Monkeypox (hMPXV)

Investigative Guidelines

August 22, 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 monkeypox.
3. To better characterize the epidemiology of this infection.
4. To identify communities most at risk for disease or severe illness and inform equity-centered outreach.

1.2 Laboratory and Clinician Reporting Requirements

Healthcare providers and laboratories are required to report probable (presumptive) and confirmed cases of monkeypox to the local public health authority (LPHA) immediately.

1. Collect and report information about the ill person's clinical presentation and epidemiological 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 electronically (e.g., cases identified through clinical evaluation or in advance of ELR) by entering them into Orpheus with disease "Orthopox" and subtype "Monkeypox."
2. Interview presumptive and confirmed cases and trace their contacts.
3. Provide education for 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 monkeypox to be vaccinated.
5. Consult with OHA as needed about patient isolation and protection of contacts, including healthcare personnel, and about strategies for vaccination, and access to therapeutics.

2. THE DISEASE AND ITS EPIDEMIOLOGY

Overview

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

Historically, monkeypox 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" stems 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, monkeypox emerged in humans in several countries without enzootic or endemic disease. Anyone may be infected with monkeypox if they have close contact with the rash of an infected person, regardless of gender identity or sexual orientation. In the current outbreak, many of those affected had intimate, skin-to-skin contact, frequently among men who have sex with men. Household transmission has also been documented.

2.1 Etiologic Agent

Monkeypox is a double-stranded DNA virus of the genus *Orthopoxvirus*. There are two distinct strains. To avoid stigma and discrimination against people from the areas after which these two strains originally 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

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 monkeypox compared to other common febrile rash illnesses. When the prodrome is present, it is typically followed within 1–3 days by a rash.

In the current outbreak lesions often are present on the genitals or in the perianal area, and there may be scattered lesions elsewhere, including the face, trunk and limbs. The rash typically 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 crust over. Lesions can display umbilication. The illness typically lasts 2–4 weeks.

2.3 Modes of Transmission

Historically transmission of monkeypox has often resulted from animal exposure in endemic areas; however, most cases in the current outbreak have resulted from direct, prolonged skin-to-skin contact with active lesions. Although not observed in the current outbreak, theoretically, contact with contaminated objects (e.g., towels, bedding, or other fomites containing body fluids) or prolonged face-to-face close contact (i.e., >3 hours, within 6 feet) with an ill person could result in transmission. Transmission risk overall is low (basic reproduction number ~2), and the greatest risk occurs following intimate, skin-to- skin 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 leaving a healed and fresh layer of skin.

2.7 Treatment, Prevention, and Limitation of Spread

2.7.1 Treatment

Many people infected with monkeypox have relatively mild, self-limited disease that resolves without treatment. However, antiviral treatment should be considered for people with severe disease requiring hospitalization and 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 monkeypox to infants.

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

Clinicians seeking to initiate treatment for a presumptive or confirmed monkeypox patient can order tecovirimat through OHA using the following link.

2.7.2 Vaccine (options, source, indications)

JYNNEOS™ (also known as Imvamune or Imvanex) is a replication-deficient vaccinia-based live virus vaccine for prevention of monkeypox infection. It may be used for post-exposure prophylaxis (PEP), and in certain circumstances, for pre-exposure protection (PrEP) of health professionals or others at increased risk of *Orthopoxvirus* exposure. It is given subcutaneously or intradermally, typically as a 2-dose series (0 and 4 weeks). Current OHA guidance on use and administration of JYNNEOS is available in OHA's Model Immunization Protocol for monkeypox, formerly known as standing orders.

Further details for PEP and patient eligibility are available in OHA's Interim hMPXV Vaccine Guidance.

For post-exposure prophylaxis (PEP), the initial dose 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. Given current supply constraints, first doses should be prioritized, with second doses administered 2-3 months later rather than at 28 days except for people who are immunocompromised or pregnant, who should receive their second dose four weeks after the initial dose. 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 monkeypox infection.

LPHAs, clinics and health systems seeking vaccine may order JYNNEOS through OHA using the following link. Distribution of vaccine is prioritized to ensure access to those who are the highest risk of infection. OHA is taking an intersectional approach to ensure equitable access to vaccine by coordinating with LPHAs, community-based organizations, and health care partners.

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 rash[1]
  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 with similar presentations to 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
  - 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 Non-monkeypox *Orthopoxviruses*

If you have reason to suspect a patient is infected with an *Orthopoxvirus* species other than monkeypox, contact the OHA Acute and Communicable Disease Prevention Section immediately, day or night, at 971-673-1111.

3.6 Laboratory Testing

3.6.1 Test Methods

Available testing for *Orthopoxviruses* and monkeypox virus is predominantly

[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.

polymerase chain reaction (PCR). Serology is available at CDC but is extremely limited and requires consultation with OHA. There are no commercial serology tests known to be available.

3.6.2 Testing at Commercial Laboratories

Commercial laboratories should be used when available. We are aware of the following commercial laboratories offering testing for *Orthopoxvirus*: Aegis Scientific, ARUP, LabCorp, Mayo Clinic Labs, Molecular Vision Lab, Quest Diagnostics, and Sonic Healthcare. Healthcare providers should follow the specimen collection, handling, and transport guidance of the laboratory that will test the specimens.

