Episode 65 – Monkeypox July 22, 2022

Background

- Monkeypox[1] is a rare zoonotic infectious disease (i.e., transferred from animals to humans) caused by monkeypox virus (MPXV), an enveloped double-stranded DNA virus within the *Orthopoxvirus* genus of the *Poxviridae* family. [1]
- Viruses of the *Poxviridae* family include variola (causes smallpox), vaccinia (used in smallpox vaccines), cowpox, orf virus, and molluscum contagiosum.
- Viruses of the *Orthopoxvirus* genus include variola, vaccinia, and cowpox. [2]
- Monkeypox first discovered in 1958 when outbreaks of a poxlike disease occurred in research monkeys in a Danish laboratory.
- In 1970, the first human case was identified in a 9-month-old boy in the Democratic Republic of the Congo (DRC), in a region where smallpox had been eliminated in 1968. [1]
- Since 1970, human monkeypox has been reported in several countries in Central and West Africa, especially the DRC and Nigeria.
- Countries endemic for monkeypox include: Benin, Cameroon, the Central African Republic, the DRC, Gabon, Ghana (identified in animals only), Ivory Coast, Liberia, Nigeria, the Republic of the Congo, Sierra Leone, and South Sudan.
- Two clades (strains) of MPXV have been identified:
    - West African clade, which causes milder disease, and
    - Congo Basin (Central African) clade, which has historically caused more severe disease and is thought to be more transmissible. [1]
- In Africa, MPXV infection has been found in many animals (e.g., African rope squirrels, tree squirrels, striped mice, Gambian pouched rats, dormice, different species of monkeys).
- Natural reservoir of monkeypox is unknown, though rodents are the most likely. Further research is required to determine the reservoir(s) and how virus circulation is maintained in nature. [1] [2]
- Human monkeypox cases are increasingly reported in West and Central Africa, likely due to:
    - Increased exposure to infected animals as a result of deforestation;
    - Conflict and displacement;
    - Waning immunity of smallpox vaccine;[2]
    - A growing population unimmune against smallpox; and
    - Improved surveillance and laboratory capacity in the African region.

[1] Refer to Episode 61 for initial discussion on monkeypox.
[2] Historical data suggests smallpox vaccination is at least 85% effective in preventing monkeypox. [1]

- In 2003, the first incidence of monkeypox outside of Africa occurred in the United States, with 47 confirmed and probable human cases. Individuals became ill after contact with pet prairie dogs infected with the virus. The prairie dogs became infected after being housed near imported small mammals (mostly rodents) carrying the virus imported from Ghana to Texas. The virus was further spread to other states (Illinois, Indiana, Kansas, Missouri, Ohio, Wisconsin) via the pet prairie dogs. No further human-to-human transmission was identified in this outbreak. [3] [4]

Monkeypox outbreak 2022

- Since early May 2022, cases of monkeypox have been reported from countries where the disease is not endemic, and continue to be reported in several endemic countries. Most confirmed cases with travel history reported travel to countries in Europe and North America, rather than endemic areas (i.e., West or Central Africa). This was the first time many monkeypox cases and clusters have been reported concurrently in nonendemic and endemic countries. [5]
- The sudden simultaneous appearance of monkeypox in several nonendemic countries suggests there may have been undetected transmission for some time. [6]
- West African clade has been implicated in this outbreak. [2]
- A large portion of the global population is susceptible to MPXV, since smallpox vaccination was discontinued. It is estimated over 70% of the global population is no longer protected against smallpox, and through cross-immunity, to the closely related orthopox virus monkeypox. [7]
- Canadians born in 1972 or later have not been routinely immunized against smallpox,[3] unless immunized for travel to other countries. World Health Organization (WHO) recommended vaccination discontinuation for travel in 1980 and by 1982, vaccination was no longer required by any country. Globally, only a relatively small number of military personnel, frontline health professionals, and laboratory workers have been vaccinated against smallpox in recent years. Smallpox vaccination is recommended for laboratory workers who handle smallpox virus or other orthopox viruses in specialized research facilities. [8] [9]
- On May 19, 2022, Public Health Agency of Canada (PHAC) confirmed the first cases of monkeypox in Canada. [10]
- In some European countries, epidemiological and clinical features of the 2022 outbreak suggest human-to-human transmission via close contact, including sexual and intimate contact. [4]
- While many affected in the current global outbreak are gay, bisexual, or other men who have sex with men (MSM), anyone who has been in close contact with someone who has monkeypox can become infected. [11] [12]
- Potential factors contributing to the global surge in cases include:

[3] Evidence of prior smallpox vaccination can usually be found as a scar on the upper arm because older generations of smallpox vaccine are administered by scarification into the epidermis using a multiple-puncture technique with a bifurcated needle. When vaccinia virus is inoculated into the epidermis the virus induces an immune response termed "a take". On day 3 to 4 a papule appears, progressing to a vesicle surround by erythema. About 1 week after vaccination, the vesicle umbilicates and pustulates, followed by crusting (dark brown or black scab). After 3 weeks, the scab detaches leaving a scar. The vaccination site is inspected 6-8 days after vaccination to ensure “a take” has occurred. If there is no evidence of papules or vesicles and erythema, the individual should be vaccinated again. [1] [8]

