Mpox

Investigative Guidelines

December 2024

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. To identify and stop chains of person-to-person transmission.
2. To identify potential outbreaks of mpox.
3. To characterize the epidemiology of this infection in Oregon.
4. To identify communities most at risk for disease or severe illness to inform equity-centered outreach efforts, in support of OHA's strategic goal of eliminating health inequities in Oregon by 2030.

1.2 Laboratory and Clinician Reporting Requirements

Healthcare providers and laboratories are required to report probable (presumptive) and confirmed cases of mpox to the local public health authority (LPHA) immediately. Healthcare providers are also asked to report clinically diagnosed cases of mpox and patients empirically treated with tecovirimat as suspect cases.

1. Collect and report information about the ill person's clinical presentation and epidemiologic risk factors to inform risk assessment.
2. 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 all confirmed and presumptive cases not already transmitted through electronic lab reporting (ELR; e.g., cases identified through clinical evaluation or in advance of ELR) by entering them into Orpheus as disease "Mpox."
2. Interview presumptive and confirmed cases and trace their contacts.
3. Provide education to confirmed and presumptive cases on best practices to prevent disease spread, including self-isolating to limit additional close contacts, informing their close contacts about monitoring for symptoms, testing and seeking care when appropriate.
4. Encourage symptomatic persons to be tested and follow isolation recommendations; encourage high-risk close contacts of confirmed and presumptive cases of mpox to be vaccinated.
5. Consult with OHA as needed about patient isolation and protection of contacts including healthcare personnel, strategies for vaccination, and access to therapeutics.

2. THE DISEASE AND ITS EPIDEMIOLOGY

Overview

Mpox is caused by infection with monkeypox virus, an orthopoxvirus. The *Orthopoxvirus* genus also includes variola virus (which causes smallpox), vaccinia virus (used in the ACAM2000® smallpox vaccine), and cowpox virus.

Historically, mpox, formerly known as monkeypox or hMPXV, has been a zoonotic disease and is endemic to forested areas of Central and West Africa. Reservoir species in endemic areas aren't well documented, but rodents are prime suspects. The name "monkeypox" stemmed from the first recognized outbreak, which occurred among monkeys in a Danish laboratory in 1958. The first human case was identified in 1970.

In May 2022, mpox emerged in humans in several countries without prior enzootic or endemic disease. While anyone may be infected with mpox if they have close contact with the affected skin of an infected person, regardless of gender or sexual orientation, this outbreak primarily affected men who have sex with men and transgender and nonbinary people in the same sexual networks. Household transmission has also been documented. Mpox has continued to circulate in humans at a low level in many countries, including the United States, since this emergence.

2.1 Etiologic Agent

Mpox virus is a double-stranded DNA virus of the genus *Orthopoxvirus*. There are two distinct strains. Clade I (formerly known as the Congo Basin or Central African Clade) is typically more severe and has a case-fatality rate of up to 10%. Clade II (formerly known as the West African Clade) 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 **§2.6.1**). Clade I is regulated as a Category A select biological agent, whereas Clade II is regulated as Category B. The 2022 outbreak involving non-endemic countries was caused by viruses within a Clade II subclade, Clade IIb.

2.2 Description of Illness

Historically, the distinctive rash has typically been preceded by fever, headache, and muscle aches. However, in the 2022 outbreak, many patients have not reported prodromal symptoms. Lymphadenopathy is common and is a distinctive feature of mpox compared to other common febrile rash illnesses. When the prodrome is present, it is typically followed in 1–4 days by a rash.

In cases during and since the 2022 outbreak, lesions are often present on the genitals or the perianal area. Scattered lesions may erupt elsewhere, including on the face, trunk and limbs. The often painful rash typically evolves through several stages—beginning as flat macules or patches that progress to firm, deep-seated papules that then may fill with fluid or pus, eventually scabbing and crusting over. Lesions can display umbilication. The illness typically lasts 2–4 weeks. Illness in

previously vaccinated patients is usually less severe, with fewer lesions and reduced systemic symptoms.[1,2] Mpox may resemble other rash illnesses including primary or secondary syphilis, herpes simplex infection, chickenpox, or zoster.

