The Commonwealth of Massachusetts

Executive Office of Health and Human Services

Department of Public Health

Bureau of Infectious Disease and Laboratory Sciences

305 South Street, Jamaica Plain, MA 02130



KATHLEEN E. WALSH

Secretary

ROBERT GOLDSTEIN, MD, PhD Commissioner

**Tel: 617-624-6000**

**www.mass.gov/dph**

MAURA T. HEALEY

Governor

KIMBERLEY DRISCOLL

Lieutenant Governor

**TO:** Massachusetts Healthcare Providers, Hospitals, Community Health Centers, and EMS

Local Boards of Health

**FROM:** Catherine M. Brown, DVM, MSc, MPH, State Epidemiologist

Nicolas Epie, PhD, HCLD, TS (ABB); MLS (ASCP), Director, Massachusetts State Public Health Laboratory

Larry Madoff, MD, Medical Director

Dylan Tierney, MD, MPH, Associate Medical Director

**SUBJECT:** Clinical and Laboratory Testing Guidance for Mpox

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**Key Messages and Updates**

* Mpox incidence in Massachusetts has increased over the period from October 2023 to March 2024. Providers should be vigilant for mpox in people with potential exposure, including previously vaccinated individuals.
* A concurrent but geographically distinct outbreak of mpox due to MPXV Clade I is occurring in central Africa. No cases have been detected in the U.S., but local health authorities should remain vigilant.
* Jynneos vaccination is associated with a reduced risk of mpox. Outreach to individuals with potential exposure to mpox should continue and the two-dose series should be completed to lower their risk for infection. People with immunocompromise, including those with HIV, may have more severe disease due to mpox so vaccination is important if they are at risk for exposure.
* Testing of mpox is available through the State Public Health Laboratory (SPHL) and commercial laboratories. Testing at the SPHL is encouraged to facilitate turnaround and clade determination. See guidance on page 5 of this advisory with guidance about specimen submission to the SPHL.
* Specimens collected from patients with travel history to central Africa or recent close contact with someone who recently travelled to central Africa should be sent to the SPHL, rather than to a commercial laboratory, for testing.
* Tecovirimat (TPOXX) is available for treatment of mpox. Therapy can be obtained by participating in the STOMP clinical trial. If trial participation is not feasible or of interest to the individual, certain patients may be eligible to receive the drug through the CDC EA-IND protocol by a healthcare provider. Contact MDPH for additional details.

**ABOUT MPOX**

[**RECOMMENDATIONS FOR CLINICIANS**](#RECOMMENDATIONS)

[**LABORATORY TESTING AND SPECIMEN COLLECTION**](#LABORATORY)

[**Laboratory testing at SPHL**](#SPHL)

[**Laboratory testing at commercial/reference laboratories**](#COMMERCIAL)

[**TREATMENT FOR MONKEYPOX**](#TREATMENT)

[**POST-EXPOSURE VACCINATION FOR HIGH RISK MONKEYPOX CONTACTS**](#VACCINE)

**ABOUT MPOX:**

Mpox is a viral disease with an incubation period of 1 to 21 days (typically 1 -2 weeks). Illness may begin with flu-like signs and symptoms (fever, chills, malaise, headache, muscle aches/back aches) and swelling of the lymph nodes and progresses to a rash that can look like pimples or blisters that appears on the face, inside the mouth, and on other parts of the body, like the hands, feet, chest, genitals, or anus. Cases may present only with rash illness without any other symptoms or may only develop mucosal lesions or proctitis. Most infections last 2-to-4 weeks and people are considered infectious throughout duration of symptoms. The infectious period may precede the development of skin lesions by several days in some individuals.

The virus does not spread easily between people; transmission most frequently occurs through direct contact with mpox rash lesions, scabs, or body fluids. The virus can also be spread through contact with fomites on items that touched the rash lesions or body fluids (e.g., clothing, bedding, etc.) or through large respiratory droplets following prolonged face-to-face contact.

Mpox lesions typically progress through specific stages—macules, papules, vesicles, and pustules— before scabbing and falling off. The characteristic lesions are deep-seated and well-circumscribed, often with central umbilication.

Mpox can occur concurrently with other diseases, including other rash illnesses such as varicella-zoster virus, herpes simplex virus or syphilis.

More information supporting clinical recognition of the disease is available through the Centers for Disease Control and Prevention website at: <https://www.cdc.gov/poxvirus/mpox/clinicians/clinical-recognition.html>.