    - Attendance at large-scale international events may have facilitated spreading the virus globally.
    - Lack of awareness of monkeypox among healthcare providers outside of endemic areas may have contributed to under-detection and subsequent low-level circulation of MPXV.
    - Lack of cross-protection from smallpox vaccination in younger populations from discontinuation of immunization programs following smallpox global eradication.
    - Potential for mutations leading to increased transmissibility (e.g., 50 single nucleotide polymorphisms have been detected in the 2022 outbreak strain of virus, compared to MPXV isolated in 2018 and 2019). [4]
- On June 14, 2022, WHO announced it was working with experts across the globe to change the name of MPXV, its clades, and the disease it causes after a group of international scientists stressed the need for non-discriminatory and non-stigmatizing virus nomenclature. The scientists explained the historic clade names are counter to best practice of avoiding geographic locations in disease nomenclature and disease groups, noting recent implementation for SARS-CoV-2 should be the norm. WHO stated the new names would be announced as soon as possible. [13] [14]
- Effective June 16, 2022, Ontario's Chief Medical Officer of Health designated monkeypox a Disease of Public Health Significance (DOPHS) under the *Health Protection and Promotion Act* (HPPA). Regulated health professionals required to report under HPPA must report suspected cases of monkeypox directly to the local Medical Officer of Health in accordance with reporting requirements in HPPA. [15] [16]
- On June 23, 2022, WHO held a meeting of the International Health Regulations (IHR) Emergency Committee regarding the global monkeypox outbreak. WHO announced on June 25, 2022 it concurred with advice offered by the IHR Emergency Committee and, at present, the outbreak did not constitute a public health emergency of international concern (PHEIC). WHO acknowledged the emergency nature of the outbreak and controlling further spread required intense response efforts. WHO would closely monitor the outbreak and review the decision after a few weeks, once more information about current unknowns was available, to determine if significant changes have occurred warranting reconsideration. [11] [17]
- On July 14, 2022, WHO announced it will reconvene its IHR Emergency Committee for a second meeting on July 21, 2022. The committee will provide its views on whether the outbreak constitutes a PHEIC, and if so, propose temporary recommendations on how to better prevent and reduce disease spread and manage the global public health response. WHO will issue a statement a few days after the meeting. [8] [9]

Global [18]

	Total confirmed cases	Number of locations
Historically has not reported cases	12333	62
Historically has reported cases	233	6
Total (As of July 15, 2022)	**12556**	**68**

Countries with high case counts [18]

Country	Confirmed cases (As of July 15, 2022)
Spain	2835
Germany	1859
United Kingdom	1856
United States	1469
France	912
Netherlands	549
Canada	539
Portugal	515
Italy	339
Brazil	310
Belgium	224
Switzerland	198

Canada [19]

Province	Confirmed cases
Quebec	299
Ontario	194
British Columbia	32
Alberta	12
Saskatchewan	2
Total (As of July 15, 2022)	**539**

Ontario [20]

Public Health Unit	Confirmed cases
Toronto Public Health	151
Ottawa Public Health	13
Middlesex-London Health	6
City of Hamilton Public Health Services	4
Halton Region Public Health	4
Wellington-Dufferin-Guelph Public Health	3
Durham Region Health	2
Haldimand-Norfolk Health	2
Peel Public Health	2
Brant County Health	1
Eastern Ontario Health	1
Grey Bruce Health	1
Peterborough Public Health	1
Public Health Sudbury & Districts	1
Simcoe-Muskoka District Health	1
York Region Public Health	1
Total*	**194**

*As of July 14, 2022, 193/194 confirmed cases were male with average age of 37 years (range: 20-66 years); 9/194 cases have been hospitalized; 1/194 case has been in ICU; no deaths have been reported. Most commonly reported symptoms included rash, fever, oral/genital lesions, lymphadenopathy, fatigue, chills, headache, and myalgia.

Routes of transmission

Infection is thought to occur when the virus enters the body through skin, respiratory tract, or mucous membranes. Three forms of transmission are animal-to-human (zoonotic), person-to-person, and fomite-mediated.

Animal-to-human

- From infected animals through bites, scratches, and licking.
- Direct contact with blood, body fluids, or lesions of infected living or deceased animals.
- Handling or preparing living or deceased animals for consumption, especially if meat is raw or undercooked.
- Consuming inadequately cooked meat or other animal products of infected animals.

Person-to-person

- Direct contact with skin lesions, scabs, blood, body fluids, or mucosal surfaces (mouth, throat, genitalia, perianal area, eyes). MPXV is not considered a sexually transmitted infection (STI); however, transmission may occur via intimate contact.
- Respiratory transmission (e.g., contact with infected droplets generated by coughing and sneezing) during direct and prolonged face-to-face contact.
    - It is not known whether airborne transmission of MPXV occurs, although it does not appear to be a primary mode of transmission. More evidence is required to determine routes of transmission for the 2022 outbreak.
- Transplacentally from an infected pregnant individual to the fetus, which can lead to congenital monkeypox.[4]

Fomites

- Direct, unprotected contact with contaminated clothing or linens, sharing objects that have been in contact with an infectious person (e.g., drinking cups), or unprotected contact with objects in contact with an infectious animal.