3.6.3 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*. Submission of specimens for testing does not require approval from public health.

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 *Orthopox* genus such as vaccinia, cowpox, monkeypox, camelpox, ectromelia, and gerbilpox, but neither assay will differentiate between the species. Neither test will detect molluscum or orf virus.

OSPHL *Orthopoxvirus* PCR results may be the only result received. OSPHL no longer sends every *Orthopoxvirus*-positive PCR to CDC for speciation. CDC notes that monkeypox is currently the only *Orthopoxvirus* species circulating in the United States. In alignment with CDC guidance, OSPHL will send a sub-set of *Orthopoxvirus*-positive specimens to CDC for public health surveillance.

3.6.4 Clinical Considerations for Testing

Orthopoxvirus testing could be considered for suspect cases OR if the clinician has a strong clinical suspicion for monkeypox. Clinical suspicion may exist if presentation is consistent with illnesses with similar presentations to 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. Furthermore, all patients tested for monkeypox 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.

3.6.5 Test Result Interpretation

Most laboratories offering testing use assays for the *Orthopoxvirus* genus broadly,

rather than the monkeypox species specifically, though some (e.g. Quest Diagnostics) test for both. Patients with specimens positive for *Orthopoxvirus* are presumptive cases, and those with specimens positive for both *Orthopoxvirus* and monkeypox virus are confirmed cases. When reading a laboratory result, look closely to determine whether the specimen warrants a presumptive or a confirmed case status.

If *Orthopoxvirus* is detected, given epidemiologic data currently available, it is reasonable to assume that this represents monkeypox 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 the presence of monkeypox virus (in addition to *Orthopoxvirus*), create a confirmed case in Orpheus and conduct case investigation. If OSPHL or commercial laboratory testing identifies only the presence of *Orthopoxvirus*, create a presumptive case and proceed with case investigation. If CDC subsequently confirms presence of monkeypox, change the case status in Orpheus to "Confirmed." (Few specimens are likely to have confirmatory testing.) If CDC does not confirm the presence of monkeypox, keep the case status as presumptive.

During the case investigation, complete the Orpheus interview, which includes 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 monkeypox 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. Ask cases to describe their symptoms and record in Orpheus.

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 (see note), any of the high- or intermediate risk exposures described in **§5.2** occurred.

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. Contact each of the identified contacts to conduct a risk assessment, as described in **§5.2.**

NOTE: While monkeypox 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 be considered a contact and/or eligible for PEP at LPHA discretion.

5. CONTROLLING FURTHER SPREAD

5.1 Isolation and Prevention

Home isolation precautions are recommended for all suspect monkeypox cases (those awaiting *Orthopoxviru*s testing results) until PCR results come back negative. All presumptive and confirmed cases must isolate until they meet criteria for discontinuation of isolation. A handout describing home isolation precautions is available in multiple languages at https://www.oregon.gov/oha/PH/Monkeypox/Pages/healthcare-providers-clinical-laboratories.aspx under Guidance for Patient Isolation. Full CDC guidance on home isolation can be found at https://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 Assessing 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. Contact between an exposed individual's broken skin or mucous membranes and the lesions, scabs, or bodily fluids of a person with monkeypox, **OR**
   2. Any sexual or intimate contact involving mucous membranes (e.g., kissing, oral-genital, oral-anal, vaginal, or anal sex (insertive or receptive) with a person with monkeypox, **OR**
   3. Contact between an exposed individual's broken skin or mucous membranes with materials (e.g., linens, clothing, objects, sex toys) that have contacted the skin lesions or bodily fluids of a person with monkeypox (e.g., sharing food, handling or sharing of linens used by a person with monkeypox without having been disinfected or laundered).

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

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

1. Contact between an exposed individual's intact skin and the lesions or bodily fluids from a person with monkeypox, **OR**
2. Being within 6 feet of an unmasked person with monkeypox for **at least three hours** (cumulatively) without wearing a surgical mask or respirator, **OR**
3. Contact between an exposed individual's intact skin with materials (e.g., linens, clothing, sex toys) that have contacted the skin lesions or bodily fluids from a person with monkeypox without having been disinfected† or laundered, **OR**
4. Contact between an exposed individual's clothing with the person with monkeypox's skin lesions or bodily fluids, or their soiled linens or dressings (e.g., during turning, bathing, or assisting with transfer).

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

C. **Low risk** exposures include:

1. Entry into the living space of a person with monkeypox (regardless of whether the person with monkeypox is present), and in the absence of any exposures above.

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

D. **No risk** exposures include:

1. No contact with the person with monkeypox, their potentially infectious contaminated materials, nor entry into their living space.

Management: Monitoring not indicated; post-exposure vaccination not indicated.

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 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 ≥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 a heads-up to the evaluating provider that the person has been exposed to monkeypox.

5.4 Post-Exposure Prophylaxis

As noted, those with a high- or intermediate-risk exposure may consider post-exposure prophylaxis as described in **§2.7**.

UPDATE LOG

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

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).

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).