2.3 Modes of Transmission

Historically, transmission of mpox often resulted from animal exposure in endemic areas. Since 2022, most cases have resulted from direct, prolonged skin-to-skin contact with another person's active lesions. Transmission could theoretically occur from contact with contaminated objects (e.g., towels, bedding, or other fomites containing body fluids or skin scrapings) or via prolonged face-to-face close contact (i.e., >3 hours, within 6 feet) with an ill person. Transmission risk overall is low (basic reproduction number ~2), and the greatest risk is from intimate, skin-to- skin contact.

2.4 Incubation Period

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

2.5 Period of Communicability

The known communicable period is from symptom onset until the lesions scab over and fall off leaving a healed and fresh layer of skin. Transmission may be possible before symptom onset, particularly when individuals have delayed recognition of symptoms such as with early internal lesions.

2.6 Treatment, Prevention, and Limitation of Spread

2.6.1 Treatment

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

No medication is currently FDA-approved for treatment of mpox. 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 (TPOXX), Brincidofovir, Cidofovir, and Vaccinia Immune Globulin Intravenous (VIGIV).

A randomized controlled trial of tecovirimat showed no difference in time to lesion resolution or pain reduction for patients with mild to moderate mpox.[3] The role of tecovirimat for patients with severe disease or at high risk for severe disease was not established through this trial. For patients meeting EA-IND criteria, tecovirimat can be obtained through CDC's Emergency Operations Center in conjunction with OHA. Information on the EA-IND can be found on CDC's website at Tecovirimat (TPOXX) for Treatment of Mpox. Tecovirimat treatment may be started empirically. Some evidence indicates that tecovirimat is most effective when started as soon as possible after symptom onset, especially for people with immunocompromising conditions.[4,5]

2.6.2 Vaccine (options, source, indications)

Two vaccines against orthopoxviruses, including mpox, are available: JYNNEOS and ACAM2000. JYNNEOS (also known as Imvamune or Imvanex) is a replication-deficient vaccinia-based live virus vaccine for prevention of mpox infection. It is recommended as a 2-dose series with doses given 4 weeks apart. It is typically given subcutaneously but may also be given intradermally in certain circumstances. JYNNEOS is the preferred orthopoxvirus vaccine given its favorable adverse event profile.

ACAM2000 is a replication-competent attenuated vaccinia-based live virus vaccine. Because the vaccine virus can replicate, 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 it is not contraindicated for the patient or individual at risk for mpox infection.

JYNNEOS can be given as either pre-exposure prophylaxis or post-exposure prophylaxis (PEP). JYNNEOS is recommended as pre-exposure prophylaxis for individuals at increased risk of exposure to mpox, as outlined in the CDC mpox vaccination recommendations. Current OHA guidance on use and administration of JYNNEOS is available in OHA's Model Immunization Protocol for mpox.

JYNNEOS can be used as post-exposure prophylaxis (PEP) for contacts who have not previously received 2 doses. Assessing which contacts should receive PEP is described in **§5.2**. For PEP the initial dose should be administered as soon as possible following exposure, ideally within 4 days. After 4 days, PEP is still recommended as it may decrease illness severity if given within 14 days of exposure.

As of April 1, 2024, JYNNEOS is commercially available.

3. CASE DEFINITIONS, DIAGNOSIS AND LABORATORY SERVICES

3.1 Confirmed Case

- Detection of mpox (monkeypox) virus DNA by molecular testing in a clinical specimen **OR**
- Isolation of mpox (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 orthopoxvirus vaccine) **AND** detection of
  - Orthopoxvirus DNA by molecular testing in a clinical specimen
    OR
  - Orthopoxvirus in a clinical specimen using immunohistochemical or electron microscopy testing
    OR
  - Anti-orthopoxvirus IgM antibody in serum drawn 4 to 56 days after rash onset, with no vaccination against smallpox or mpox in the preceding 60 days.