Transmission risk increases:

- During sexual contact (including oral and non-penetrative sexual contact)
- Providing care (e.g., healthcare workers and family members who provide care)
- Living in the same household [1] [2] [4] [21] [22]

It is not clear whether asymptomatic individuals can spread the disease. It is not known with certainty if individuals can transmit the infection before developing symptoms. It is believed contagiousness may begin with symptom onset. Individuals remain contagious until scabs have fallen off on their own and lesions have epithelialized. [2] [23]

Clinical signs and symptoms

Symptoms of monkeypox are similar to but less severe than smallpox.

[4] Adverse pregnancy outcomes (e.g., spontaneous pregnancy loss, stillbirth) and preterm delivery have been reported in pregnant individuals with monkeypox infection. [66]

Typical presentation:

Incubation period

- Usually 6-13 days (range 5-21 days)

Prodrome phase

- 1-4 days, occurs prior to rash onset, or concurrently
- May involve fever, chills, headache, myalgia (muscle aches), arthralgia (joint pain), back pain, weakness, fatigue
- Lymphadenopathy may occur (i.e., submandibular, cervical, axillary, inguinal; may be bilateral or unilateral), which is a feature that helps differentiate monkeypox from other diseases with a similar rash (e.g., chickenpox, syphilis, herpes simplex virus[5])

Rash phase

- Usually begins in the mouth or on the face
- May then spread to body, extremities, anogenital area, palms and soles
- Typical lesions are described as deep-seated, well-circumscribed, often with central umbilication (resembles a dot on top of the lesion)
- Rash can last for 2-4 weeks and progress through the following stages before falling off: macules (flat lesions), papules (raised lesions), vesicles (filled with clear fluid), pustules (filled with pus), and ulcers that eventually scab over (crust)
- Lesions tend to evolve synchronously
- Rash may be localized, or generalized. If generalized, it may be similar to smallpox, with a centrifugal distribution (i.e., greatest concentration of lesions on face and distal extremities)

Recovery phase

- Rashes scab (crust), fall off, and new skin forms

Atypical presentation

Prior to the 2022 outbreak, monkeypox infections usually followed the typical presentation. However, some jurisdictions with new monkeypox outbreaks have noted atypical presentations.

Atypical features may include:

- Presenting with lesions at initial site of inoculation (e.g., mouth, genital, or perianal areas) prior to onset of systemic symptoms
- Presenting with only a few or just a single lesion
- Absence of skin lesions, with anal pain and bleeding
- Lesions in the genital or perineal/perianal area which do not spread further
- Lesions appearing at different stages of development (evolve asynchronously)
- Absence of prodromal phase (i.e., lesions appear before fever, malaise, etc.) [2] [9] [24] [25]

[5] Refer to Episode 61 for clinical features of chickenpox, syphilis, and herpes simplex virus.

Individuals are to contact a medical healthcare provider immediately if they:
- Develop monkeypox symptoms
- Had contact with a known or suspect monkeypox case [26]

Diagnosis
Monkeypox is diagnosed based on a combination of factors, such as:
- Clinical signs and symptoms
- Risk factors (e.g., exposure to a case, travel history)
- Laboratory testing [26]

Individuals with a compatible clinical illness where monkeypox is suspected should be tested. Diagnosis is confirmed by the presence of MPXV DNA by PCR. [27]

Specimens for PCR testing include:
- Swabs of lesion surface or lesion fluid
- Lesion crusts (scabs)
- Nasopharyngeal and/or throat swab (useful if testing during prodrome phase [e.g., pre-rash in febrile individuals who are contacts of cases], or in individuals with macular or papular rash)

Nasopharyngeal and throat swabs are generally **not** recommended if there are skin lesions that can be swabbed, or if there is skin lesion material (e.g., scab) that can be tested. Skin lesions usually have higher viral loads; thus, skin swabs or lesion material are more sensitive (~90%) for MPXV detection. Currently, serology is not ideal because of significant cross-reactivity with other *Orthopoxviruses* and previously smallpox vaccinated individuals. However, blood samples may be taken to supplement nasal or throat swabs. [2] [27]

Case definitions [21] [28]

Case type	Description		
Confirmed	A person who is laboratory confirmed for monkeypox virus by detection of monkeypox virus DNA by polymerase chain reaction (PCR) from an appropriate clinical specimen OR Isolation of monkeypox virus in culture from an appropriate clinical specimen		
Probable	A person who meets the criteria in 1, 2, OR 3:		
	1. a) Presents with an unexplained acute rash[6] or lesion(s) AND b) Meets at least one of the following within the 21 days before their symptom onset:	2. a) Presents with an unexplained acute rash or lesion(s) AND b) Has an indeterminate *Orthopoxvirus* or	3. a) Has a positive *Orthopoxvirus* PCR result AND b) Is pending monkeypox virus PCR

[6] Common causes of acute illness with rash include coxsackieviruses (e.g., hand, foot, and mouth disease), varicella zoster, herpes zoster, measles, herpes simplex, syphilis, chancroid, lymphogranuloma venereum. [28]

Case type	Description		
	• High risk exposure to a probable or confirmed monkeypox case[7] • History of travel to a region that has reported confirmed cases of monkeypox • A relevant zoonotic exposure[8]	monkeypox virus PCR result.	
Suspect	A person monkeypox virus has not been ruled out by a negative PCR result and meets the criteria in 1 OR 2:		
	1. a) An unexplained acute rash AND b) Has at least one of the following signs or symptoms: • Fever (>38.5°C) • Chills and/or sweats • Lymphadenopathy • Headache • Myalgia • Sore throat • Cough • Coryza • Prostration or asthenia (profound weakness)	2. An unexplained acute genital, perianal or oral lesion(s)	
Person under investigation (PUI)	A person with a pending *Orthopoxvirus* or monkeypox virus PCR result, AND Does not meet criteria for a suspect, probable, or confirmed case of monkeypox.		

