Manifestations

Incubation period: 7-14 days (average, 12 days)

Signs and Symptoms: Clinically, monkeypox is similar to smallpox, although monkeypox is often milder and less transmissible from person-to-person. Signs and symptoms include fever, headache, backache, lymphadenopathy (not commonly seen in smallpox), sore throat and cough. One to three days after fever onset, a papular rash develops which often first appears on the face, but may present on other parts of the body. The rash lesions usually develop through several stages, including a vesiculopustular stage, before crusting and falling off. Illness typically lasts for 2 to 4 weeks. Case-fatality rates among people with monkeypox in central and West Africa have ranged from 1% – 10%. During the 2003 U.S. monkeypox outbreak, out of approximately 70 reported human cases, there were no reported deaths due to monkeypox. The differential diagnosis of monkeypox includes smallpox, generalized vaccinia, chickenpox, disseminated herpes zoster, disseminated herpes simplex, erythema multiforme, contact dermatitis, enteroviral infection, molluscum contagiosum, secondary syphilis, and atypical measles.

2. Identification and Isolation of Cases

Any patient who presents with fever and vesicular or pustular rash (including those with suspected monkeypox) should be assessed by a healthcare worker for risk of smallpox, using the Centers for Disease Control and Prevention (CDC) algorithm based upon clinical symptoms (see CDC website <http://www.bt.cdc.gov/agent/smallpox/diagnosis>). Patients with monkeypox may present with symptoms suggestive of smallpox, and need to be managed as a suspected case of smallpox until variola virus has been ruled out. If a patient is assessed to be at high risk for smallpox, the healthcare worker should immediately verify that the patient is under contact and

airborne precautions, placed in an isolation room, and urgently notify hospital epidemiology/infection control, who in turn should notify laboratory personnel, other healthcare professionals and the local health department. The local health department should immediately notify the Division of Surveillance and Investigation (DSI) or the Division of Zoonotic and Environmental Epidemiology (DZEE) in the central office of the Virginia Department of Health (VDH) about the suspect case. DSI or DZEE staff can be reached during work hours at 804-864-8141 or on the VDH emergency phone at 866-531-3068 after work hours, at night and on weekends.

While waiting for laboratory results, collect information about the patient's travel and exposure history for the two weeks prior to illness onset. The diagnosis of monkeypox becomes more likely if the patient had exposure during that time to an exotic or wild mammalian animal or to any mammalian animal housed with an exotic or wild mammalian animal that originates from a geographic area where the occurrence of monkeypox is biologically plausible (e.g., Africa or a location in the U.S. where monkeypox was confirmed during the 2003 outbreak). The animal constituting the exposure must have clinical signs of illness consistent with monkeypox (e.g., conjunctivitis, respiratory symptoms, and/or rash).

For infection control of monkeypox, a patient should be placed under standard, contact, and droplet precautions in all healthcare settings. In addition, because of the theoretical risk of airborne transmission, airborne precautions should be followed whenever possible.

Under certain circumstances, the State Health Commissioner may invoke control measures that include quarantine and isolation of humans and/or certain animals as described in Article 3.02 of Title 32.1 of the Code of Virginia regarding *Quarantine and Isolation of Persons with Communicable Diseases of Public Health Threat*. Monkeypox patients who do not require hospitalization may be isolated at home.

3. Handling Laboratory Specimens

If a patient is determined to be at high risk for smallpox, specimen collection and biosafety/infection control should follow the guidelines for smallpox (see VDH website http://www.vdh.state.va.us/EPR/Agents_Biological_Smallpox.asp). Upon consultation, VDH may deploy a vaccinated public health physician with a smallpox kit obtained from the state public health laboratory, Virginia Division of Consolidated Laboratory Services (DCLS), to collect specimens for laboratory testing at DCLS and CDC.

When monkeypox is the suspected agent and specimens are submitted for routine laboratory testing (e.g. chemistry, hematology, bacteriology), laboratory personnel should be informed that the specimens are from a patient with suspected monkeypox to ensure that appropriate biosafety precautions are followed. Biosafety guidelines for laboratory personnel handling specimens from patients with suspected monkeypox are available at the CDC website <http://www.cdc.gov/ncidod/monkeypox> (see: Interim Biosafety Guidelines for Laboratory Personnel Handling Human and Animal Specimens for Monkeypox Testing). Monkeypox and related viruses grow easily in cell culture; therefore, specimens from patients with suspected monkeypox should not be placed into viral culture except in specialized laboratories with suitable biocontainment and appropriately trained, vaccinated laboratory personnel.