3.3 Suspect Case

- New rash characteristic of mpox*
  OR
- Meets one of the epidemiologic criteria below, in a patient in whom mpox is highly suspected clinically. Clinical suspicion may exist if presentation is consistent with illnesses that present similarly to mpox (e.g., secondary syphilis, herpes, and varicella zoster).

  Epidemiologic Criteria (within 21 days before illness onset)
  - Contact with a person with a similar-appearing rash or who received a diagnosis of confirmed or presumptive mpox
    OR
  - Close or intimate in-person contact with individuals in a social network experiencing mpox activity. Such networks include men who have sex with men (MSM) who meet partners through an online website, app, or social event (e.g., a bar or party); or any cohort defined by public health authorities as experiencing mpox activity.
    OR
  - Residence in or travel to a country where mpox is endemic.
    OR
  - 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.).

* Mpox lesions are typically deep-seated and well-circumscribed, often with central umbilication. The lesions generally progress through specific sequential stages—macules, papules, vesicles, pustules, and scabs.

3.4 Non-mpox Orthopoxviruses

If you have reason to suspect a patient is infected with an orthopoxvirus species other than mpox virus, contact the OHA Acute and Communicable Disease Prevention Section immediately, day or night, at 971-673-1111. This may apply in situations where there is very low suspicion for mpox, such as patients reporting no skin-to-skin contact during their exposure window or those with no plausible contact with people in communities where mpox is known to be circulating. Suspicion for non-mpox orthopoxviruses may also exist in the setting of potential exposure to another orthopoxvirus, such as recent vaccination with ACAM2000 or close contact with someone who was vaccinated with ACAM2000. Concern for non-mpox orthopoxviruses also includes cases who are orthopoxvirus-positive, but mpox virus-negative. In such cases, consult with ACDP immediately to determine the best course of action.

In the rare situation where you suspect mpox virus clade I, such as in patients with recent travel to an area with an outbreak of clade I, call ACDP immediately to coordinate clade-specific testing and public health follow-up. Information on the clade I mpox outbreak that began in 2023 is available from CDC at Clade I Mpox Outbreak Originating in Central Africa.

3.5 Laboratory Testing

3.5.1 Test Methods

Available testing for orthopoxviruses and mpox virus is predominantly polymerase chain reaction (PCR). Some assays test only for orthopoxvirus broadly, while others additionally test specifically for mpox virus. Serology is available at CDC, but interpretation of results is difficult and requires consultation with OHA. No commercial serologic tests are available. If there is suspicion for clade I mpox, clade-specific testing should be arranged through OHA.

3.5.2 Testing at Commercial Laboratories

Commercial laboratories should be used when available; many offer orthopoxvirus PCR testing. Healthcare providers should follow the specimen collection, handling, and transport guidance of the laboratory that will test the specimens.

3.5.3 Services Available at the Oregon State Public Health Laboratory

OSPHL will prioritize orthopoxvirus testing for patients and healthcare facilities without access to commercial laboratory testing services. OSPHL performs real-time PCR testing for orthopoxviruses but does not offer species-level identification. Specimens that meet the submission criteria may be submitted; approval from public health is not required.

Collect, store, and transport specimens in accordance with OSPHL's Lab Test Menu for *Orthopoxvirus* Real-Time PCR. Complete the Virology/Immunology Test Request Form, **one per specimen** submitted. Specify the **location of the lesion** collected in the *Specimen Source* section.

OSPHL utilizes CDC's orthopoxvirus PCR procedure and CDC's FDA-cleared non-variola orthopoxvirus DNA PCR assay. Both assays will detect the members of the *Orthopoxvirus* genus such as vaccinia, cowpox, mpox, camelpox, ectromelia, and gerbilpox, but neither assay will differentiate among the species. Neither test will detect Molluscum contagiosum or Orf viruses, which are members of different genera of poxviruses.