Differential diagnosis

Differential diagnosis includes, but not limited to:

- Chickenpox (varicella)[9]
- Primary syphilis (with a painless chancre)
- Secondary syphilis (with widespread rash)
- Shingles (herpes zoster)[10]
- Herpes simplex
- Hand, foot, and mouth disease[11]
- Measles[12]
- Allergic reactions

[7] High-risk exposure includes living in the same household, having direct physical contact including sexual contact, and direct contact with a skin lesion or bodily fluid without appropriate PPE. [21]
[8] Relevant zoonotic exposure may include contact with a dead or live wild animal or exotic pet of African endemic species, or use of a product derived from such animals (e.g., game meat, creams, lotions, powders, etc.). [28]
[9] Chickenpox rash tends to favour a truncal distribution while monkeypox is usually more predominant on the face or extremities. Chickenpox presents with lesions of different stages in close proximity, monkeypox lesions tend to have a similar size and stage of development on a single site of the body.
[10] Refer to Episode 61 for discussion on clinical features of shingles.
[11] Refer to Episode 61 for discussion on clinical features of hand, foot, and mouth disease.
[12] Refer to Episode 61 for discussion on clinical features of measles.

- Molluscum contagiosum[13]
- Disseminated gonorrhea infections (DGI) (in cases with proctitis [inflammation of lining of rectum] and rash)[14]
- Lymphogranuloma venereum (LGV)[15]
- Chancroid[16]
- Ecthyma[17]
- Ecthyma gangrenosum[18]
- Less common diseases to consider include other poxvirus infections, such as orf virus (ecthyma contagiosum). [2]

Given some of the atypical presentations with early lesions in the mouth, genital or anorectal areas, consider monkeypox alongside other sexually transmitted infections. It is possible for monkeypox to occur concurrently with other rash diseases (e.g., herpes zoster and herpes simplex infections). [2] [24]

[13] Molluscum contagiosum is caused by a poxvirus (molluscum contagiosum virus), which can cause small, firm, dome-shaped flesh-coloured papules with umbilication anywhere on the body, but are uncommon in mouth or on palms and soles. [29] [39]
[14] DGI is an uncommon but a severe complication of untreated gonorrhea. It occurs when the sexually transmitted pathogen *Neisseria gonorrhoeae* invades the bloodstream and spreads to distant sites in the body, leading to clinical manifestations such as petechial/pustular skin lesions, septic arthritis, polyarthralgia, tenosynovitis, bacteremia, or, on rare occasions, endocarditis or meningitis. [55]
[15] LGV is a STI caused by a strain of chlamydia bacteria. It can cause fever, fatigue; painless, small papule(s) (1–6 mm), at the site of inoculation (vulva, vagina, penis, rectum, oral cavity, occasionally cervix) that may ulcerate. and lymphadenopathy in the genital area. It can be prevented through safer sex practices and treated with antibiotics. [56] [57]
[16] Chancroid is a sexually transmitted bacterial infection caused by *Haemophilus ducreyi*. It is rare in Canada. Symptoms can include painful genital ulcers and painful, swollen regional lymph nodes. Symptoms appear up to 2 weeks after exposure. Chancroid is a risk factor in HIV transmission and acquisition. It can be prevented through safer sex practices and treated with antibiotics. [58] [59]
[17] Ecthyma is caused by streptococci, staphylococci, or both. Lesions begin as pustules that erode and form an ulcer with adherent crust. Ecthyma is an ulcerative form of impetigo. [60] [61]
[18] Ecthyma gangrenosum is a skin infection most commonly occurring in immunocompromised individuals with *Pseudomonas* bacteremia. Lesions begin as painless, round erythematous macules and patches with surrounding erythema before rapidly progressing to bullae and necrotic, ulcerative eschars. [62] [63]

Comparison of monkeypox with other rash inducing infections [23] [28] [29] [30]

