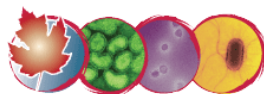


Canadian Public Health Laboratory Network



The Canadian Public Health Laboratory Network (CPHLN)

Best Practices for Responding to Monkeypox Cases in Canada

June 2022

Introduction

Since the initial report of sustained human transmission of monkeypox outside of Africa in May 2022, several countries have now reported lab-confirmed cases of monkeypox. As of June 10th/2022, 28 WHO member states have reported cases in non-endemic areas. The sudden appearance of this illness suggests that monkeypoxvirus (MPXV) was circulating undetected for some time before a variety of events led to the spike in cases. MPXV is a double-stranded DNA virus, and a member of the orthopoxvirus genus within the Poxviridae family [which also includes variola (smallpox) and cowpox virus]. The circulating MPXV belongs to the West African clade and is associated with milder disease and lower fatality rates as compared to the clade from Central Africa.

The National Microbiology Laboratory Branch (NMLB) at the Public Health Agency of Canada (PHAC) in collaboration with its provincial and territorial partners formed a working group to assess and respond to the monkeypox outbreak in Canada.

Case Definition

Case definitions have been established by WHO and CDC.

Table 1: Summary of case definitions by WHO and CDC as of June 9/2022

Case Definitions for Monkeypox in non-endemic countries			
	WHO	CDC	Canadian Case Definition
Suspect	A person of any age presenting in a monkeypox non-endemic country ^[1] with an unexplained acute rash	<ul style="list-style-type: none">• New characteristic rash* OR <ul style="list-style-type: none">• Meets one of the epidemiologic criteria and has a high clinical	A person who presents with unexplained ¹ acute genital, perianal, or oral lesion(s) OR A person who presents with an unexplained ¹

	<p>AND</p> <p>One or more of the following signs or symptoms, since 15 March 2022:</p> <ul style="list-style-type: none"> • Headache • Acute onset of fever (>38.5°C), • Lymphadenopathy (swollen lymph nodes) • Myalgia (muscle and body aches) • Back pain • Asthenia (profound weakness) <p>AND</p> <p>For which the following common causes of acute rash do not explain the clinical picture: varicella zoster, herpes zoster, measles, Zika, dengue, chikungunya, herpes simplex, bacterial skin infections, disseminated gonococcus infection, primary or secondary syphilis, chancroid, lymphogranuloma venereum, granuloma inguinale, molluscum contagiosum, allergic reaction (e.g., to plants); and any other locally relevant common causes of papular or vesicular rash.</p>	<p>suspicion[†] for Monkeypox.</p> <p>*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.; this can sometimes be confused with other diseases that are more commonly encountered in clinical practice (e.g., secondary syphilis, herpes, and varicella zoster). Historically, sporadic accounts of patients co-infected with Monkeypox virus and other infectious agents (e.g., varicella zoster, syphilis) have been reported, so patients with a characteristic rash should be considered for testing, even if other tests are positive.</p> <p>†Clinical suspicion may exist if presentation is consistent with illnesses confused with monkeypox (e.g., secondary syphilis, herpes, and varicella zoster).</p>	<p>acute rash² AND has at least one of the following signs or symptoms:</p> <ul style="list-style-type: none"> • Headache • Acute onset of fever (>38.5°C), • Lymphadenopathy (swollen lymph nodes) • Myalgia (muscle and body aches) • Back pain • Asthenia (profound weakness) <p>AND</p> <p>The lesions or the rash are not explained by other common illnesses; varicella zoster, herpes zoster, measles, Zika, dengue, chikungunya, herpes simplex, bacterial skin infections, disseminated gonococcus infection, primary or secondary syphilis, lymphogranuloma venereum, molluscum contagiosum, allergic reaction (e.g., to plants); and any other locally relevant common causes of papular or vesicular rash. (Note: be aware of the possibility of co-infections of MPXV with one or more of these).</p> <p>AND</p> <ul style="list-style-type: none"> • Compatible epidemiological criteria
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<p>Probable</p>	<p>A person meeting the case definition for a suspected case AND one or more of the following:</p> <ul style="list-style-type: none"> • has an epidemiological link (face-to-face exposure, including health workers without eye and respiratory protection); direct physical contact with skin or skin lesions, including sexual contact; or contact with contaminated materials such as clothing, bedding or utensils to a probable or confirmed case of monkeypox in the 21 days before symptom onset • reported travel history to a monkeypox endemic country in the 21 days before symptom onset • has had multiple or anonymous sexual partners in the 21 days before symptom onset • has a positive result of an orthopoxvirus serological assay, in the absence of smallpox vaccination or other known exposure to orthopoxviruses • is hospitalized due to the illness 	<p>No suspicion of other recent <i>Orthopoxvirus</i> exposure (e.g., <i>Vaccinia virus</i> in ACAM2000 vaccination) AND demonstration of the presence of:</p> <ul style="list-style-type: none"> • <i>Orthopoxvirus</i> DNA by polymerase chain reaction of a clinical specimen OR • <i>Orthopoxvirus</i> 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 	<p>A person who presents with unexplained¹ acute rash or lesion(s) AND has one or more of the following:</p> <ul style="list-style-type: none"> • Epidemiological link to a probable or confirmed MPXV case in the 21 days before symptom onset • Reported travel history to or residence in a location where MPXV is endemic in the 21 days before symptom onset • <i>Orthopoxvirus</i> DNA detected in a specimen by nucleic acid amplification test (NAAT) assay (e.g. real-time PCR)
<p>Confirmed</p>	<p>A case meeting the definition of either a</p>	<p>Demonstration of the presence of <i>Monkeypox virus</i></p>	<p>A person in whom MPXV-specific DNA as well as a</p>

