

A case of human monkeypox in Canada

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A previously healthy 33-year-old man presented to an ambulatory clinic with rectal pain and a pustular rash involving the face, extremities and torso. Twenty-one days before presentation (day 0), he had unprotected, receptive orogenital and oroanal intercourse with a new, anonymous male partner. On day 12, he developed enlarged, painful, tender inguinal and cervical lymphadenopathy, chills and night sweats. On day 13, he developed rectal pain and tenesmus, followed by the appearance of 4 pruritic, painless macules on his forearm and wrist on day 15, which became vesicular and then pustular over the subsequent 7 days. He presented to an emergency department and was prescribed valacyclovir for presumptive herpes simplex virus (HSV) infection. He subsequently developed similar lesions on the face, extremities and torso. He had no urethral discharge, dysuria, urgency or frequency and no respiratory symptoms. He had not travelled or been exposed to animals.

On day 21, the patient presented to our infectious disease clinic, where we noted about 40 painless pustules on his face, scalp and extremities (Figure 1), some with central umbilication (Figure 2). One macule appeared on the left plantar surface (Figure 3). We did not observe any perianal or genital lesions; we deferred digital rectal examination owing to pain. The patient had no palpable lymphadenopathy.



Figure 1: Photograph of the right forearm of a 33-year-old man with monkeypox showing two 3 mm pustular lesions with surrounding erythema, captured on day 7 following the emergence of the lesions (illness day 10).

Key points

- Monkeypox is classically a zoonotic infection; its recent spread by person-to-person contact led to the declaration of a new monkeypox pandemic in June 2022.
- In the current outbreak, pleomorphic mucocutaneous lesions in various body locations (including the genitals, oropharynx, palms, soles) are the predominant clinical manifestation, which progress from macules and papules to vesicles and pustules that umbilicate, ulcerate, crust and desquamate, revealing re-epithelialized skin.
- Understanding the epidemiologic and clinical features of monkeypox is important for rapid identification of suspected and probable cases and for the development of public health campaigns to limit the spread of disease through isolation, contact tracing and strategies for pre- and postexposure prophylaxis.

Using sterile nylon flocked swabs, we sampled the nasopharynx and pustules from each arm and also collected pustular roof tissue and serum, which were sent to the Public Health Ontario Laboratory. Roof tissue and pustule swabs were positive



Figure 2: Photograph of the flexor surface of the left wrist of a 33-year-old man with monkeypox showing two 10 mm pustular lesions with central umbilication, captured on day 7 following the emergence of the lesions (illness day 10).

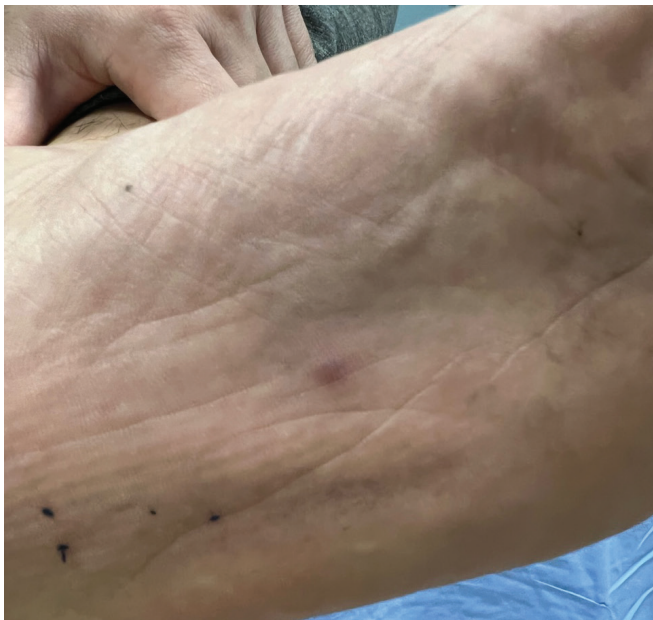


Figure 3: Photograph of the plantar aspect of the left foot of a 33-year-old man with monkeypox showing a 3 mm macular lesion, captured on day 1 of the emergence of the lesion (illness day 10)