Characteristic	Monkeypox	Chickenpox (Varicella)	Shingles (Herpes zoster)	Hand, foot, & mouth disease	Herpes simplex virus infection	Syphilis	Molluscum contagiosum
Etiology	Monkeypox virus (MPXV)	Varicella-zoster virus (VZV) [31]	Varicella-zoster virus (VZV) [32] [33]	Enteroviruses (e.g., coxsackievirus A16, enterovirus 71)	Herpes simplex virus (HSV-1 & HSV-2) [34] [35] [36] [37]	*Treponema pallidum* [38]	Poxvirus (molluscum contagiosum virus) [39] [40] [41]
Incubation period	5-21 days	10-21 days Can be up to 28 days in breakthrough infections.[19]	Reactivation of varicella zoster virus.	3-7 days	2-12 days	3-90 days	14-180 days
Fever	May occur, most commonly 1-3 days before rash onset.	Unvaccinated: mild if present, 1-2 days before rash. Breakthrough: less common.	Minority have fever.	1-2 days before oral vesicles.	Primary infection: fever followed by lesions.	Uncommon	No
Lymphadenopathy	Tender, regional	Generalized	Regional	Cervical	Primary: tender, regional	Primary: painless, regional Secondary: generalized	No
Other systemic symptoms	Malaise, myalgia, headache, arthralgia, fatigue.	Malaise, pharyngitis, anorexia.	Minority have malaise, headache.	Malaise, headache	Primary: malaise, myalgias, headache. Reactivation: prodromal tingling or shooting pains.	Primary: uncommon Secondary: headache, myalgia, arthralgia, pharyngitis, hepatosplenomegaly, alopecia, malaise.	None

[19] Breakthrough varicella is an infection occurring in an individual >42 days after varicella vaccination.

Characteristic	Monkeypox	Chickenpox (Varicella)	Shingles (Herpes zoster)	Hand, foot, & mouth disease	Herpes simplex virus infection	Syphilis	Molluscum contagiosum
Rash appearance & progression	Progresses through macules, papules, vesicles, pustules that umbilicate, then ulcerate, crust & fall off. Local pain & pruritis until crusting. Lesions may number from a few to several thousand. [23] Atypical presentation includes initial signs of a genital or peri-anal rash (prior to or without prodromal symptoms) which may not spread to other body parts, & lesion pleomorphism.	Unvaccinated: pruritic, rapidly progresses through macules, papules, vesicles, & crusting/scabs. All stages may be simultaneously present; lesions numbering 250-500 are superficial & may appear in crops. Breakthrough: usually, maculopapular lesions numbering ≤50 that do not progress to vesicles.	Usually pain, itching, tingling along the affected dermatome, followed 2-3 days later by painful vesicles on erythematous base that rupture, ulcerate & crust by 7–10 days.	Macules, sometimes with vesicles. Vesicles may break open & progress to crusting/scabs. Lesions may be at different stages of development. Local pruritis.	Primary: painful, pruritic cluster of vesicles on erythematous base. May progress to pustules, erosions, & ulcerations. Lesions crust then resolve. Recurrent: cluster of 2–4 mm vesicles on an erythematous base. May progress to vesicopustules & ulcers. Local pain & pruritis.	Primary: small papule develops rapidly into chancre (large, painless ulcer with indurated border) at inoculation site, painless. Secondary: maculopapular, may coalesce. Superficial mucosal erosions. Pustules. Condyloma lata. Rarely vesicular	2-5-mm firm, dome-shaped flesh-coloured papules with umbilication. Usually painless, but may become pruritic, red, & swollen. Papules usually disappear spontaneously within 6-12 months without scarring but may take up to 4 years.
Rash location	Appears at inoculation site, then may appear on other body parts, e.g., oral mucosa, genital area, conjunctiva, palms, soles.	Usually on chest, back, & face then spreads to other body parts. Rarely appear on palms & soles immunodeficient individuals.	Lesions distributed unilaterally within a single dermatome (e.g., torso, face). Dermatome is an area of skin whose sensory nerves all come from a single spinal nerve root.	Mouth, palms, soles, legs, arms, buttocks, genital area.	Primary: orofacial, genitalia Recurrent: orofacial, genitalia, rectum, hands, eyes.	Primary: site of inoculation. Secondary: most commonly on palms & soles, trunk, & extremities, intertriginous & mucosal areas.	Anywhere on body, e.g., face, neck, arms, legs, abdomen, & genital area, alone or in groups. Uncommon on palms & soles.

Characteristic	Monkeypox	Chickenpox (Varicella)	Shingles (Herpes zoster)	Hand, foot, & mouth disease	Herpes simplex virus infection	Syphilis	Molluscum contagiosum
Rash duration	14-28 days	Unvaccinated: 4-7 days Breakthrough: shorter duration of illness compared to unvaccinated.	2-4 weeks but the pain may continue.	7-10 days	Primary: 2-3 weeks Recurrent: 7-10 days	Primary chancre will resolve without treatment. If untreated, primary syphilis can progress to secondary syphilis. Secondary lesions resolve without treatment, then progresses to early or latent phase with no clinical manifestations.	6-12 months, up to 4 years
Oral signs	Small lesions develop on tongue & oral mucous membranes, which ulcerate.	Small vesicles develop on oral mucosa that rupture to form shallow ulcers.	Vesicular eruption may follow the sensory distribution of trigeminal nerve or one of its branches.	1–5-mm erythematous vesiculoulcerative stomatitis.	Primary: Labial vesicles rupture & crust, intraoral vesicles quickly ulcerate; extremely painful. Acute gingivitis, foul breath odour. Reactivation: labial vesicles coalesce, rupture creating painful weeping ulcers that crust. Intraoral vesicles rupture to form small painful ulcers.	Secondary: maculopapular lesions of oral mucosa, 5-10 mm in diameter with central ulceration covered by grayish membrane.	Lesions uncommon in mouth
Public health reportable disease	Yes	Yes	No	No	No	Yes	No

