

Monkeypox

Section 1: ABOUT THE DISEASE

A. Etiologic Agent

Monkeypox is a zoonotic disease caused by the monkeypox virus of the family *Orthopoxviridae*. This genus also includes variola virus (smallpox), vaccinia virus (the virus in the smallpox vaccine), and cowpox. The disease is called monkeypox because the agent was first discovered in laboratory monkeys in 1958, but the natural hosts of the virus are rodents.

Note: Variola virus is covered in detail in the “Smallpox” chapter of this manual.

B. Clinical Description

The symptoms of monkeypox are similar to human smallpox, although they are milder. They include fever, headache, muscle aches, swollen lymph nodes, and fatigue. A rash typically develops within three days of the onset of fever. The rash typically becomes vesiculopustular (blisters with clear, progressing to cloudy, contents). The rash usually starts on the face, but may begin on other body parts. The raised bumps of the rash go through stages, much like the smallpox rash, before becoming crusted, scabbing, and falling off. The duration of illness ranges from 2–4 weeks.

C. Vectors and Reservoirs

Recent evidence suggests that African squirrels may be the natural reservoir for monkeypox, but other rodents including Gambian rats, mice, and the elephant shrew, and mammals including rabbits, monkeys, and pigs, can be carriers.

D. Modes of Transmission

Monkeypox is transmitted through direct contact with infected animals, including a bite from the animal as well as contact with the animal’s blood, body fluids, or rash. Evidence exists for transmission through contaminated objects such as bedding or clothing. Person-to-person transmission also occurs, primarily through large respiratory droplets spread during periods of prolonged face-to-face contact. While airborne transmission has never been documented, it is theoretically possible using the smallpox model, and thus, cannot be excluded.

E. Incubation Period

The incubation period for monkeypox ranges from 10–14 days, but is usually 12 days.

F. Period of Communicability or Infectious Period

The communicable period for monkeypox generally lasts about three weeks, or from the time of the development of the first lesion to the disappearance of all scabs.

G. Epidemiology

Monkeypox is rare and occurs mostly in central and western Africa, with fatality rates of up to 10%, primarily in children. Monkeypox was first reported in humans in 1970. One factor behind the spread of human monkeypox infection is the discontinuation of smallpox vaccination in Africa in the 1980s, as the vaccine provided protection against monkeypox. An outbreak of monkeypox, which occurred in June of 2003 in the Midwestern U.S., has focused recent attention on the disease. These cases are believed to be the first monkeypox cases ever to occur in the Western Hemisphere. Infections were acquired after close contact with pet prairie dogs that were infected with the monkeypox virus through close contact with animals imported from Africa.

H. Bioterrorist Potential

This pathogen is not considered to be of risk for use in bioterrorism. However, monkeypox could be used to generate fear of smallpox in a population, and this would be a bioterrorism challenge.

Section 2: REPORTING CRITERIA AND LABORATORY TESTING

A. What to Report to the Massachusetts Department of Public Health (MDPH)

Report any suspect case of monkeypox based on a health care provider's medical judgment or on a positive laboratory result pertaining to monkeypox virus or any other orthopox virus in humans.

Note: See Section 3C for information on how to report a case.

B. Laboratory Testing Services Available

The MDPH State Laboratory Institute (SLI) performs testing for orthopox viruses by real-time detection polymerase chain reaction (PCR). Tests will be performed on specimens after individual case review and approval by a MDPH epidemiologist, at (617) 983-6800 or (888) 658-2850. Appropriate specimens include vesicular "touch prep," vesicle roof, vesicular swab, ocular swab or impression slide, and biopsy specimens. Swabs should be submitted in a dry tube without viral transport medium. All specimens will be forwarded to the Centers for Disease Control and Prevention (CDC) for further testing and confirmation. To identify other potential causes of pox-like illness, the SLI will also perform laboratory screening for other pox-like viral agents.

For additional information on testing or specimen submission, contact the SLI Virus Isolation Laboratory at (617) 983-6382. Please call the laboratory prior to specimen submission. Detailed instructions for specimen collection for cases of suspect monkeypox can be found on the CDC website at www.cdc.gov/ncidod/monkeypox/diagspecimens.htm.

Section 3: REPORTING RESPONSIBILITIES AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- To identify clusters of infection as soon as possible.
- To identify potential sources of infection.
- To design effective control and prevention methods, as necessary.

B. Laboratory and Health Care Provider Reporting Requirements

Monkeypox is reportable to the local board of health (LBOH). The MDPH requests that health care providers immediately report to the LBOH in the community where the case is diagnosed, all confirmed or suspect cases of monkeypox, as defined by the reporting criteria in Section 2A.