Figure 4: Photograph of the flexor surface of the right wrist of a 33-year-old man with monkeypox showing 2 crusted pustular lesions, captured on day 12 following the emergence of the lesions (illness day 15).

for orthopoxvirus using real-time polymerase chain reaction (PCR) assay, and confirmed by monkeypox probe PCR assay at the National Microbiology Laboratory. Nasopharyngeal and serum samples were negative for orthopoxvirus by PCR. Serology tests for HIV and syphilis, anal swab cultures for HSV and nucleic acid amplification tests of a urine sample and swabs of the throat and rectum for gonorrhoea and chlamydia were negative.

The patient developed new lesions until day 26, and then all lesions crusted (Figure 4) and desquamated. He received supportive management with no antiviral treatment. We identified no specific cause for his rectal pain, but it resolved when the skin lesions crusted.

Discussion

Monkeypox is a zoonotic disease caused by the monkeypox virus, a double-stranded DNA virus classified in the orthopoxvirus genus of the Poxviridae family. The reservoir is unknown but is likely rodents; monkeys and humans are incidental hosts. Two clades have been identified. The Central African clade, first recognized in humans in 1970, has higher morbidity and more human-to-human transmission. The West African clade causes milder disease with limited human-to-human transmission, and was implicated in a 2003 human outbreak in the United States that was traced to infected prairie dogs.¹

Before 2022, transmission of monkeypox to humans was predominantly zoonotic, via animal bites or scratches, and human-to-human transmission (through contact with infected bodily fluid, mucocutaneous lesions or respiratory droplets) was uncommon. Fomites such as linen and clothing have been implicated in transmission, and airborne transmission is theoretically possible but remains unproven.

In May 2022, new cases of monkeypox appeared in nonendemic countries across Europe and North America.³ Canada reported its first cases in Montréal on May 19, 2022.⁴ On June 22, 2022, the World Health Network declared the outbreak a pandemic (<https://www.worldhealthnetwork.global/monkeypoxdeclaration>). Initial case reports have been predominantly among men who have had sex with men; this observation may be biased by sexual health-seeking behaviours of those with lesions that mimic a sexually transmitted infection.⁵ Reports of proctitis, genital lesions and PCR-positive semen samples raise the possibility of sexual transmission.

In previous outbreaks, the incubation period of monkeypox was 5–21 days, with a febrile prodrome of 8–12 days preceding the rash by 2 days. Cases were described as having tender, pruritic lesions that began on the face or trunk, and then spread peripherally to the palms, soles and mucous membranes. Lesions progressed over 2–4 weeks through stages of macules, papules, vesicles and pustules that umbilicate, ulcerate, crust and desquamate.² Oropharyngeal lesions sometimes presented as a sore throat or cough. Increased disease severity was loosely defined by high rash burden or need for hospital admission and was associated with greater exposures, extremes of age, immunocompromising condition and pregnancy. Previous smallpox vaccination may have attenuated disease severity.

Observations from case series have shown important differences in the 2022 outbreak (S.W., unpublished data, 2022). Human-to-human transmission is predominant, with patients in nonendemic countries having had no exposure to infected animals. The rash may occur before, with or without the febrile systemic illness. Initial lesions may appear at sites of inoculation, such as the face and neck with kissing, and the penis and perianal region with sexual exposure.⁵ Lesions display pleomorphism, presenting in various stages simultaneously. Vesicles and pustules may be smaller than

classically described, sometimes noticed only with surrounding pain, pruritis or erythema. Complications have been reported, including myocarditis, proctitis and epiglottitis, but there have been no reported deaths.