Disease severity

- Usually a mild, self-limiting disease with symptoms lasting 2-4 weeks. Most recover without the need for treatment. However, severe illness can occur in some individuals.
- Although vaccination against smallpox was historically protective, today individuals <40-50 years of age (depending on the country) may be more susceptible to monkeypox due to cessation of global smallpox vaccination campaigns after disease eradication.
- Newborns, children, and individuals with immune deficiencies may be at risk of more serious symptoms, complications, and death from monkeypox.
- Pregnant individuals are at high risk of severe disease.
- Complications from infection can include secondary infections, pneumonia, sepsis, encephalitis, corneal infection (may lead to vision loss), and death.
- Monkeypox case fatality ratio has historically ranged from 0-11% in the general population and has been higher among young children. In recent times, case fatality ratio has been around 3-6%, often in children or individuals who may have underlying health conditions. [1] [2]

Monkeypox and COVID-19

- It is currently unknown whether having COVID-19[20] or post COVID-19 condition (long COVID)[21] makes an individual more vulnerable to monkeypox. More research is needed on individuals with COVID-19 or post-COVID-19 condition and concurrent MPXV infection. [1] [23]

Managing illness

- Those diagnosed with monkeypox should self-isolate until all scabs have fallen off and healed (i.e., new intact skin has formed below, typically takes 2-4 weeks).
- Management of the illness is mainly focused on supportive care (e.g., analgesics for pain, antipyretics for fever).
- Tecovirimat (TPoxx®) may be recommended for individuals who are severely ill or disabled due to monkeypox infection or at high risk for severe disease.

Home self-isolation[22]

In Ontario, local public health units will provide self-isolation guidance for confirmed or probable cases, such as:

- Stay in a separate room/area away from other household members if possible and use a separate bathroom if available/feasible

[20] Refer to Episodes 10, 13, 22, 27, 28, 31, 33, 34, 39, 40, 56, 57, & 59 for additional information on COVID-19

[21] Refer to Episodes 28, 38, 48 & 59 for discussion on post COVID-19 condition (long COVID).

[22] For additional information on self-isolation refer to: Monkeypox Virus: Interim Case and Contact Management Guidance for Local Public Health Units https://www.publichealthontario.ca/-/media/Documents/M/2022/monkeypox-virus-interim-case-contact-management-guidance-phu.pdf
Ontario Public Health Standards: Requirements for Programs, Services and Accountability Infectious Disease Protocol, Appendix 1: Case Definitions and Disease Specific Information, Disease: Smallpox and other Orthopoxviruses including Monkeypox
https://www.health.gov.on.ca/en/pro/programs/publichealth/oph_standards/docs/smallpox_chapter.pdf

- Avoid contact with those at higher risk of severe monkeypox illness (e.g., individuals who are immunosuppressed or pregnant, children <12 years)
- Avoid leaving the home unless necessary (e.g., to seek essential medical care)
- Avoid non-essential household visitors
- Wear a mask for source control (medical mask preferred), especially if respiratory symptoms are present
- Cover skin lesions as much as possible (e.g., long sleeves, long pants)
- Avoid contact with animals, including household pets. [21] [28]

Therapeutics
Canada's National Emergency Strategic Stockpile (NESS) has a supply of vaccines and drugs in the event of a smallpox emergency. The NESS stockpile includes TPoxx® (tecovirimat) capsules and the Imvamune® vaccine, which are available to address monkeypox outbreaks in Canada. [2] [42]

Treatment

TPoxx®

- TPoxx® (tecovirimat) is an antiviral medication that targets and inhibits an orthopoxviral envelope protein required for viral maturation and dissemination (i.e., prevents viral replication; therefore, slowing down its spread throughout the body, allowing the body to build an immune response[23] to fight the infection).
- TPoxx® was authorized for use in Canada in 2021 to treat smallpox in adults and children weighing at least 13 kg (29 lbs).
- TPoxx® does not have approval for the treatment of monkeypox in Canada. However, a licensed healthcare professional may request this drug for eligible patients based on their clinical judgement for treating severe monkeypox infections.
- Ontario is able to access TPoxx® through the federal government. Given the current limited supply, the product is available for individuals who are severely ill or disabled due to monkeypox infection or at high risk for severe disease.
- TPoxx® is a capsule taken by mouth within 30 minutes after a full meal of moderate of high fat to ensure absorption of tecovirimat. It is taken twice a day for 14 days. [24] [43] [44] [45]

Treatment course [43]

Body weight	Dosage
13 kg to less than 25 kg	200 mg twice daily for 14 days
25 kg to less than 40 kg	400 mg twice daily for 14 days
40 kg and above	600 mg twice daily for 14 days
TPoxx® should be taken within 30 minutes after a full meal of moderate or high fat to ensure proper tecovirimat absorption	

[23] Refer to Episodes 44 & 45 for discussion on the immune system.