**Epidemiology**

There has been a global outbreak of mpox associated with monkeypox virus (MPXV) Clade IIb, beginning in 2022 and continuing to the present. The first mpox case of this MPXV Clade IIb global outbreak in the USA was identified in Massachusetts in May 2022. The Massachusetts outbreak continued through the remainder of 2022, with the peak incidence in August 2022. Cases of mpox declined to near zero from the end 2022 through October 2023. There has been an uptick in mpox cases in Massachusetts, with 32 confirmed or probable cases reported from October 2023 to date. There may also be unrecognized cases occurring since not all identified cases can be linked directly to other identified cases. Healthcare providers should be vigilant for mpox in people with potential exposure, including previously vaccinated individuals.

To date, mpox cases have been disproportionately reported within networks of self-identified gay and bisexual men, other men who have sex with men (MSM), and transgender individuals who have sex with men. Recent cases have included an increase in the number of individuals identifying as Hispanic. However, people of any sexual orientation or gender identity can become infected and transmit mpox.

A concurrent but geographically distinct outbreak of mpox with MPXV Clade I has also been underway in central Africa in 2023-2024, particularly in the Democratic Republic of Congo. Infections due to MPXV Clade I may be more severe than those from Clade IIb. MPXV Clade I human-to-human transmission traditionally has occur through non-sexual contact but some sexual transmission has been observed during the current outbreak. There have been no cases of mpox due to MPVX Clade I detected in the U.S. to date. Importantly, vaccination and therapeutics effective against MPVX Clade II are also likely to be effective for MPVX Clade I.

**RECOMMENDATIONS FOR CLINICIANS:**

**Mpox considerations**

Clinicians should consider testing for mpox in patients with a new onset and a clinically compatible skin rash (exhibiting macular, papular, vesicular, or pustular lesions; generalized or localized; discrete or confluent; mucosal lesions; or proctitis). Known risk factors that increase the likelihood of MPXV infection include individuals who in the previous 21 days:

1. report close contact with a person or people with confirmed or suspected mpox; OR
2. report close contact with a person or people who have a similar rash; OR
3. report they are a man (individual assigned male sex at birth; cisgender man) who has sex with men, a transgender woman who has sex with men, or a transgender man who has sex with men, who regularly has proximate physical, sexual, or other close contact with other men, including encounters with individuals met through online dating applications or in social venues; OR
4. report residence in or travel to endemic areas of Africa.

**However, clinicians should consider testing clinically compatible patients regardless of whether they have known risk factors for mpox and regardless of gender or sexual orientation.**

Although transmission of mpox from patients to healthcare workers happens rarely and is primarily associated with needlestick injuries, suspect mpox cases should be evaluated clinically using contact and droplet precautions [gloves, eye protection, surgical mask (N95 optional unless aerosol generating procedures are being performed), and a gown or disposable covering].

**Co-infection considerations**

Patients who are at risk for exposure to MPXV through sexual activity are also at risk for sexually transmitted infections and diagnostic testing should be comprehensive; coinfections are common. All patients with mpox who are not known to have HIV, should be tested for HIV.

Clinicians should also rule out other causes of rash illness while considering mpox. Other diseases that can cause similar appearing rash lesions include:

* herpes
* secondary syphilis
* chancroid
* varicella-zoster virus

**LABORATORY TESTING AND SPECIMEN COLLECTION:**

Testing for non-variola orthopoxvirus (presumptive MPXV) infection is available from the State Public Health Laboratory (SPHL) and from commercial laboratories. Testing through SPHL is encouraged for all patients, and in particular for

* Patients for whom there is a strong clinical suspicion of mpox who are hospitalized; OR
* Patients for whom there is a strong clinical suspicion of mpox and are at high risk of more severe disease† (e.g. pregnant people, children under 8 years of age, individuals with immune compromise, or people with concurrent disease/co-morbidities); OR
* Patients for whom there is a strong clinical suspicion of mpox in a congregate setting; OR
* Patients for whom cost of commercial testing is a concern.

**All specimens from patients with travel history to central Africa or recent close contact with someone with travel history to central Africa should be sent to the State Public Health Laboratory for testing.**

†More information about individuals at high risk for severe disease is available from CDC here: <https://www.cdc.gov/poxvirus/monkeypox/clinicians/treatment.html>.

**Laboratory testing at SPHL**

***Pre-approval for submission of specimens is not required.*** Questions about specimen submission should be directed to the MDPH Division of Epidemiology at 617-983-6800 (available 24/7).