Laboratory tests to detect and identify monkeypox are available at DCLS and CDC, but must be pre-arranged by consultation with DCLS. It is essential to contact DCLS before collecting specimens to assure appropriate specimen collection and transport, and to arrange for test availability at DCLS and CDC. The DCLS Emergency Services Officer may be paged at 804-418-9923 (24 hours a day/7days a week).

Healthcare personnel who collect specimens from patients with suspected monkeypox should use personal protective equipment (PPE) in accordance with recommendations for standard, contact and airborne precautions. Current recommendations for vaccinia vaccination of healthcare workers who may be exposed to monkeypox should also be followed. Details of specimen collection for monkeypox are available at the CDC website <http://www.cdc.gov/ncidod/monkeypox> (see: Interim Guidance for Collection of Diagnostic Specimens from Persons with Suspect Monkeypox). An overview of the specimens to collect from a patient with acute symptoms of monkeypox is provided in Table 1. DCLS specimen collection kits designed for smallpox or for vaccinia virus contain materials and directions needed to collect specimens for monkeypox testing.

Table 1. Summary of Clinical Specimens for Monkeypox Testing

<i>Source</i>	<i>Specimen</i>	<i>Container</i>	<i>Comment</i>
Vesicle or Pustule Note: all 5 types of specimens are collected from each vesicle or pustule sampled	1. Roof of lesion	2 ml tube	
	2. Swab of lesion fluid	15 ml tube	
	3. Touch preparation (slide)	Microscope slide (plastic preferred)	
	4. Touch preparation (EM grid)	EM (electron microscopy) grid	Collect 3 per lesion, using varying degrees of pressure in touch prep
	5. Swab of cells from base of lesion	Viral Transport Medium tube	
Scab lesion	Collect at least 4 scabs	2 ml tube (1 or 2 scabs per tube)	
Macule or Papule (or any lesion from which biopsy is indicated)	Biopsy using a 3.5-4mm biopsy punch (2.5 mm if pediatric). Bisect into 2 halves, or collect 2 biopsies.	Place half of biopsy into dry sterile container ("fresh"); place other half into formalin ("fixed")	Ship fixed biopsy in formalin at room temperature; ship fresh biopsy frozen on dry ice
Tonsillar tissue swab	Swab tonsillar tissue with a polyester or dacron swab	Place swab in dry 2 ml tube	
Whole blood	5 ml of blood	Purple topped tube (EDTA anticoagulant), preferably plastic	
Acute and convalescent serum	7 to 10 ml of blood	Serum separator tube, preferably plastic	Collect convalescent serum 4 to 6 weeks after acute

Depending upon the urgency of the public health situation, specimens to be tested for monkeypox virus may be sent simultaneously to both DCLS and to CDC. Alternatively, screening tests may first be performed at DCLS, with positive screening results from DCLS confirmed by other testing at CDC. The monkeypox screening test performed at DCLS is the non-variola generic orthopoxvirus polymerase chain reaction using the approved Laboratory Response Network protocol. CDC offers many different tests, including viral culture, polymerase chain reaction, electron microscopy, and immunohistochemistry. Coordination of specimen collection, shipment and testing for both DCLS and CDC must be arranged through DCLS.

4. Diagnosis

The case classifications for the diagnosis of monkeypox are outlined below.

A. Clinical criteria

- Rash: macular, papular, vesicular, or pustular; generalized or localized; discrete or confluent.
- Fever: subjective or measured temperature of greater than or equal to 99.0 degrees F (37.4 degrees C).
- Other signs and symptoms: chills and/or sweats, headache, backache, lymphadenopathy, sore throat, cough, shortness of breath.

B. Epidemiologic criteria

- Exposure to an exotic or wild mammalian animal or to any mammalian animal housed with exotic or wild mammalian animal that originates from a geographic area where the occurrence of monkeypox is biologically plausible (e.g., Africa, locations in the U.S. where monkeypox was confirmed during the 2003 outbreak). The pet or animal constituting the exposure must have clinical signs of illness consistent with monkeypox (e.g., conjunctivitis, respiratory symptoms and/or rash).
- Exposure to an exotic or wild mammalian animal (with or without clinical signs of illness) that has been in contact with a mammalian animal infected with monkeypox or a human infected with monkeypox.
- Exposure to a suspect, probable or confirmed human case of monkeypox.