Laboratories performing examinations on any specimens derived from Massachusetts residents that yield evidence of monkeypox or other orthopox virus infection shall report such evidence of infection directly to the MDPH within 24 hours.

Note: Confirmatory testing for monkeypox will be done either at the SLI or at the CDC, but will be coordinated through the SLI in both cases. However, the LBOH could be the initial recipient of a report of a suspect case.

C. Local Board of Health (LBOH) Reporting and Follow-Up Responsibilities

Reporting Requirements

MDPH regulations (*105 CMR 300.000*) stipulate that monkeypox is reportable to the LBOH and that each LBOH must report any confirmed case of monkeypox or suspect case of monkeypox, as defined by the reporting criteria in Section 2A. Cases should be reported to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS) using a MDPH *Generic Confidential Case Report Form* (found at the end of this chapter). Refer to the *Local Board of Health Timeline* at the end of this manual's *Introduction* section for information on prioritization and timeliness requirements of reporting and case investigation.

Under *105 CMR 300.140, Reporting of Animal Diseases with Zoonotic Potential by Veterinarians*, any veterinarian or LBOH with knowledge of an animal disease potentially infectious to humans must also report the disease to the Massachusetts Department of Agricultural Resources (MDAR), Division of Animal Health, Dairy Services and Biosecurity (DAH). Specific disease in animals which veterinarians must also report directly to the MDPH are anthrax, plague, West Nile virus infection, and Eastern equine encephalitis virus infection. For questions related to monkeypox in animals or to report a suspect case of monkeypox infection in an animal, contact the DAH at (617) 626-1795, or fax the information to the DAH at (617) 626-1850.

Case Investigation

If a LBOH learns of a suspect or confirmed case of monkeypox, it should promptly call the MDPH Division of Epidemiology and Immunization with initial information at (617) 983-6800 and (888) 658-2850. Case investigation of suspect or confirmed cases of monkeypox in Massachusetts residents will, in most circumstances, be led by the MDPH Division of Epidemiology and Immunization.

1. The LBOH may be asked to assist in completing an official MDPH *Generic Confidential Case Report Form* (found at the end of this chapter). Use the following guidelines to assist in completing the form:
 - a. Accurately record the demographic information.
 - b. Accurately record clinical information, including “monkeypox” as the disease being investigated, date of symptom onset, symptoms, whether the case was hospitalized, and hospital and clinician contact information.
 - c. Include all diagnostic laboratory test information that is available.
 - d. Record information relevant to prevention and control. Use the incubation period range for monkeypox (10–14 days). Specifically, focus on the period beginning 14 days prior to the case’s onset date for the following exposures:
 - i. Travel history: Determine the date(s) and geographic area(s) traveled to by the case.
 - ii. Animal contact: Ask the case about potential direct or indirect occupational or recreational exposures to animals. This information can then be documented in the “Comments” section.
 - e. Include any additional comments regarding the case.
 - f. If you have made several attempts to obtain case information but have been unsuccessful (e.g., the case or health care provider does not return your calls or respond to a letter, or the case refuses to divulge information or is too ill to be interviewed), please fill out the form with as much information as you have gathered. Please note on the form the reason(s) why it could not be filled out completely.
2. After completing the form, attach laboratory report(s) and fax or mail (in an envelope marked “Confidential”) to ISIS. The confidential fax number is (617) 983-6813. Call ISIS at (617) 983-6801 to confirm receipt of your fax. The mailing address is:

MDPH, Office of Integrated Surveillance and Informatics Services (ISIS)
305 South Street, 5th Floor
Jamaica Plain, MA 02130
Fax: (617) 983-6813

3. Institution of disease control measures is an integral part of case investigation. It is the responsibility of the LBOH to understand, and if necessary, institute the control guidelines listed in Section 4.

Section 4:

CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements (105 CMR 300.200)

Minimum Period of Isolation of Patient

Until lesions have dried and crusts have separated. If no lesions, until seven days after onset of fever. (If a rash does not develop within seven days, the patient does not have monkeypox, and isolation procedures can be discontinued.)

Minimum Period of Quarantine of Contacts

Personal surveillance; otherwise, no restrictions. Additional control measures may be recommended by the MDPH.

B. Protection of Contacts of a Case

Vaccination with smallpox (vaccinia) vaccine is recommended for health care workers and household contacts of monkeypox cases. (See smallpox vaccine information in Section 4D.)