The general approach to evaluating suspected monkeypox begins with an epidemiologic history of exposures, sexual history, attendance in crowded places or gatherings with body contact, travel to current outbreak regions in the previous 21 days

and a review of the symptoms and chronology. Preliminary differentiation of monkeypox from other infections, including HSV, varicella zoster virus, syphilis, enteroviral infections and molluscum contagiosum, relies on epidemiological risk factors, clinical features and concurrent testing (Table 1).

Management of suspected, probable or confirmed cases may differ by jurisdiction. Patients with suspected monkeypox can be evaluated in ambulatory settings, though current regulations for

Table 1 (part 1 of 2): Distinguishing infectious causes of vesicular lesions

Characteristic	Monkeypox	Chickenpox and herpes zoster	HSV-1 and HSV-2	Syphilis	Hand, foot and mouth disease	Molluscum contagiosum
Infectious cause	Monkeypox virus	Varicella zoster virus	Herpes simplex virus	<i>Treponema pallidum</i>	Coxsackievirus A and several other enterovirus serotypes	Poxvirus (molluscum contagiosum virus)
Subclinical shedding	No*	Yes	Yes	No	Yes	No
Incubation period, d	5–21	10–21	2–12	3–90	3–5	14–180
Systemic symptoms	Possible prodrome of fever, malaise, myalgias, headache.	Primary: a prodrome of fever, malaise, pharyngitis, anorexia. Reactivation: minority have fever, malaise, headache.	Primary: fever, malaise, myalgias, headache, tender lymphadenopathy. Reactivation: prodromal tingling or shooting pains.	Uncommon	Prodrome is uncommon	None
Lymphadenopathy	Tender, regional	Primary: generalized. Reactivation: regional.	Tender, regional	Primary: painless, regional. Secondary: generalized.	Cervical	No
Rash	Macules to papules to vesicles to pustules that umbilicate, ulcerate, crust and desquamate. Local pain and pruritis until crusting. Lesion pleomorphism.	Primary: maculopapular, vesicles, scabs appearing in crops. Lesions in all stages. Pruritic. Reactivation: erythematous papules to pustules. Can be hemorrhagic. Crust by 7–10 days.	A cluster of 2–4 mm vesicles on an erythematous base. May progress to vesicopustules and ulcers. Local pain and pruritis.	Primary: chancre. Secondary: maculopapular, may coalesce. Superficial mucosal erosions. Pustules. Condyloma lata. Rarely vesicular.	Oral: 1–5-mm erythematous vesiculoulcerative stomatitis. Exanthem: macular, maculopapular, or 1–10-mm vesicular on palms, soles, legs, and arms. Lesions may be at different stages of development. Local pruritis.	2–5-mm firm, dome-shaped flesh-coloured papules with umbilication. Rarely painful.
Location	Primary: site of inoculation. Secondary: spreads to extremities.* Can involve palms and soles.	Primary: head, scalp, trunk, extremities. Reactivation: dermatomal.	Orofacial, genitalia, rectum, hands, eyes	Primary: site of inoculation. Secondary: most commonly on palms and soles, trunk and extremities, intertriginous and mucosal areas.	Oral, palms, soles, arm, legs, buttocks	Anywhere on body, but uncommon in mouth or on palms and soles

Table 1 (part 2 of 2): Distinguishing infectious causes of vesicular lesions

Characteristic	Monkeypox	Chickenpox and herpes zoster	HSV-1 and HSV-2	Syphilis	Hand, foot and mouth disease	Molluscum contagiosum
Diagnosis	Viral PCR of unroofed lesion (dry flocced swab), throat or nasopharyngeal swab, serum sample or urine sample (currently all samples are being investigated)	Viral PCR of lesion swab	Viral culture or viral PCR of lesion swab	Serology	Clinical	Skin biopsy showing keratinocytes with eosinophilic cytoplasmic inclusion bodies
Treatment	Supportive; antiviral drugs restricted to high-risk cases and are not widely available outside of a clinical trial	Acyclovir, valacyclovir	Acyclovir, valacyclovir	Penicillin	Supportive	Supportive