Contraindications

- Individuals who are hypersensitive to this drug or to any ingredient in the formulation, or component of the container should not take it. A list of ingredients can be found in the product monograph.
- Children under 13 kg (29 lbs) in weight. [43] [45] [46]

Eligibility criteria

TPoxx® should be considered for the following:

- Hospitalized patients with severe disease (e.g., hemorrhagic disease, sepsis, encephalitis, myocarditis, or other conditions requiring hospitalization);
- Persons who may be at high risk of severe disease such as:
    - Individuals who are severely immunocompromised;
    - Children, particularly <8 years of age;
    - Pregnant or breastfeeding individuals;[24]
    - Individuals with one or more complications (e.g., secondary bacterial skin infection; gastroenteritis with severe nausea/vomiting, diarrhea, or dehydration; pneumonia; concurrent disease; or other comorbidities).
- Individuals with MPXV infections with lesions that are leading to significant disability (e.g., proctitis, keratitis or other ocular involvement, pharyngitis/epiglottitis or other breathing/swallowing compromise). [24] [43]

Potential side effects of TPoxx®

- In adults, the most commonly reported side effects were headache, nausea, abdominal pain, and vomiting.
- Less common side effects may include:
    - Dry mouth, joint pain, itchiness, rash, mood changes, and a “pins and needles” sensation. Refer to drug monograph for more information.
- TPoxx® may interact with other medications. Individuals should speak to their healthcare provider about potential drug interactions. [43] [45]

Vaccination

Imvamune®

- Imvamune® (also called Jynneos®, Imvanex®) is a third-generation smallpox vaccine initially authorized by Health Canada in 2013 for emergency situations for active immunization against smallpox infection in adults ≥18 years with a contraindication to the first- or second-generation smallpox vaccines. Authorization was expanded in 2020 for immunization against smallpox, monkeypox, and other pox viruses in adults ≥18 years who are at high risk of exposure.
- Imvamune® was developed to provide an alternative vaccine for immunocompromised individuals and those with atopic dermatitis, who could not safely receive earlier generation (replicating) smallpox vaccines. These individuals

[24] TPoxx® has not been studied in pregnant individuals, benefits of use should outweigh risks. It is unknown if TPoxx® is excreted in human milk. Health benefits of breastfeeding should be considered, along with the pregnant individual’s clinical need for TPoxx® and any potential adverse effects on the breastfed child from TPoxx® or the underlying infection.

were a risk group with severe outcomes for earlier generations of smallpox vaccines.[25]

- Imvamune® is a live-attenuated, and non-replicating viral vaccine[26] produced from the *Orthopoxvirus* strain Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN).
- Primary vaccination schedule in vaccinia-naïve individuals consists of 2 doses of 0.5 mL 4 weeks apart administered by subcutaneous injection, preferably in deltoid region of the nondominant arm. [47] [48]

Contraindications

- Individuals who are hypersensitive to the vaccine or to any ingredient in the formulation or component of the container should not receive the vaccine. A list of ingredients can be found in the product monograph.
- Individuals with signs or symptoms of monkeypox infection should not receive the vaccine as it is not indicated to treat monkeypox.
- Individuals with a history of myocarditis or pericarditis linked to a previous dose of a first- or second-generation smallpox vaccine should speak to their healthcare provider. [44] [49] [50]

Use of Imvamune® in Ontario

- Currently due to limited supply, Ontario is utilizing a ring vaccination approach[27] by using a single 0.5mL dose of Imvamune® in locations with confirmed cases to limit ongoing transmission, with the goal of preventing spread of monkeypox to unaffected areas. Ontario Ministry of Health will continually evaluate this approach as the epidemiology evolves and vaccine supply increases.
- Based on Ministry of Health June 2022 guidelines, Imvamune® vaccine can be used for pre-exposure prophylaxis (PrEP) in locations with confirmed cases, or for post-exposure prophylaxis (PEP) throughout Ontario. [44] [49]

<u>Pre-exposure prophylaxis (PrEP)</u>

- Imvamune® should be considered for transgender or cisgender individuals who self-identify as belonging to the gay, bisexual, and other men who have sex with men (gbMSM) community AND at least one of the following:
    - Have received a diagnosis of bacterial STI (i.e., chlamydia, gonorrhea, syphilis) in the past 2 months;
    - Have had 2 or more sexual partners within the past 21 days or may be planning to;

[25]First- and second-generation smallpox vaccines, based upon vaccinia virus (VACV) are highly protective and were used extensively during the global eradication program. However, these live replication competent VACV vaccines have the potential to cause serious complications including progressive vaccinia, eczema vaccinatum, generalized vaccinia, encephalitis, and myo-/pericarditis, especially in individuals with immunodeficiency or skin disorders (e.g., atopic dermatitis). [54]
[26] Refer to Episode 15 for discussion on types of vaccines.
[27] Ring vaccination is a vaccine strategy where close contacts of a person exposed to a virus are vaccinated against the virus. Public health officials use it as part of a public health response to limit spread of vaccine-preventable diseases. Ring vaccination helped put an end to smallpox in the last half of the 1900s. [53]

    - Have attended venues for sexual contact within the past 21 days (i.e., bath houses, sex clubs) or may be planning to, or who work/volunteer in these settings;
    - Have had anonymous sex in the past 21 days (e.g., using hookup apps) or may be planning to;
    - Engage in sex work or may be planning to, and their sexual contacts.
- Individuals who are immunocompromised, pregnant, or breastfeeding may be at higher risk for severe illness from a monkeypox infection. They should contact their local public health unit (PHU) for PrEP consideration if they are at risk for contracting monkeypox. [24] [44] [49]