Acceptable specimen types include dry swabs of crusts and/or fluid from an active, open lesions; dry swabs of an intact vesicle or pustule; or a scab from a lesion. Providers may submit specimens from up to 2 sites. Selection of lesions for sampling should focus on identifying lesions that appear different from each other. The rationale for this recommendation is that patients may have multiple diseases and sending swabs from two different appearing lesions enhances the ability to identify MPXV if it is present. SPHL is not able to test submitted specimens for other pathogens. Note that there are no acceptable specimen types for testing PRIOR to the development of rash lesions.

**Complete specimen collection, labelling and packaging and shipping guidance for specimens sent to the State Public Health Laboratory is available and can be viewed here:** [**https://www.mass.gov/doc/instructions-for-specimen-collection-for-orthopoxvirus-testing/download**](https://www.mass.gov/doc/instructions-for-specimen-collection-for-orthopoxvirus-testing/download)**. Please note that duplicate specimens are no longer necessary and should not be submitted; however, swabs from up to two different lesions per patient may be submitted. Please, do not submit throat swabs in the absence of oropharyngeal lesions, but swabs of oropharyngeal lesions are acceptable.**

**Laboratory testing at commercial/reference laboratories**

When patients are being tested through commercial or reference laboratories, healthcare providers should consider ordering diagnostic tests for other infections, as clinically indicated, in addition to MPXV. As of the date of this guidance, testing is available through:

* **Labcorp** [https://www.labcorp.com/tests/140230/mpox-orthopoxvirus-dna-pcr](https://www.labcorp.com/tests/140230/mpox-orthopoxvirus-dna-pcr%20)
* **Quest Diagnostics** <https://testdirectory.questdiagnostics.com/test/test-detail/12084/monkeypox-virus-dna-qualitative-real-time-pcr?q=monkeypox&cc=MASTER>
* **Aegis Sciences Corporation** <https://www.aegislabs.com/our-services/monkeypox>
* **Sonic Reference Laboratory** [<https://directory.sonicreferencelab.com/tests?iframe_layout=srl>](https://directory.sonicreferencelab.com/tests?iframe_layout=srl)
* **ARUP** <https://ltd.aruplab.com/Tests/Pub/3005716>

**Questions about testing should be directed to the MDPH Division of Epidemiology at (617) 983-6800 available 24/7.**

**PREVENTING TRANSMISSION:**

Anyone who is suspected to have mpox and is being tested or who has already tested positive should take precautions to help prevent spread of the virus. Isolation at home or in another private location is recommended but may not always be possible. If isolation is not possible, individuals should completely cover all their rash lesions and wear a mask when in public or around others. Individuals should avoid having bare skin physical contact, including sexual contact, with others and should avoid sharing bed linens, clothing, towels, wash cloths, drinking glasses or eating utensils.

Routine disinfection of high touch surfaces in a shared bathroom and kitchen after use is recommended. Standard household cleaning/disinfectants may be used in accordance with the manufacturer’s instructions. More guidance on how to safely isolate at home is available from CDC at <https://www.cdc.gov/poxvirus/monkeypox/clinicians/infection-control-home.html>.

**IDENTIFYING CONTACTS:**

After a person tests positive for mpox it is important to identify others who may have been exposed to the virus to advise them of their possible exposure and to offer post-exposure prophylaxis (see VACCINATION FOR MPOX further on in this document). The local Board of Health in the town of residence of the case will speak with the individual and assess for close contacts. However, the clinician can facilitate this conversation by educating their patient about what constitutes an exposure.

People should be considered a contact, and therefore potentially exposed to the virus that causes mpox, if they had skin-to-skin physical contact (including sexual contact) at any time while the case had symptoms. Sharing clothes, bed linens, towels, drinking glasses or eating utensils with a symptomatic case can also result in exposure. Because of emerging evidence that some people with mpox can transmit the virus up to 4 days before symptom onset, any sexual or intimate contact involving mucous membranes [e.g., kissing, oral-genital, oral-anal, vaginal, or anal sex (insertive or receptive)] within 4 days of symptoms onset with a person who developed mpox should also be considered exposed. Lower risk exposures that are less likely to result in transmission include sustained, face-to-face interactions (within 6 feet for more than 3 hours) with a symptomatic case.

**TREATMENT FOR MPOX:**

Most cases associated with the recent outbreak have had self-limiting disease not requiring hospitalization. However, certain conditions are associated with the possibility of more severe disease. Tecovirimat (TPOXX or ST-246) is an antiviral drug FDA-approved for the treatment of smallpox disease. There is minimal evidence, however, demonstrating clinical efficacy of tecovirimat for the treatment of mpox in humans.