C. Laboratory criteria

- Isolation of monkeypox virus in culture.
- Demonstration of monkeypox virus DNA by polymerase chain reaction testing of a clinical specimen.
- Demonstration of virus morphologically consistent with an orthopoxvirus by electron microscopy in the absence of exposure to another orthopoxvirus.
- Demonstration of presence of orthopoxvirus in tissue using immunohistochemical testing methods in the absence of exposure to another orthopoxvirus.

D. Case classification

- **Suspect case:** meets one of the epidemiologic criteria AND has fever or unexplained rash AND two or more other signs or symptoms with onset of

first sign or symptom less than or equal to 21 days after last exposure meeting epidemiologic criteria.

- **Probable case:** meets one epidemiologic criteria AND has fever AND vesiculopustular rash with onset of first sign or symptom less than or equal to 21 days after last exposure meeting epidemiologic criteria.
- **Confirmed case:** meets one of the laboratory criteria.

E. Exclusion criteria

A case may be excluded as a suspect or probable monkeypox case if:

- An alternative diagnosis can fully explain the illness OR
- The case was reported on the basis of primary or secondary exposure to an exotic or wild mammalian pet or a human (see epidemiologic criteria) subsequently determined not to have monkeypox, provided other possible epidemiologic exposure criteria are not present OR
- A case without a rash does not develop a rash within 10 days of onset of clinical symptoms consistent with monkeypox OR
- The case is determined to be negative for non-variola generic orthopoxvirus by polymerase chain reaction testing of a well-sampled rash lesion by the approved Laboratory Response Network (LRN) protocol.

5. Treatment and Prophylaxis

Treatment: Generally, treatment is supportive. However, cidofovir, an antiviral medication, is available for monkeypox treatment through CDC as an Investigational New Drug. Consult with the local health department for details about requesting cidofovir. Otherwise, there is currently no recommended treatment for monkeypox.

Prophylaxis: Vaccination may be indicated before or after exposure to monkeypox (see: **6. Vaccine**).

6. Vaccine

The vaccinia vaccine (used for smallpox) likely protects against monkeypox. The following is a summary of recommendations for pre- and post-exposure vaccinia vaccination for persons at risk for specific monkeypox exposures.

Pre-monkeypox exposure: Data suggest that vaccinia vaccination before exposure to monkeypox is highly effective (greater than or equal to 85%) in protecting those exposed to monkeypox from developing disease. Ideally, persons who know in advance that they may be exposed to monkeypox virus (e.g., monkeypox outbreak investigators, healthcare workers caring for monkeypox patients, laboratory workers and veterinarians) should have received a recent (within the previous 3 years) vaccinia vaccination with a confirmed take. If not previously vaccinated, such persons should be vaccinated as soon as possible prior to beginning their duties. Vaccinia vaccine recipients should follow vaccine site precautions. Contraindications to vaccinia vaccine must be considered before vaccination or work assignment.

Post-monkeypox exposure: Less is known about post-exposure prophylaxis. However, because vaccinia vaccination after smallpox exposure is effective in preventing or ameliorating smallpox, it is likely that vaccinia vaccination should have similar impact against monkeypox. Therefore, it is recommended that those exposed to monkeypox (e.g., close contacts of confirmed monkeypox cases, persons with close contact with ill prairie dogs or other ill small mammals, and laboratory workers who handle specimens from ill persons and/or prairie dogs or other ill small mammals meeting the probable or confirmed case definitions for monkeypox) should receive vaccinia vaccination as soon as possible, preferably within 4 days from the initial exposure. Vaccination should be considered only for persons who are within 2 weeks of the most recent monkeypox exposure. Contraindications to vaccinia vaccination must be considered before vaccination.

Note: Irrespective of vaccination status, all persons exposed to or potentially exposed to monkeypox should follow recommended infection control precautions.

Certain persons (including those with severe immunodeficiencies, life-threatening allergies to smallpox vaccine or any of its components) are at risk of severe complications from vaccinia vaccination that may approach or exceed the risk of disease from monkeypox exposure. Consult with VDH to discuss vaccination of such persons.