Close contacts, defined as household contacts, as well as others who have had close or intimate contact with confirmed human cases and who are within four days of initial direct exposure to a monkeypox case should be vaccinated. Vaccination should be considered for persons who are within two weeks of most recent exposure. As general guidance, for purposes of smallpox exposure, close contact has been defined as ≥ 3 hours of direct exposure within 6 feet, and this is reasonable guidance for monkeypox exposure as well. Intimate contact refers to contact resulting in exposure to body fluids or lesions of affected persons. However, judgment must be applied to determine the significance of contact in individual exposure situations. The MDPH should be consulted regarding decisions about vaccination of contacts, and in particular, for contacts who may not meet the strict definitions of close or intimate contact above, especially in childcare, school, or health care settings.

Smallpox vaccination should also be recommended for persons who have, within the past four days, had direct physical (intimate) contact with ill animals meeting the animal case definition for monkeypox. Vaccination should be considered for persons who are within two weeks of most recent exposure. In addition, vaccination can be considered for persons who have close contact with an ill animal that meets the probable or confirmed animal case definition. Close contact is defined as direct exposure within six feet of a probable or confirmed monkeypox case in an animal with respiratory symptoms, such as nasal discharge, cough, or conjunctivitis in a setting where the animal has been manipulated (e.g., an exam room). Smallpox vaccination is not recommended for persons exposed to a healthy animal.

The animal case definition for monkeypox is available on the CDC website at www.cdc.gov/ncidod/monkeypox/animalcasedefinition.htm.

Asymptomatic contacts of animals or humans suspected to have monkeypox should be placed under symptom surveillance for 21 days after their last exposure. Symptoms of concern include fever (temperature $\geq 99.3^{\circ}\text{F}$), sore throat, cough, or skin rash. Contacts should monitor their temperatures twice daily. In addition, they should maintain daily telephone contact with designated health department personnel. Asymptomatic contacts should not donate blood, cells, tissue, organs, breast milk, or semen while they are under symptom surveillance. Asymptomatic contacts should continue routine daily activities such as going to work and attending school, but should remain close to home for the duration of surveillance. It may, however, be prudent to exclude pre-school children from daycare or other group settings.

C. Managing Special Situations

Reported Incidence Is Higher Than Usual/Outbreak Suspected

If you suspect a case of monkeypox in your city/town or if you suspect an outbreak, investigate to determine the source of infection and the mode of transmission. Consult with the epidemiologist on-call at the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850. The Division can help determine a course of action to prevent further cases and can perform surveillance for cases across town lines, which would otherwise be difficult to identify at the local level.

Personal Preventive Measures/Education

Smallpox Vaccine

Because the monkeypox virus is related to the virus that causes smallpox (variola), the smallpox vaccine (vaccinia) can protect people from getting monkeypox as well as smallpox. Smallpox vaccine is effective at protecting people against monkeypox when it is given before they are exposed to monkeypox, and it may help prevent the disease or make it less severe when administered to people after exposure. Reports from outbreaks in Africa indicate the vaccine is 85% effective in preventing the development of monkeypox.

Specific information on the use of smallpox vaccine for the prevention of monkeypox, including which individuals should and should not get smallpox vaccine to prevent monkeypox, is available in a CDC Fact Sheet, Smallpox Vaccine and Monkeypox, on the CDC website at www.cdc.gov/ncidod/monkeypox/smallpoxvaccine_mpx.htm.

ADDITIONAL INFORMATION

The following is the formal CDC surveillance case definition for monkeypox. It is provided for your information only and should not affect the investigation and reporting of a case that fulfills the criteria in Section 2A of this chapter. (The CDC and the MDPH use the CDC case definitions to maintain uniform standards for national reporting.) For reporting to the MDPH, always use the criteria outlined in Section 2A.

Note: The most up-to-date CDC case definitions are available on the CDC website at www.cdc.gov/epo/dphsi/casedef/case_definitions.htm.

Clinical Criteria

- Rash (macular, papular, vesicular, or pustular; generalized or localized; discrete or confluent).
- Fever (subjective or measured temperature of $\geq 99.3^{\circ}\text{F}$ [$\geq 37.4^{\circ}\text{C}$]).
- Other signs and symptoms:
 - Chills and/or sweats,
 - Headache,
 - Backache,
 - Lymphadenopathy,
 - Sore throat,
 - Cough, and
 - Shortness of breath.

Epidemiologic Criteria

- Exposure¹ to an exotic or wild mammalian pet,² obtained on or after April 15, 2003, with clinical signs of illness (e.g., conjunctivitis, respiratory symptoms, and/or rash).
- Exposure¹ to an exotic or wild mammalian pet,² with or without clinical signs of illness, that has been in contact with either a mammalian pet³ or a human with monkeypox.
- Exposure⁴ to a suspect, probable, or confirmed human case of monkeypox.

1 Includes living in a household, petting or handling, or visiting a pet-holding facility (e.g., pet store, veterinary clinic, pet distributor).