More information about tecovirimat is available here: <https://www.cdc.gov/poxvirus/mpox/clinicians/Tecovirimat.html>.

**Accessing treatment**

Tecovirimat is available for the treatment of mpox in adults and children through regulated access.

Individuals with mild-to-moderate mpox disease can access the drug by participating in the Study of Tecovirimat for Human Mpox Virus (STOMP) trial, sponsored by the National Institute of Allergy and Infectious Disease. Eligible participants with mild-to-moderate disease will be randomized 2:1 to receive either tecovirimat or placebo. (Note: STOMP is the only option for tecovirimat access for patients with mild-to-moderate diseases.) Individuals with severe disease, significant skin conditions, or with severe immunocompromise will receive open-label tecovirimat through the STOMP trial should they choose to participate. Regardless of disease severity, individuals must have mpox illness for less than 14 days prior to study entry to be eligible to participate in STOMP.

The study is being conducted through the AIDS Clinical Trial Group (ACTG). There are two ACTG sites in Massachusetts that are conducting the STOMP trial: Massachusetts General Hospital (617-726 -5598) and Brigham and Women’s Hospital (617-732-5635). Participants can enroll in the study through an initial in-person visit to either site. Providers caring for individuals with mpox as outpatients should contact an ACTG site Monday through Friday 9 AM – 5 PM to arrange for an intake appointment. Enrollment is also possible on nights and weekends through the Brigham and Women’s Hospital Emergency Department. For individuals who are hospitalized with mpox and require treatment, transfer to a hospital with an ACTG site should be considered.

If an eligible participant cannot enroll at an in-person study site, remote enrollment in the STOMP trial via study sites outside of Massachusetts is possible. (Note: remote enrollment may not be available on weekends.) More information about the STOMP trial is available here: [STOMP (stomptpoxx.org)](https://www.stomptpoxx.org/main) or by calling 855-876-9997 Monday through Friday 9 AM to 10 PM, Saturday 9 AM to 4 PM and Sunday 1 PM to 6 PM.

If enrollment in STOMP is not feasible (e.g., a clinical trial site is not geographically accessible) or of interest, individuals with severe mpox disease can also access TPOXX through a Massachusetts health care provider using the EA-IND pathway in concert with CDC’s guidance for treatment if they qualify for the EA-IND.

Access to tecovirimat treatment through EA-IND access is limited to:

* People with severe disease
  + Hemorrhagic disease
  + Large number of confluent lesions
  + Necrotic lesions
  + Severe lymphadenopathy that can be necrotizing or obstructing (such as in airways)
  + Involvement of multiple organ systems and associated comorbidities (for example, pulmonary involvement with nodular lesions, sepsis, encephalitis, myocarditis, ocular or periorbital infections)
  + Other conditions requiring hospitalization
* People with involvement of an anatomic area which might result in serious sequelae that include scarring or strictures
  + Lesions involving pharynx causing dysphagia, inability to control secretions or need for parenteral feeding
  + Lesions involving penile foreskin, vulva, vagina, urethra or anorectum with the potential for causing strictures or requiring catheterization
  + Anorectal lesions interfering with bowel movements (for example, severe pain)
  + Severe infections (including secondary bacterial skin infections), especially those that require surgical intervention such as debridement
* People who may be at high risk of severe disease:
  + People with severe immunocompromise (e.g., advanced or poorly controlled human immunodeficiency virus/acquired immune deficiency syndrome infection, leukemia, lymphoma, generalized malignancy, solid organ transplantation, therapy with alkylating agents, antimetabolites, radiation, tumor necrosis factor inhibitors, high-dose corticosteroids, being a recipient with hematopoietic stem cell transplant <24 months post-transplant or ≥24 months but with graft-versus-host disease or disease relapse, or having autoimmune disease with immunodeficiency as a clinical component)
  + Pediatric populations, particularly patients younger than 1 year of age
  + People with a condition affecting skin integrity including atopic dermatitis, eczema, burns, impetigo, varicella zoster virus infection, herpes simplex virus infection, severe acne, severe diaper dermatitis with extensive areas of denuded skin, psoriasis, or Darier disease [keratosis follicularis])
  + Pregnant or breastfeeding people

The regulatory requirements for treating patients with tecovirimat through the EA-IND are available here: <https://www.cdc.gov/poxvirus/mpox/clinicians/obtaining-tecovirimat.html>. Providers should contact Massachusetts DPH for additional details and facilitation of communication with the US Centers for Disease Control to access tecovirimat through the EA-IND program.