OSPHL orthopoxvirus PCR results may be the only result received from OSPHL. OSPHL no longer sends every orthopoxvirus-positive PCR to CDC for speciation. CDC notes that mpox is currently the only orthopoxvirus species circulating in the United States. In alignment with CDC guidance, OSPHL will send a subset of orthopoxvirus-positive specimens to CDC for public health surveillance. If testing to the species level is needed (e.g., if there is suspicion for non-mpox orthopoxvirus), please consult with ACDP to request forwarding to CDC.

3.5.4 Clinical Considerations for Testing

Orthopoxvirus testing may be considered for suspect cases or if a clinician has a strong clinical suspicion for mpox. Clinical suspicion may exist if presentation is consistent with illnesses that present similarly to mpox (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 mpox cases. Mpox specimen collection guidance is available from CDC. Furthermore, all patients tested for mpox should be offered comprehensive sexual health screening, including HIV, syphilis, and gonorrhea and chlamydia testing at exposed sites (urogenital, rectal, pharyngeal) regardless of condom use.

3.5.5 Test Result Interpretation

Most laboratories offering testing use assays for the *Orthopoxvirus* genus broadly, rather than the mpox species specifically, though some (e.g. Quest Diagnostics) test for both. Patients with specimens positive only for genus "orthopoxvirus" are presumptive cases, and those with specimens also positive for mpox (monkeypox)-specific sequence are confirmed cases. Review laboratory results closely to determine whether they warrant a presumptive or confirmed case status.

If orthopoxvirus is detected and none of the situations in **§3.4** apply, given available epidemiologic data, it is reasonable to presume that this represents mpox infection and begin public health interventions as outlined in this investigative guideline.

4. ROUTINE CASE INVESTIGATION

4.1 Case Investigation

If commercial laboratory or CDC testing identifies either orthopoxvirus or mpox virus, create a case in Orpheus and investigate. If a clinician reports a clinically diagnosed case of mpox, create a suspect case. At LPHA discretion, if mpox is highly suspected, proceed with case investigation until lab results are received to

facilitate timely PEP and contact tracing. If testing for orthopoxvirus genus is positive and testing for mpox species is negative, alert ACDP for possible non-mpox orthopoxvirus.

During the case investigation, complete the Orpheus interview module, including questions about the following: 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 mpox or symptoms compatible with it, and 4) any intimate contact with persons and any contacts with their clothing, skin lesions, bodily fluids, soiled linens, or dressings.

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 mpox case. Ask about family, friends, sexual contacts, work or school contacts, and any medically fragile persons who might have been exposed. LPHAs are also encouraged, at their discretion, to follow up on suspect cases prior to receiving test results to facilitate timely PEP when indicated. A person is considered exposed if, during the time that the confirmed or presumptive case was ill and still had a rash or in the 5 days before symptom onset (see note), any of the high- or intermediate-risk exposures described in **§5.2** occurred.

Request from the case the name, age, and contact information of any person meeting the exposure criteria. Enter the information into Orpheus as contacts to the case. Contact each of the identified contacts to conduct a risk assessment, as described in **§5.2**, and facilitate PEP where indicated.

NOTE: Although mpox is considered transmissible from the time of symptom onset, cases may not always notice or accurately recall their earliest symptoms (e.g., rash not readily visible to case, imprecise recollection of timing). If a case had high-risk contact with individuals in the 5 days preceding symptom onset, they may, at LPHA discretion, be considered a contact and eligible for PEP.

5. CONTROLLING FURTHER SPREAD

5.1 Isolation and Prevention

All confirmed and presumptive cases of mpox should isolate to the best of their ability until they meet criteria for discontinuation of isolation. Isolation may be discontinued when a case has been afebrile for at least 24 hours, any systemic symptoms are resolved, and all lesions have crusted over and new, healed skin is in their place. Isolation is also recommended for suspect cases as defined in **§3.3** until PCR results come back negative. Full CDC guidance on home isolation can be found on CDC's website at: Isolation and Infection Control At Home.