	<p>suspected or probable case AND is laboratory confirmed for monkeypox virus by detection of unique sequences of viral DNA either by real-time polymerase chain reaction (PCR) and/or sequencing.</p>	<p>DNA by polymerase chain reaction testing or Next-Generation sequencing of a clinical specimen OR isolation of <i>Monkeypox virus</i> in culture from a clinical specimen.</p>	<p>confirmatory additional test including Orthopox DNA which was detected by a validated nucleic acid amplification test (NAAT) assay (e.g. real-time PCR or nucleic acid sequencing) at a hospital or reference laboratory (the National Microbiology Laboratory or a provincial public health laboratory).</p>
<p>Epidemiologic Criteria</p>		<p>Within 21 days of illness onset:</p> <ul style="list-style-type: none"> • Reports having contact with a person or people with a similar appearing rash or who received a diagnosis of confirmed or probable 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 US to a country with confirmed cases of monkeypox or where <i>Monkeypox virus</i> is endemic OR <p>Had contact with a dead or live wild 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.)</p>	<p>Within 21 days of symptoms onset:</p> <ul style="list-style-type: none"> • Reported having contact with a probable or confirmed case of monkeypox OR • Had close or intimate contact with individuals in a social network experiencing a monkeypox outbreak; this would include gbMSM with multiple partners; intimate contacts in sex-on-premises venues • Traveled to a country where monkeypox is endemic.

<p>Exclusion Criteria</p>	<p>A suspected or probable case for which laboratory testing by PCR and/or sequencing is negative for monkeypox virus.</p>	<p>A case may be excluded as a suspect, probable, or confirmed case if:</p> <ul style="list-style-type: none"> • 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 <i>Orthopoxvirus</i> or <i>Monkeypox virus</i> or antibodies to orthopoxvirus 	
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Footnotes

¹Common causes of acute rash can include Varicella zoster, herpes zoster, measles, herpes simplex, syphilis, chancroid, lymphogranuloma venereum, hand-foot-and-mouth disease

²Acute rash. Monkeypox illness includes a progressively developing rash that usually starts on the face and then spreads elsewhere on the body. The rash can affect the mucous membranes in the mouth, tongue, and genitalia. The rash can also affect the palms of hands and soles of the feet. The rash can last for 2 to 4 weeks and progresses through the following stages before falling off:

- Macules
- Papules
- Vesicles
- Pustules
- Scabs

N.B. It is not necessary to obtain negative laboratory results for listed common causes of rash illness in order to classify a case as suspected.

³Reported travel history includes regional, national, or international travel in the 21 days before symptom onset to any area where monkeypox may be reported.

⁴Epidemiologic Criteria

Within 21 days of illness onset:

- Reports having contact with a person or people with a similar appearing rash or who received a diagnosis of confirmed or probable MPXV **OR**
- Had close or intimate in-person contact with individuals experiencing MPXV activity **OR**
- Traveled outside Canada with confirmed cases of MPXV or where Monkeypox virus is endemic **OR**
- Had contact with a dead or live wild animal or exotic pet that is an African endemic species or used a product derived from such animals

Laboratory Testing Recommendations

The WHO has recommended that an individual that meets the suspected case definition should be offered testing. Testing should be based on both clinical and epidemiological factors tied to the likelihood of infection.

Confirmation of a monkeypox infection is based on nucleic acid amplification testing based on real-time or conventional polymerase chain reaction (PCR), used alone or in combination with sequencing. Currently, monkeypox PCR is conducted at the NMLB and some provincial laboratories.

Virus isolation is limited to facilities that have licensed containment level 3 or 4 capabilities and is not necessary for diagnosis of monkeypox cases. MXPV is a security sensitive biological agent (SSBA) and requires additional security requirements such as obtaining a Human Pathogens and Toxin Act security clearance. At NMLB, virus isolation is used to propagate virus for the generation of positive control DNA material for diagnostic tests.

At this time, the NMLB is not offering serology for monkeypox as the assays (ELISAs, IgG and IgM) are not available and there is a lack of immediate clinical utility for serology for the current monkeypox outbreak. More information regarding serology testing for monkeypox may become available.

Sequencing Recommendations

Laboratories sequencing monkeypox samples may see ‘Monkeypox Sample Selection for Sequencing Guide v1’ developed by NMLB, PHAC. If unable to access the document, please email CPHLN at CPHLN-RLSPC@phac-aspc.gc.ca.

Specimen Collection

According to WHO, the recommended specimen type for diagnostic confirmation of monkeypox in suspected cases is skin lesion material, including swabs of lesion exudate, roofs from more than one lesion, or lesion crusts.

After checking with your local or provincial laboratory, other specimen types should be considered for testing for probable cases that do not present with lesions (i.e. in prodromal stage). They may include: upper respiratory tract, blood, serum, urine, rectal and/or genital swab.

Specimen Type	Minimum Volume	Collection Kit	*Store-transport
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Lesion or vesicular fluid, crust material or scab	Not Applicable	Sterile container (without viral transport media preferred)	2-8°C
Biopsy of lesion (fresh or frozen tissue)	Not Applicable	Sterile container	2-8°C
Nasopharyngeal and/or throat swab	Particularly useful specimens if testing during the prodrome	Viral transport media	2-8°C

Biosafety Considerations as per Centre for Biosecurity, PHAC

MXPV is a risk group 3 pathogen. Propagation of virus should be conducted in licensed CL3 and CL4 laboratories. MXPV is a security sensitive biological agent (SSBA) and requires additional security requirements such as obtaining a Human Pathogens and Toxin Act security clearance.

Biosafety advisory for Monkeypox virus can be found here: [Biosafety advisory: Monkeypox virus \(MPXV\) - Canada.ca](#)

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References

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