<u>Post-exposure prophylaxis (PEP)</u>

- Imvamune® for PEP requires an exposure risk assessment by a PHU. A single dose of the vaccine should be offered ideally within 4 days (up to 14 days) from date of last exposure to individuals who are a high-risk contact of a confirmed or probable case of monkeypox.
- Vaccine must be given within 4 days from exposure date to prevent disease onset.
- Vaccination given between 4 to 14 days after date of exposure may reduce disease symptoms, but may not prevent disease.
- Anyone who self-identifies as a high-risk contact of a confirmed or probable case of monkeypox should contact their local PHU for assessment to see if PEP is recommended.
- Additional risk/benefit discussion is indicated for immunocompromised, pregnant, and breastfeeding individuals, and individuals <18 years of age prior to receiving vaccine as PEP since:
    - There is limited data on use of Imvamune® in severely immunosuppressed individuals and pregnant individuals.
    - There is no data on whether the vaccine is excreted in breastmilk, although it is unlikely as the vaccine is nonreplicating.
    - The vaccine is not authorized for use in individuals <18 years, and has not been studied in this age group, although it has been offered to children as PEP in previous United Kingdom (UK) monkeypox incidents as cited in UK PEP guidance. Clinical trials have studied other vaccines (TB, malaria) using Modified Vaccinia Ankara (MVA) as a vector in children with a reassuring safety profile.
- Intermediate risk contacts may also be offered PEP, following a PHU assessment of risks and benefits (i.e., balance risks from exposure, protection from vaccination, and potential vaccine side effects). [24] [44] [49]

Potential side effects of Imvamune®

- Most common side effects at the injection site are pain, erythema, induration, and swelling.[28]

[28] Imvamune® does not leave a scar like previous smallpox vaccines since it is not given through scarification. It is delivered subcutaneously where the needle is placed into the fatty tissue below the skin and above the muscle tissue.

- Most common systemic reactions observed after vaccination are fatigue, headache, myalgia, and nausea.
- Most of the reported adverse drug reactions observed in clinical trials were mild to moderate and resolved within the first 7 days following vaccination.
- No cases of myocarditis or pericarditis were identified in clinical trials of Imvamune®. Individuals who develop any cardiac symptoms after receiving the vaccine should contact their healthcare provider.
- Refer to drug monograph for additional information. [48]

Vaccine coadministration

Data on coadministration of Imvamune® with other vaccines are not available. Thus, it is not recommended to administer Imvamune® with other vaccines, and to reschedule other vaccinations until at least 14 days after Imvamune® administration. However, PEP should not be delayed in an individual who has recently received another vaccine. [44]

Infection prevention and control (IPAC) recommendations in healthcare settings

Public Health Ontario has developed IPAC recommendations for monkeypox healthcare settings, such as hospitals and outpatient settings (e.g., primary care, sexual health clinics, vaccine clinics). Personal protective equipment (PPE) for healthcare workers includes:

- Gloves
- Gown
- Eye protection (e.g., face shields, safety glasses or goggles)
- Fit-tested and seal checked N-95 respirator (or equivalent); perform seal check after donning N95 respirator. [51]

Travel health notice for Canadian travellers

PHAC has issued a travel health notice for monkeypox:

- Travel health notices outline potential health risks to Canadian travellers and recommend ways to reduce them.
- As of July 15, 2022, the notice is Level 2 - Practise enhanced health precautions for the following locations: Argentina, Australia, Austria, Belgium, Bosnia and Herzegovina, Brazil, Bulgaria, Chile, Colombia, Croatia, Czech Republic, Denmark, Dominican Republic, Ecuador, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, India, Ireland, Israel, the West Bank and the Gaza Strip, Italy, Jamaica, Latvia, Lebanon, Luxembourg, Malta, Mexico, Morocco, Netherlands, New Zealand, Norway, Panama, Peru, Poland, Portugal, Puerto Rico, Romania, Russia, Saudi Arabia, Serbia, Singapore, Slovakia, Slovenia, South Africa, South Korea, Spain, Sweden, Switzerland, Taiwan, Turkey, United Arab Emirates, United Kingdom, United States, Venezuela.
- Notices remain in effect until removed from the website.[29] [22] [52]

[29] For more travel health information refer to https://travel.gc.ca/travelling/health-safety/travel-health-notices/515 and https://travel.gc.ca/travelling/health-safety/travel-health-notices

Take home messages

- Oral health professionals should be aware of the clinical signs and symptoms of monkeypox for prompt client referral for diagnosis, self-isolation, and contact tracing. Monkeypox is a reportable disease.
- Support public health efforts to prevent spread of the monkeypox virus by educating clients on routes of transmission, precautions to prevent infection, and signs and symptoms of infection.[30]

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Client resources

Monkeypox, City of Toronto
Provides information on transmission, symptoms, PrEP & PEP vaccine eligibility, etc.
https://www.toronto.ca/community-people/health-wellness-care/health-programs-advice/monkeypox/

Monkeypox virus, Ottawa Public Health
Provides information on symptoms, vaccine eligibility, etc.
https://www.ottawapublichealth.ca/en/public-health-topics/monkeypox-virus.aspx

Monkeypox, Canadian Centre for Occupational Health and Safety
Provides information on symptoms, transmission, risk of contracting, etc.
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