For a full discussion see: *Centers for Disease Control and Prevention. Vaccinia (smallpox) vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001. MMWR 2001;50 (No. RR-10:[1-26].*

7. Decontamination guidelines for monkeypox

In the hospital setting:

- Use standard precautions when handling an ill patient's clothing, dressings, bedding, etc. to avoid direct contact with contaminated material.
- Contain and dispose of contaminated waste (e.g., dressings) in accordance with facility-specific guidelines.
- Launder/disinfect clothing or linens contaminated with body fluids according to hospital protocol.
- Soiled laundry should not be shaken or otherwise handled in a manner that could aerosolize infectious particles.
- Handle used patient care equipment in a manner that prevents contamination of skin and clothing. Ensure that used equipment has been cleaned and reprocessed appropriately.
- Ensure procedures are in place for cleaning and disinfecting surfaces in the healthcare environment. Use any EPA-registered hospital detergent/disinfectant currently used by healthcare facilities for environmental surfaces. Follow manufacturer's recommendations for specific concentrations, contact time and care in handling. Monkeypox virus is inactivated by 0.5% sodium hypochlorite solution (1 part bleach to 9 parts water).

In the home setting:

- Wear disposable gloves for direct contact with weeping lesions. Dispose of gloves after use. Wash hands after removing gloves.
- Use proper hand hygiene (i.e., hand washing with soap and water or use of an alcohol-based hand rub) after touching patient body sites, handling patient clothing, dressings, bedding or environmental surfaces.
- Launder bedding, towels, clothing, etc., in a standard washing machine with warm water and detergent; bleach may be added but is not necessary. Take care when handling soiled laundry to avoid direct contact with contaminated material. Soiled laundry should not be shaken or otherwise handled in a manner that could aerosolize infectious particles.
- Do not share dishes or other eating utensils of suspected or confirmed monkeypox cases. Segregation of specific utensils for use by the infected person is not necessary. Wash soiled dishes and eating utensils in a dishwasher or by hand with warm water and soap.
- Clean and disinfect contaminated surfaces using standard household cleaning/disinfectants in accordance with manufacturer's instructions. Monkeypox virus is inactivated by 0.5% sodium hypochlorite solution (1 part bleach to 9 parts water).
- Bag dressings, bandages, gloves and other materials contaminated with lesion drainage and place inside a second closed container for disposal with other household waste.

8. Postmortem Practices

If monkeypox is suspected as a cause of death, the district Office of the Chief Medical Examiner (OCME) should be notified immediately. Consult with OCME to determine if an autopsy should be conducted, the parties responsible for conducting the autopsy and the appropriate personal protective procedures to follow.

9. Public Health Measures

- A. Suspected cases should be reported to hospital epidemiology/infection control, who in turn should notify laboratory personnel, other medical care professionals, and the local health department. The local health department should immediately notify the DSI or DZEE in the central office of VDH about the suspect case. DSI or DZEE staff can be reached during work hours at 804-864-8141 or on the VDH emergency phone at 866-531-3068 after work hours, at night and on weekends.
- B. Laboratory testing of clinical specimens for monkeypox is available at DCLS and at CDC. DCLS must be notified prior to specimen collection to assure proper specimen collection, transport, coordination with CDC, and availability of testing personnel. The DCLS Emergency Services Officer can be paged 24 hours a day/7days a week at 804-418-9923.
- C. Designated public health authorities should begin an epidemiologic investigation to include the following:
 - a. Collection of detailed information from the patient (or his/her designee) about possible exposures (including exposure to a wild or exotic mammalian animal or to any mammalian animal housed with exotic or wild mammalian animal that originates from a geographic area where exposure to monkeypox is biologically plausible).
 - b. Investigation of contacts of the case for compatible illness that may be due to a common exposure.

- c. Notification of Virginia Department of Agriculture and Consumer Services (VDACS) at 804-786-2483 and Virginia Department of Game and Inland Fisheries (VDGIF) at 804-367-1000 so they may initiate an investigation of animals that could potentially be involved in the transmission of monkeypox to humans, and so they may develop appropriate disease control measures and surveillance tools for potential animal disease.
- d. Review the VDH *Public Health Emergency Response Plan for Zoonotic Diseases Using Monkeypox as a Prototype*.

References

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