For patients with severe manifestations of disease, prolongation of treatment length beyond the standard 14-day course may be advisable. Addition of other therapeutics such as brincidofovir, cidofovir or Vaccinia Immune Globulin may also be indicated. In these cases, providers should seek consultation with MDPH.

**VACCINATION FOR MPOX**

Jynneos vaccination is associated with a reduced risk of mpox, based upon retrospective clinical studies, with two doses providing the best protection. People who have been vaccinated can still get mpox, but vaccination may make illness less severe. Outreach to individuals with potential exposure to mpox should be prioritized. People with immunocompromise, including those with HIV, may have more severe disease due to mpox so vaccination is important if they are at risk for exposure.

**Post-Exposure Prophylaxis**

Individuals with potential exposure to mpox should complete the recommended two-dose series. The second dose should be given four weeks after the first dose.

Vaccination is available to individuals who live or work in Massachusetts and meet current eligibility criteria, which include individuals with possible recent exposure to an individual with mpox.

Persons eligible for post-exposure prophylaxis (PEP) using vaccine include:

* Known contacts identified by public health via case investigation, contact tracing, and risk exposure assessments (this may include sexual partners, household contacts, and healthcare workers); as well as
* Presumed contacts who meet the following criteria:
  + Know that a sexual partner in the past 14 days was diagnosed with mpox
  + Had multiple sexual partners in the past 14 days in a jurisdiction with known mpox

As PEP, vaccine should be given as soon as possible, ideally within four days of exposure; administration 4-14 days after exposure may still provide some protection against mpox and reduce the severity of infection if it occurs. After 14 days, clinicians should consider the benefits and risks of receiving vaccine on a case-by-case basis.

**Pre-Exposure Prophylaxis**

In addition, pre-exposure vaccination (PrEP) is recommended for persons at risk for mpox, including:

* Gay, bisexual, and other men who have sex with men, transgender, gender non-conforming, or nonbinary people (including adolescents who fall into any of the aforementioned categories) who
  + Have had a diagnosis of or have sought testing for one or more sexually transmitted diseases (i.e., chancroid, chlamydia, gonorrhea, or syphilis) in the past year
  + Are living with HIV infection
  + Are on or are eligible to be on HIV PrEP
  + Have recently had more than one sex partner
* People who:
  + Have had sex at a private or commercial sex venue (e.g., sex party, bathhouse)
  + Have had sex in association with a large public event (e.g., rave, circuit party) in a geographic area where mpox transmission is occurring
* Sexual partners of people with the above risks
* People who anticipate experiencing the above risks

When an individual at risk requests vaccine, they will not be asked which of these criteria applies. It is sufficient to say that they consider themselves to be at risk for mpox.

General information about mpox vaccination for healthcare professionals is available here: <https://www.cdc.gov/poxvirus/mpox/clinicians/vaccines/vaccine-basics-healthcare.html>.

Current information about who is eligible to receive vaccine and where to access it in Massachusetts is available on the DPH website here: <https://www.mass.gov/info-details/mpox-vaccination>.

**Additional information is available on the CDC website:**

* [Interim Clinical Considerations for Use of JYNNEOS](https://www.cdc.gov/poxvirus/monkeypox/interim-considerations/jynneos-vaccine.html#interim)
* [Video on Administering JYNNEOS Intradermally](https://www.youtube.com/watch?v=TLv1mR6mECQ)
* [Intradermal Vaccine Preparation and Administration Summary](https://www.cdc.gov/poxvirus/monkeypox/files/interim-considerations/guidance-jynneos-prep-admin-alt-dosing.pdf)
* [Vaccine Administration Errors and Deviations](https://www.cdc.gov/poxvirus/monkeypox/interim-considerations/errors-deviations.html)
* [Vaccine Administration Considerations for Specific Populations](https://www.cdc.gov/poxvirus/monkeypox/interim-considerations/special-populations.html)
* [FDA EUA Fact Sheet for Providers](https://www.fda.gov/media/160774/download)
* [FDA EUA Fact Sheet for Patients and Caregivers](https://www.fda.gov/media/160773/download)
* [JYNNEOS Vaccine Information Statement](https://www.cdc.gov/vaccines/hcp/vis/vis-statements/smallpox-monkeypox.pdf)