

Monkeypox (MPXV)

Investigative Guidelines

June 2022

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. To identify and prevent chains of person-to-person transmission.
2. To identify potential outbreaks of MPXV.
3. To better characterize the epidemiology of this infection.

1.2 Clinician Reporting Requirements

Report suspect, probable (presumptive), and confirmed cases to the state epidemiologist on call **immediately**, any time of day, at 971-673-1111.

1. **Collect and report** information about the ill person's clinical presentation and epi risk factors to inform the risk assessment and help determine whether the patient meets criteria for testing.
2. Share available photos of any rash via secure email or fax (971-673-1100).
3. Provide additional information to public health as requested during case investigation.

1.3 Local Public Health Authority (LPHA) Reporting and Follow-Up Responsibilities

1. **Report** suspect, presumptive, and confirmed cases to the state epidemiologist on call **immediately**, any time of day, at 971-673-1111. ACDP will conduct screening for testing approvals, except for Multnomah County residents, for whom screening will be done by Multnomah County Health Department Health Officers.
2. **Conduct case investigation** for presumptive and confirmed cases and contact tracing of their contacts.

2. THE DISEASE AND ITS EPIDEMIOLOGY

Overview

Monkeypox is a rare disease caused by infection with monkeypox virus (MPXV). The *Orthopoxvirus* genus, which includes MPXV, also includes variola virus (which causes smallpox), vaccinia virus (used in the ACAM2000[®] smallpox vaccine), and cowpox virus.

Historically, it has been a zoonotic disease and is endemic to forested areas of Central and West Africa. It is unclear which animals are reservoirs for monkeypox; however, rodents in endemic areas appear to be likely candidates.

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The name stems from the first recognized outbreak, in monkeys in a Danish laboratory in 1958. The first human case was identified in 1970 in the Democratic Republic of the Congo.

In May 2022, monkeypox emerged in humans in several countries without enzootic or endemic disease. CDC maintains a list of these countries:

<https://wwwnc.cdc.gov/travel/notices/alert/monkeypox>

2.1 Etiologic Agent

MPXV is a double-stranded DNA virus of the genus *Orthopoxvirus*. There are two genetic clades of MPXV: In an effort to avoid stigma and discrimination against people from the areas after which these two strains were named, we refer to them as MPXV-1, which is typically more severe and has a case-fatality rate of up to 10% and MPXV-2, which causes milder illness with an estimated case fatality rate in endemic countries of about 1%. Severe illness might be more common in certain groups. (See §2.7.1.) MPXV-1 is regulated as a Category A select biological agent; whereas MPXV-2 is regulated as Category B. The 2022 outbreak involving non-endemic countries is caused by MPXV-2

2.2 Description of Illness

The distinctive rash is typically preceded by a prodrome of fever, headache, and muscle aches, however in the 2022 outbreak, many cases have not reported prodromal symptoms. Lymphadenopathy is common and is a distinctive feature of monkeypox, compared to other common febrile rash illnesses. The prodrome is followed within 1–3 days by a rash, often on the face, spreading to the trunk and limbs. The rash evolves through several stages — starting with flat macules or patches that progress to firm, deep-seated papules, which then may fill with fluid or pus, and eventually scab and fall off. Lesions can display umbilication. Lesions typically develop simultaneously and evolve together on any given part of the body. The illness typically lasts 2–4 weeks.

2.3 Modes of Transmission

Historically, transmission has often resulted from animal exposure in endemic areas. Human-to-human spread is from direct or indirect contact with body lesions, including skin-to-skin contact with lesions, contact with contaminated objects such as towels, bedding, or other fomites containing such fluids, or potentially from large respiratory droplets. Transmission risk is low (basic reproduction number ~2) and usually requires close, prolonged contact.

2.5 Incubation Period

The typical incubation period is 7–14 days (range: 5–21 days).

2.6 Period of Communicability

The communicable period is from symptom onset until the lesions scab over and fall off.

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2.7 Medical Countermeasures

2.7.1 Treatment

Many people infected with monkeypox virus have mild, self-limited disease that resolves without treatment. However, antiviral treatment should be considered for people with severe disease requiring hospitalization. Immunocompromised people, children younger than eight years old, and those experiencing clinical complications might also be candidates for treatment, because they are considered at an increased risk for severe illness. Those who are pregnant or breastfeeding are also candidates, due to the risk of transmitting monkeypox to infants.

No medication is currently FDA-approved for treatment of MPXV infection. However, several are available from the Strategic National Stockpile (SNS) for the treatment of *Orthopoxviruses*, under Expanded Access Investigational New Drug (EA-IND) Protocols, including Tecovirimat, Cidofovir, and Vaccinia Immune Globulin Intravenous (VIGIV).

Clinicians seeking to initiate treatment for a presumptive or confirmed monkeypox patient can contact the ACDP on-call line at 971-673-1111 to request access through the CDC's SNS.

2.7.2 Vaccine (options, source, indications)

JYNNEOS™ (also known as Imvamune or Imvanex) is a replication-deficient vaccinia-based live virus vaccine approved for prevention of monkeypox infection. It may be used for post-exposure prophylaxis, and, in certain circumstances for pre-exposure protection of health professionals at increased risk of orthopox exposure. It is given subcutaneously as a 2-dose series (0 and 4 weeks). The Advisory Committee on Immunization Practices (ACIP) recommends that people whose jobs may expose them to *Orthopoxviruses* receive JYNNEOS. This includes laboratorians performing *Orthopoxvirus* testing, researchers handling animals or cultures that might be contaminated with *Orthopoxvirus*, clinicians administering ACAM2000®, and healthcare and public health professionals designated by a public health authority to be vaccinated for preparedness purposes. JYNNEOS may be ordered from the SNS for post-exposure prophylaxis of high-risk contacts and may be considered for intermediate-risk contacts as described in §5.2. It should be administered as soon as possible following exposure and ideally within 4 days in order to prevent illness. It may provide benefit in decreasing illness severity if given within 14 days of exposure. JYNNEOS is the preferred *Orthopoxvirus* vaccine, given its favorable adverse event profile.

ACAM2000® is a replication-competent vaccinia-based live virus vaccine. Because the vaccine is replication competent, it has a higher side effect profile and can result in virus spread to others. ACAM2000® should only be used if JYNNEOS is not available and if it is not contraindicated for the patient or individual at risk for *Orthopoxvirus* infection.

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Clinicians seeking vaccine for pre-exposure prophylaxis of individuals at risk for *Orthopoxvirus* infection or post-exposure prophylaxis for those with a high- or intermediate-risk exposure to a presumptive or confirmed monkeypox case may contact the ACDP on-call line at 971-673-1111 to request access through the CDC's SNS.

3. CASE DEFINITIONS, DIAGNOSIS AND LABORATORY SERVICES

3.1 Confirmed Case

- Demonstration of the presence of *monkeypox virus* DNA by polymerase chain reaction (PCR) testing or Next-Generation sequencing of a clinical specimen
OR
- Isolation of *monkeypox virus* in culture from a clinical specimen.

3.2 Probable (Presumptive) Case

- No suspicion of other recent *Orthopoxvirus* exposure (e.g., *Vaccinia virus* in *Orthopoxviruses* vaccination) **AND** demonstration of the presence of
 - *Orthopoxvirus* DNA by PCR testing of a clinical specimen
OR
 - *Orthopoxvirus* using immunohistochemical or electron microscopy testing methods
OR
 - Demonstration of detectable levels of anti-orthopoxvirus IgM antibody during the period of 4 to 56 days after rash onset.

3.3 Suspect Case

- New characteristic rash¹
OR
- Meets one of the epidemiologic criteria **AND** has a high clinical suspicion for monkeypox. Clinical suspicion may exist if presentation is consistent with illnesses confused with monkeypox (e.g., secondary syphilis, herpes, and varicella zoster).

Epidemiologic Criteria (within 21 days before illness onset)

- Reports having contact with a person with a similar appearing rash or who received a diagnosis of confirmed or presumptive monkeypox
OR
- Had close or intimate in-person contact with individuals in a social network experiencing monkeypox activity, this includes men who have sex with men (MSM) who meet partners through an online website, digital application ("app"), or social event (e.g., a bar or party)
- **OR**

¹ The characteristic rash associated with monkeypox lesions involve the following: deep-seated and well-circumscribed lesions, often with central umbilication; and lesion progression through specific sequential stages—macules, papules, vesicles, pustules, and scabs.

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- Traveled outside the U.S. to a country with confirmed cases of monkeypox or where monkeypox is endemic
- OR**
- Had contact with a dead or live animal or exotic pet that is an African endemic species or used a product derived from such animals (e.g., game meat, creams, lotions, powders, etc.).

3.4 Exclusion Criteria

A case may be excluded as a suspect, presumptive, or confirmed case if:

- An alternative diagnosis can fully explain the illness

OR

- An individual with symptoms consistent with monkeypox does not develop a rash within 5 days of illness onset

OR

- A case where high-quality specimens do not demonstrate the presence of *Orthopoxvirus* monkeypox virus or antibodies to *Orthopoxvirus*.

3.5 Services Available at the Oregon State Public Health Laboratories

OSPHL performs real-time PCR testing for *Orthopox* viruses.

Submission of specimens for testing requires approval from ACDP and, through them, from CDC. *Orthopox* virus testing could be considered for suspect cases **OR** if the clinician (particularly an infectious disease specialist) has a strong clinical suspicion for monkeypox. Clinical suspicion may exist if presentation is consistent with illnesses confused with monkeypox (e.g., primary or secondary syphilis, herpes, varicella zoster, or lymphogranuloma venereum). Patients with a characteristic rash should be considered for testing, even if other tests are positive as co-infections with STI and varicella zoster virus have been reported among monkeypox cases.

OSPHL's *Orthopox* DNA PCR assay will detect the following species but will not differentiate or report which species is present: variola; smallpox; vaccinia; cowpox; monkeypox; camelpox; ectromelia; gerbilpox.

- If *Orthopox* species are **detected** at OSPHL, identification of specific species (e.g., (monkeypox virus) will be completed through immediate specimen referral to CDC.
- If *Orthopox* species are **not detected** at OSPHL, no further testing will be conducted on specimens submitted.

Each specimen submission must be accompanied by the following two forms:

1. One per specimen: OSPHL Virology/Immunology Test Request Form (www.bitly.com/phl-forms) Specify the location of the lesion collected in the *Specimen Source* section.
2. One per patient: [CDC 50.34 Specimen Submission Form](#). Completing this form will ensure public health has all information needed to forward specimens to CDC for confirmation, if indicated.

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3.6 Specimen Collection

Have the submitting facility **collect**, prepare, and store specimens for transport to OSPHL if testing is approved.

Complete instructions are available on the [OSPHL Test Menu for Orthopox Virus, Real-Time PCR](#). CDC's [Monkeypox – Laboratory Procedures](#) webpage might also be useful.

1. More than one lesion should be sampled, preferably from different anatomic sites or from lesions with different appearances. Collect paired swabs from each lesion sampled. Swab or brush lesion vigorously with two dry swabs. Place each swab in a separate, sterile container.
2. Use sterile synthetic swabs, such as polyester, to collect. DO NOT use cotton swabs or wooden-shafted swabs. DO NOT place swab in transport medium or saline.
3. Label each specimen with at least two unique patient identifiers **and** a brief description of anatomic site of the lesion.
4. Refrigerate or freeze within one hour after collection. Refrigerate at 2-8° C.

3.7 Specimen Transport

Transport specimens to OSPHL promptly. **Note: OSPHL cannot receive specimens on weekends or state holidays.**

1. Specimens should be transported using fully frozen cold packs to maintain necessary temperature during transit. Specimens must be *tested* within 7 days of collection.
2. If specimens cannot be tested within 7 days, store frozen (-20°C or below) and ship to OSPHL to maintain frozen temperatures during transit. If shipping on dry ice, store at -70°C prior to shipping.

Per CDC, specimens may be packaged and shipped to OSPHL as Category B.

4. ROUTINE CASE INVESTIGATION

4.1 Case Investigation

If ACDP and CDC approve testing, enter a new *Orthopox* (subtype monkeypox) suspect case into Orpheus. If OSPHL testing identifies the presence of *Orthopox* virus, change the case status in Orpheus to “Presumptive”, the designation for probable case, and conduct a case investigation. If CDC subsequently confirms presence of monkeypox, change the case status in Orpheus to “Confirmed.” If CDC does not confirm the presence of monkeypox, keep the case status as presumptive.

During the case investigation, ask about 1) timeline and progression of signs and symptoms, 2) recent domestic or international travel history and places visited, 3) any contact with a person ill with confirmed or presumptive monkeypox or symptoms compatible with it, 4) any intimate contact with persons and any

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contacts with their clothing, skin lesions, bodily fluids, soiled linens, or dressings, and 5) any exposures to animals or byproducts of animals originating from monkeypox-endemic countries in the 21 days before illness onset. Ask cases to describe their symptoms and record in Orpheus.

Complete the CDC's Orthopox case investigation form and attach the form as a document in Orpheus for the case. If consultation or support is needed during the case investigation or contact tracing, contact the ACDP on-call line at 971-673-1111.

4.2 Contact Tracing

Identify anyone exposed to a confirmed or presumptive monkeypox case-patient. Ask about family, friends, sexual contacts, work/school contacts, and any medically fragile persons who might have been exposed. A person is considered exposed if, during the time that the confirmed or presumptive case was ill and still had a rash, any of the following occurred:

- Had contact with a confirmed or presumptive case's skin or bodily fluids
- Had oral, anal, or vaginal sex with a confirmed or presumptive case
- Had contact with the clothing, bedding, dressings, or other garments or personal items, including fetish gear and sex toys, with a confirmed or presumptive case
- Was otherwise within 6 feet of an unmasked confirmed or presumptive case without wearing a surgical mask
- Was in the same room as the confirmed or presumptive case without use of eye protection.
- Had contact between the person's clothing and the confirmed or presumptive case's skin lesions, bodily fluids, soiled linens, or dressings during the time that the case had a rash while wearing gloves but not wearing a gown.

Request from the confirmed or presumptive case the name, age, and contact information of any person meeting the exposure criteria. Enter the information into Orpheus as contacts to the case. Call each of the identified contacts to conduct a risk assessment, as described in **§5.2**.

5. CONTROLLING FURTHER SPREAD

5.1 Isolation and Prevention

All presumptive and confirmed cases must isolate until they meet criteria for discontinuation of isolation. Household members who are not ill should limit their contact with the person with monkeypox. Skin lesions should be covered to the extent possible (e.g., long sleeves and pants) to minimize contact with others. People with monkeypox should avoid contact with animals, including pets, if possible. Cases must stay home and away from other people until a clinician confirms that all lesions have resolved, the scabs have fallen off, and a fresh layer of intact skin has formed. If a confirmed or presumptive case needs to

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seek in-person medical care, contact the clinician in advance to indicate confirmed or presumptive monkeypox case status.

People with monkeypox should wear a surgical mask when they are not isolated. Disposable gloves should be worn for direct contact with lesions and disposed of after use. Hand hygiene with soap and water or an alcohol-based rub should be performed by cases and by any individuals who touch lesion material, clothing, linens, or environmental surfaces in contact with lesion material.

For home isolation of cases, laundry may be washed in a standard washing machine with warm water and detergent. Care should be used when handling soiled laundry to avoid direct contact with contaminated material. Dishes and other eating utensils should not be shared. Soiled dishes and eating utensils should be washed in a dishwasher or by hand with warm water and soap. Contaminated surfaces should be cleaned and disinfected with standard household cleaning/disinfectants. More resources on infection control for home isolation can be found at: www.cdc.gov/poxvirus/monkeypox/clinicians/infection-control-home.html.

Home waste disposal for monkeypox patients isolating at home should continue as normal, using existing municipal waste management systems. The person infected with monkeypox should use a dedicated, lined trash receptacle in the room where they are isolating. Any gloves, bandages, or other waste and disposable items that have been in direct contact with skin should be sealed in plastic bags and thrown away in the dedicated trash receptacle. The person infected with monkeypox or other household occupants should use gloves when removing garbage bags and handling and disposing of trash.

5.2 Assess the risk to identified contacts

LPHAs should conduct a risk assessment for each identified contact using the following criteria:

A. **High-risk** exposures include any of the following:

1. Unprotected contact between a person's skin or mucous membranes and the skin, lesions, or bodily fluids from a case or contaminated materials, **OR**
2. Being inside the case's room or within 6 feet of a patient during any procedures that may create aerosols without wearing an N95 or equivalent respirator and eye protection, **OR**
3. Exposure that, at the discretion of public health authorities, was recategorized to this risk level because of unique circumstances.

Management: Monitoring as described in §5.3; post-exposure vaccination recommended.

B. **Intermediate-risk** exposures include any of the following:

1. Being within 6 feet of an ill, unmasked case for **at least three hours** without wearing a surgical mask, **OR**

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2. Contact between the person's clothing and the case's skin lesions, bodily fluids, soiled linens, or dressings during the time that the case had a rash while wearing gloves but not wearing a gown, **OR**
3. Exposure that, at the discretion of public health authorities, was recategorized to this risk level because of unique circumstances.

Management: Monitoring as described in §5.3; post-exposure vaccination through individual-informed clinical decision-making.

C. **Low-uncertain** exposures include either of the following:

1. Being within 6 feet an unmasked case for **less than three hours** without wearing a surgical mask, **OR**
2. Being in the same room as the case without wearing eye protection.

Management: Monitoring as described in §5.3; post-exposure vaccination not indicated.

5.3 Monitor for Symptoms

Develop a plan with any contacts of persons or animals confirmed to have monkeypox to monitor for fever and symptoms for 21 days after the last exposure. Contacts who remain asymptomatic can continue routine daily activities (e.g., work, school, sexual activity). Contacts should not donate blood, cells, tissue, breast milk, semen, or organs while they are under symptom surveillance. For high-risk contacts as defined in §5.2, direct, daily symptom checks by public health via phone or email can be considered but aren't required.

Instruct contacts to monitor for symptoms and to check their temperature twice daily. Signs and symptoms that should prompt a call to public health include fever $\geq 100.4^{\circ}\text{F}$ (38°C), chills, swelling of lymph nodes, or new skin rash. If fever or rash develop, contacts should self-isolate and contact their LPHA immediately.

5.4 Post-Exposure Prophylaxis

As noted, those with a high- or intermediate-risk exposure might consider post-exposure prophylaxis as described in §2.7 upon consultation with their clinician or a public health clinician. If the clinician requests PEP, the clinician or LPHA should contact the state epidemiologist on-call to verify the risk assessment and to submit a request for access to Medical Countermeasures from the CDC's SNS.

UPDATE LOG

June 2022 – Original (Bonner, DeBess, Leman, Sutton)