Note: HSV = herpes simplex virus, PCR = polymerase chain reaction.
 *Being challenged in the 2022 outbreak. Investigations are ongoing.

local specimen transport preclude many clinics from testing. Stable patients may be sent home with rapid referral to a specialty clinic. In the ambulatory setting, the patient should be isolated in a room with droplet and contact precautions for health care workers. Health Canada advises airborne precautions pending better evidence about transmission routes.⁶ However, many provincial guidelines require only droplet precautions.

Monkeypox is confirmed by detection of viral DNA by PCR. Dry swabs of unroofed vesiculopustular fluid or samples of lesion crust have the highest diagnostic yield and should be sent with a throat or nasopharyngeal swab, anal swab, urine sample and serum sample for PCR. In many provinces, local public health agencies perform preliminary orthopoxvirus PCR assays within 24–72 hours; positive samples are forwarded to the National Medical Laboratory for confirmatory PCR assay, with reports within 48 hours.

Health care providers must notify hospital infection control, ensure environmental decontamination of the patient room after each visit and notify the laboratory to allow for special specimen handling. Suspected and confirmed cases are reportable to the local public health agency; the agency then performs contact tracing and determines vaccine eligibility for high-risk contacts. Patients with suspected or probable monkeypox should isolate at home until results return, and patients with confirmed monkeypox should isolate at home until the end of the period of communicability (i.e., until all lesion scabs have fallen off, revealing re-epithelialized skin underneath). This period varies by individual but typically takes 2–4 weeks. During isolation, patients should not use public transportation and should isolate away from other household members, with their own bedroom and bathroom. If shared spaces are unavoidable, frequent disinfecting of high-touch surfaces is recommended. Patients should

keep lesions covered, wash their hands often with soap and water or alcohol-based hand sanitizer, and self-laundry clothing and linens to prevent spread. If patients are unable to avoid close contact with others (e.g., for urgent doctor visits), wearing a surgical mask and covering lesions are recommended.

Most individuals have mild disease and recover with supportive care; it is too early to know if lesions typically scar. No antiviral treatments have been established for monkeypox. Originally approved by Health Canada for smallpox, tecovirimat is an antiviral medication that is effective in preventing death and shortening disease duration in nonhuman primates infected with monkeypox; data for humans are limited, and clinical trials are being designed.⁷ Brincidofovir, an antiviral drug with similar evidence in primate monkeypox, is not approved in Canada.

Contacts should monitor symptoms for 21 days after last exposure, during which time they should not donate organs or bodily fluids. Imvamune is a smallpox vaccine approved by Health Canada in 2013 that received extended approval for monkeypox in 2020; it is included in the National Emergency Strategic Stockpile. Until supply is increased, the National Advisory Committee on Immunization recommends Imvamune be reserved for postexposure prophylaxis (ideally within 4 days of, but up to 14 days since, last exposure) and for occupational pre-exposure prophylaxis for those working with replicating orthopoxviruses.⁸ Additional indications are being considered and are currently being offered to high-risk men who have sex with men.

As the outbreak evolves, more insight will be gained into transmission, infection prevention, patterns of disease, diagnostic testing and treatment. In the meantime, health care providers should consider monkeypox when seeing patients with new skin lesions, which will lead to timely diagnosis, management and control of its spread.

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The section Cases presents brief case reports that convey clear, practical lessons. Preference is given to common presentations of important rare conditions, and important unusual presentations of common problems. Articles start with a case presentation (500 words maximum), and a discussion of the underlying condition follows (1000 words maximum). Visual elements (e.g., tables of the differential diagnosis, clinical features or diagnostic approach) are encouraged. Consent from patients for publication of their story is a necessity. See information for authors at www.cmaj.ca.