5.2 Assessing the Risk to Identified Contacts

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

Risk level	Exposure scenario	PEP (see §2.6)	Monitor?
High	• Contact between an exposed individual's broken skin or mucous membranes and the lesions, scabs, or bodily fluids of a person with mpox. • Contact between an exposed individual's broken skin or mucous membrane with materials that have contacted the skin lesions or bodily fluids of the person with mpox. • Any sexual or intimate contact involving mucous membranes, such as the mouth, genitalia, vagina, or anus.	Recommended	Yes
Intermediate	• Contact between an exposed individual's intact skin and the lesions, mucous membranes, or bodily fluids from a person with mpox. • Contact between an exposed individual's intact skin with materials (e.g., linens, clothing, sex toys) visibly contaminated with body fluids or lesions, exudates, or crusts from a person with mpox without having been disinfected† or laundered. • Being within 6 feet of a person with mpox who has laryngeal disease, cough, respiratory symptoms, or oral lesions for an extended period.	Consider, with individual informed clinical decision making	Yes
Uncertain to minimal	• Entry into the living space of a person with mpox regardless of whether the person with mpox is present (risk classification may vary depending on the extent of the exposed person's interaction) • Contact between a person's intact skin or clothing and the intact skin or clothing of a person with mpox who has completely covered lesions (e.g., bandaged, covered with clothing).	No	At discretion of public health authority
None	• No contact with the person with mpox, their potentially contaminated materials, and only transient time spent within 6 feet of the person with mpox.	No	No

NOTE: Exposures in any risk level may, at the discretion of public health authorities or the treating physician, be recategorized because of unique circumstances of an exposure incident.

5.3 Monitor for Symptoms

Develop a plan with any contacts of persons or animals confirmed to have mpox 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 ≥100.4°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. Medical evaluation should follow, with notification to the evaluating provider prior to examination that the person has been exposed to mpox to inform evaluation and allow for the use of appropriate personal protective equipment.

5.4 Post-Exposure Prophylaxis

As noted, those with a high- or intermediate-risk exposure who have not previously received 2 doses of JYNNEOS may consider post- exposure prophylaxis as described in **§2.6**.

UPDATE LOG

December 2024. Updated assessing the risk to contacts table to align with CDC updates. Added information on results of STOMP trial. Removed references to OHA supply and request process for JYNNEOS and tecovirimat (TPOXX) and to STOMP trial. Replaced reference to OHA Interim Jynneos Guidance with CDC vaccination recommendations. Updated CDC hyperlinks. (Sam Hawkins)

August 2024. Added recommendations for suspect case reporting, examples of situations concerning for other orthopoxviruses, and clarification that PEP is not recommended for contacts who have previously received two doses of JYNNEOS. Changed terminology from monkeypox to mpox. Modifications throughout to reflect ongoing low levels of transmission globally and continued lack of evidence for respiratory transmission. Moved risk assessment to table. (Meagan McLafferty, Sam Hawkins)

August 22, 2022. Expanded laboratory testing section, revised contact tracing and risk assessment sections to align with updated CDC guidance. (Meagan McLafferty, Kelly Cogswell, Dean Sidelinger).

August 8, 2022. Significant modifications throughout. Shifted reporting to LPHA first; no longer require reporting of suspect cases; no need to send rash photos, Commercial laboratories now testing; ACDP not required to approve OSPHL test requests; updates to disease transmission, outbreak information, risk assessment. (Meagan McLafferty, Richard Leman, Kelly Cogswell, Amanda Faulkner, Dean Sidelinger, Emilio DeBess, Paul Cieslak).

June 2022. Created. (Bonner, DeBess, Leman, Sutton)

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