2 Includes prairie dogs, Gambian giant rats, and rope squirrels. Exposure to other exotic or non-exotic mammalian pets will be considered on a case-by-case basis; assessment should include the likelihood of contact with a mammal with monkeypox and the compatibility of clinical illness with monkeypox.

3 Includes living in a household, or originating from the same pet-holding facility as another animal with monkeypox.

4 Includes skin-to-skin or face-to-face contact.

Laboratory Criteria

- Isolation of monkeypox virus in culture.
- Demonstration of monkeypox virus DNA by polymerase chain reaction (PCR) 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.

Case Classification

Suspect

- Meets one of the epidemiologic criteria; AND
- Fever or unexplained rash AND 2 or more other signs or symptoms with onset of 1st sign or symptom ≤ 21 days after last exposure meeting epidemiologic criteria.

Probable

- Meets one of the epidemiologic criteria; AND
- Fever AND vesicular-pustular rash with onset of 1st sign or symptom ≤ 21 days after last exposure meeting epidemiologic criteria.

Confirmed

- Meets one of the laboratory criteria.

Exclusion Criteria

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

- An alternative diagnosis can fully explain the illness;¹

- The case was reported on the basis of primary or secondary exposure to an exotic or wild mammalian pet or a human subsequently determined not to have monkeypox, provided other possible epidemiologic exposure criteria are not present;
- A case without a rash does not develop a rash within ten days of onset of clinical symptoms consistent with monkeypox;² or
- The case is determined to be negative for non-variola generic orthopoxvirus by PCR testing of a well-sampled rash lesion by the approved Laboratory Response Network (LRN) protocol.

1 Factors that might be considered in assigning alternate diagnoses include the strength of the epidemiologic exposure criteria for monkeypox, the specificity of the diagnostic test, and the compatibility of the clinical presentation and course of illness for the alternative diagnosis.

2 If possible, obtain convalescent-phase serum specimen from these patients.

REFERENCES

CDC. Update: Multistate Outbreak of Monkeypox—Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003. *MMWR*. 2003; 52: 642–646.

“Fact Sheet: Smallpox Vaccine and Monkeypox.” Centers for Disease Control and Prevention. July 9, 2003. <www.cdc.gov/ncidod/monkeypox/smallpoxvaccine_mpox.htm>.

“Fact Sheet: What You Should Know about Monkeypox.” Centers for Disease Control and Prevention. June 12, 2003. <www.cdc.gov/ncidod/monkeypox/factsheet2.htm>.

Heymann, D., ed. *Control of Communicable Diseases Manual, 18th Edition*. Washington, DC, American Public Health Association, 2004.

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“Updated Interim CDC Guidance for Use of Smallpox Vaccine, Cidofovir, and Vaccinia Immune Globulin (VIG) for Prevention and Treatment in the Setting of an Outbreak of Monkeypox Infections.” Centers for Disease Control and Prevention. June 25, 2003. <www.cdc.gov/ncidod/monkeypox/treatmentguidelines.htm>.

“Updated Interim Infection Control and Exposure Management Guidance in the Health-Care and Community Setting for Patients with Possible Monkeypox Virus Infection.” Centers for Disease Control and Prevention. July 18, 2003. <www.cdc.gov/ncidod/monkeypox/infectioncontrol.htm>.

Monkeypox

LBOH Action Steps

This form does not need to be submitted to the MDPH with the case report form. It is for LBOH use and is meant as a quick-reference guide to monkeypox case investigation activities.

LBOH staff should follow these steps when monkeypox is suspected in the community. For more detailed information, including disease epidemiology, reporting, case investigation and follow-up, refer to the preceding chapter.

Note: Case investigation of suspect or confirmed cases of monkeypox in Massachusetts residents will, in most circumstances, be directed by the MDPH Division of Epidemiology and Immunization.

- ☐ Notify the MDPH Division of Epidemiology and Immunization, at (617) 983-6800 or (888) 658-2850, to report all confirmed or suspect case(s) of monkeypox.
- ☐ To report a suspect case of monkeypox in an animal, contact the Massachusetts Department of Agricultural Resources (MDAR), Division of Animal Health, Dairy Services and Biosecurity (DAH) at (617) 626-1795 or fax the information to the DAH at (617) 626-1850.
- ☐ Assist MDPH with obtaining clinical specimens needed for laboratory confirmation, if necessary.
- ☐ Assist MDPH with obtaining information needed to complete a MDPH *Generic Confidential Case Report Form*.
- ☐ Work with MDPH to institute isolation and quarantine requirements (*105 CMR 300.200*), as they apply to a particular case.
- ☐ Send the completed case report form (with laboratory results) to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS).