



Mpox: A Reemerging Public Health Emergency

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ABSTRACT

Keywords:

global emergency
infectious disease
men who have sex with men
Mpox
World Health Organization

On August 14, 2024, the World Health Organization director-general declared mpox a public health emergency of international concern (PHEIC), a consequence of increased case surge in the Democratic Republic of the Congo. However, just days after, single cases were reported in Sweden and Thailand. The current strain of mpox (Clade Ib) linked to this PHEIC has been associated with enhanced communicability and increased morbidity and mortality compared with infections with the Clade IIb strain that prompted the 2022 global public health threat. This article explores the pathophysiology of mpox, epidemiologic data related to the 2024 PHEIC, and effective vaccination prevention.

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Introduction

Mpox is a virus member of the genus *Orthopoxvirus*, which also includes the variola (causing smallpox), vaccinia, and cowpox viruses.^{1,2} Mpox is a zoonotic virus with potential communication from animal to human and from human to animal.² However, communication of the virus largely occurs from close person-to-person contact, including contact with open lesions (active rashes and scabs) and body fluids (sourced as saliva, mucus, semen, feces, and vaginal secretions).^{1,3,4} Vertical transplacental transmission from mother to newborn results from close skin-to-skin contact during the intrapartum and postpartum periods.^{1,5,6} Thus, portals of entry include the oropharynx, nasopharynx, or dermis. As described by Moore and colleagues⁴:

Following viral entry from any route (oropharynx, nasopharynx, or intradermal), the mpox virus replicates at the inoculation site and then spreads to local lymph nodes. Next, an initial viremia leads to viral spread and the seeding of other organs. This represents the incubation period, typically lasting 7 to 14 days with an upper limit of 21 days. Symptom onset correlates with a secondary viremia leading to 1 to 2 days of prodromal symptoms such as fever and lymphadenopathy before lesions appear. Infected patients may be contagious at this time. Lesions start in the oropharynx and then appear on the skin. Serum antibodies are often detectable by the time lesions appear.

History, Physical Examination, Clinical Evolution and Sequelae, Prognosis, Morbidity and Mortality

Vital historic information that clinicians can obtain regarding possible exposures to mpox include recent travel to geographic

regions where incidence and prevalence of mpox is occurring.⁷ In addition, patients should be evaluated based on risk factors for transmission. Because transmission of mpox can occur through close contact during sexual activities, risk of exposure and infection increases in persons who engage in more frequent sexual activities with novel partners.⁷ Specific examples include men who have sex with men (MSM), those who engage in sex with multiple partners, those who participate in sexual activity in sex venues (eg, sex clubs or bathhouses) or at public events (eg, raves, parties, or festivals), and those who exchange sex for commodity (eg, sex workers or anyone who has sex for money, drugs, or other goods).⁷ Nurse practitioners and other clinicians must approach sexual histories with sensitivity and use an open-ended, nonjudgmental approach.⁸ Patients may report symptoms of headache, fever, myalgia, and lymphadenopathy; lymphadenopathy is clinically significant because it differentiates mpox from smallpox.⁴ Physical examination can demonstrate mucosal lesions in the mouth early in infection, followed by integumentary lesions of the face and extremities; assessment of the palms of the hands and soles of the feet is important as lesions can also appear on these structures.⁴

Moore and colleagues⁴ describe the evolution of lesions and its relationship to communication: During the following 2 to 4 weeks, the lesions evolve in 1- to 2-day increments through macular, papular, vesicular, and pustular phases. Lesions change synchronously and are characterized as firm, deep-seated, and 2 to 10 mm in size. Lesions remain in the pustular phase for 5 to 7 days before crusts begin to form. Crusts form and desquamate over the subsequent 7 to 14 days, and the condition resolves around 3 to 4 weeks after symptom onset in most cases. Patients are no longer considered infectious after all crusts fall off.

Clinical sequelae associated with mpox infections include integumentary superinfection, scarring (which can be permanent),

Table 1

2024^a Incidence Data for Mpox in the Democratic Republic of the Congo (DRC), Burundi, the Central African Republic (CAR), the Republic of the Congo (ROC), Rwanda, and Uganda^b

Country	Cases Suspected (No.)	Cases Confirmed (No.)	Deaths (No.)
DRC	14,151	2,638	511
Burundi	165	61	Not reported
CAR	223	35	Not reported
ROC	150	19	Not reported
Rwanda	Not reported	4	Not reported
Uganda	Not reported	2	Not reported

^a Data were reported by the European Centre for Disease Prevention and Control on August 16, 2024.

^b Surveillance data from the DCR and its surrounding affected countries are incomplete.¹⁶

hyperpigmentation/hypopigmentation, corneal scarring (which can also be permanent and associated with permanent vision loss), pneumonia, dehydration, and sepsis. There are no current clinical treatments that are specifically proven for eradication of mpox; thus, clinical management is aimed at symptom support.⁴ Prognosis is good, with a reported death rate of 1.3 per 10,000 patients.⁹ Mortality is much higher in persons who are immunocompromised, especially in people living with HIV.⁹

Classification and Geographic Distribution

Mpox is classified as Clade I or II (with Subclades IIa and IIb). Clade I is associated with greater communicability, higher morbidity and mortality (with an up to 11% mortality rate), and more incidences of spontaneous abortions.^{6,10–12} Subclade IIb has traditionally been associated with most global infections, including the 2022 global outbreak.¹⁰ Although Clade I is usually endemically confined to the Democratic Republic of the Congo,^{11,12} the infections that prompted the 2024 public health emergency of international concern, in addition to a 2024 Health Update to the Health Alert Network,^{9,10,13} have been with a more virulent Clade I variant strain (Ib).¹⁴ Communicability of this strain has involved both sexual and nonsexual contact, and it is easier to communicate through routine close contact.¹⁴ Clade I also has higher morbidity and mortality. Consequently, global public health efforts to prevent its spread have recently intensified.¹²

Epidemiology

Currently, the incidence of the emerging 2024 Clade Ib variant strain spread of mpox differs from the 2022 outbreak of the Clade IIb strain. This is because, so far, cases have been seen only in the Democratic Republic of the Congo, its neighboring countries, and an isolated case in Sweden.^{12,15} For a comprehensive review of the 2022 outbreak and its epidemiologic course in the United States, see Blackwell et al.¹ Since January 2023, the Democratic Republic of

the Congo has recorded its largest number of annual suspect Clade I mpox cases.¹² Although endemic to the Democratic Republic of the Congo, this outbreak is more widespread than any historic outbreaks; the Republic of the Congo, the Democratic Republic of the Congo's neighboring country to the west, declared a Clade I outbreak in April 2024.¹²

In addition, cases with probable links back to the Democratic Republic of the Congo have been reported in the Central African Republic.¹² In late July 2024, countries on the Democratic Republic of the Congo's eastern border also reported confirmed cases of mpox.¹² Despite mpox being nonendemic in Rwanda and Uganda, these countries confirmed cases as Clade I (with a probable link to the Democratic Republic of the Congo); Clade testing remains pending in Burundi.¹² Table 1 presents the incidence data reported by the European Centre for Disease Prevention and Control on August 16, 2024, for the Democratic Republic of the Congo, Burundi, the Central African Republic, the Republic of the Congo, Rwanda, and Uganda.

Surveillance data from the Democratic Republic of the Congo and its surrounding affected countries are incomplete.¹⁶ However, the data suggest a much greater concentration in males and those younger than 15 years. For example, in the Democratic Republic of the Congo, approximately 66% of total cases ($n = 1,741$) have been in those younger than 15 years. Strikingly, 419 of the 511 deaths (82%) in the Democratic Republic of the Congo from this mpox outbreak have been in those younger than 15 years. Males accounted for 73% of cases ($n = 1,926$) in the Democratic Republic of the Congo. Data are similar in the Republic of the Congo, the Central African Republic, and Burundi (Table 2). Although Swedish health officials have not released demographic data related to their single case, they did indicate that the person's infection was acquired while in Africa.¹⁵ Similarly, the single case reported in Thailand was in a 66-year-old man who had recently arrived in the country from an unspecified African country.¹⁷

To date, the US has had no detected cases of Clade I mpox. Active surveillance is ongoing. These surveillance data include wastewater monitoring for community detection, specifically for Clades I and II.¹⁸ Nonetheless, the US Centers for Disease Control and Prevention (CDC) has conducted modeling and forecasting for a potential outbreak of Clade I mpox in the US. Because the 2022 outbreak in the US was primarily seen in gay men, bisexual men, and other MSM, the CDC's forecasting and modeling efforts remain concentrated in this population. Forecasting predicts that a Clade I outbreak in the US would make less of a public health impact than the 2022 Clade II outbreak as a consequence of varying levels of transmissibility of Clade I mpox due to 1) county-specific, population-level immunity from previous infection; 2) receiving either 1 or 2 doses of the JYN-NEOS vaccine (Bavarian Nordic Inc); and/or 3) changes in the sexual behaviors of gay men, bisexual men, and other MSM.

Population-level immunity noted from the 2022 outbreak resulted from mpox Clade II infections and vaccination coverage

Table 2

2024^a Demographic Data for Mpox Cases in the Democratic Republic of the Congo (DRC), Burundi, the Central African Republic (CAR), and the Republic of the Congo (ROC)^b

Cases (No. [%])				
Country	Cases in <15-Year-Olds	Cases in >15-Year-Olds	Males	Females
DRC ^c	1,741 (66)	897 (34)	1,926 (73)	712 (27)
Burundi	Not reported ^d	Not reported	32 (52)	29 (48)
CAR	15 (43)	19 (53)	22 (62)	13 (38)
ROC	11 (56)	8 (44)	11 (58)	15 (42)

^a Data were reported by the European Centre for Disease Prevention and Control¹³ on August 16, 2024, and are rounded to the nearest whole number.

^b Surveillance data from the DCR and its surrounding affected countries are incomplete.¹⁶

^c Children <15 years old composed 419 of the 511 total deaths (82%).

^d 18 of 61 cases (29.5%) in <5-year-olds.¹³

Table 3
Indications for Mpox Vaccination⁷

- Patients with known or suspected exposure to mpox
- Patients who have had sex with a partner diagnosed as having mpox within the past 2 wk
- Male patients who have had sex with other males in the past 6 mo who have had:
 - A new diagnosis of ≥ 1 sexually transmitted diseases
 - >1 sex partner
- Patients who report any of the following in the past 6 mo:
 - Sex at a sex venue (eg, sex club or bathhouse)
 - Sex at a large commercial event or in a geographic area where mpox transmission is occurring
- Patients traveling to a country with a Clade I mpox outbreak anticipating any of these activities during travel:
 - Sex with a novel partner
 - Sex at a commercial sex venue (eg, sex club or bathhouse)
 - Sex in exchange for commodity (money, drugs, goods, other trade)
 - Sex at a large public event (eg, rave, party, or festival)
- Patients with an identified occupational risk for mpox exposure (eg, some health care and laboratory workers)
- Patients who anticipate experiencing any of the above scenarios themselves or through exposure with a sex partner anticipating experiencing any of the above scenarios

within individual counties. Because vaccination plays a major role in conveying population-level immunity, the CDC recommends that all eligible persons get vaccinated.¹⁸

Prevention Through Vaccination

The global vaccine group Gavi has up to \$500 million dedicated to efforts to administer vaccines in countries affected by the escalating mpox outbreak in Africa.¹⁹ In the US, the JYNNEOS vaccine, a smallpox and mpox live, nonreplicating injection,¹ is accessible in local health departments (see CDC⁷ for more information about accessibility). Although out-of-pocket costs for the vaccine vary depending on where patients receive the vaccination and their insurance status, the current cost for a 10-pack of 1-dose vials of the vaccine for the private sector is \$270.00; the contracted rate by the CDC for this quantity is \$198.03.²⁰ The JYNNEOS vaccine is given in 2 doses, 4 weeks apart.⁷ During the 2022 Clade II outbreak in the US, vaccination shortages resulted in variance from the traditional subcutaneous administration route to intradermal because it reduced dosage requirements from 0.5 mL to 0.1 mL, yielding an immediate 5-fold increase in national supply.¹

Using the intradermal route, 0.1 mL is administered above the triceps.⁷ Intradermal administration is noninferior to the standard subcutaneous administration in terms of immunogenicity, reactogenicity, and safety.⁷ Although immunogenicity occurs after the first dose of JYNNEOS, it is strongest 2 weeks after the second dose. Specifically, data suggest vaccine efficacy of 35.8% in those who receive just 1 dose of the vaccine; this increases to 66% in those who receive 2 doses, thus achieving full vaccination.²¹ Patients should be screened for appropriateness for receiving vaccination. Table 3 provides an outline of patient populations for which the vaccine is indicated.

In addition, patients need to be informed that length of immunogenicity and potential vaccine waning times are unknown.⁷ There are no current booster recommendations.²² Table 4 summarizes the vaccine's major contraindications and adverse events.

Summary and Conclusion

It is evident that mpox is continuing to evolve into a global public health threat that is becoming increasingly serious.

Table 4
Adverse Events and Contraindications Associated With the JYNNEOS Vaccine^{1,7}

- Adverse events:
 - Pain, erythema, and pruritus at injection site
 - Fever
 - Headache
 - Fatigue
 - Nausea
 - Chills/rigors
 - Myalgia
 - Less pain is reported with intradermal injections; however, greater adverse events in this route include:
 - Pruritus
 - Edema
 - Erythema
 - Intradermal thickening
 - Skin discoloration at site of injection
- Contraindications:
 - Allergic reaction to the vaccine or any of its components
 - Reported allergy to gentamicin, ciprofloxacin, or chicken/egg protein

Variant strands of the virus are resulting in enhanced communicability and increased morbidity and mortality. Consequently, public health nurse practitioners, nurses, physicians, and other clinicians responsible for caring for individuals at highest risk for the disease must have an intimate knowledge of the pathophysiology of mpox (especially pathologic differences between Clade I, II, and emerging variants). Although a comprehensive discussion of health assessment and physical examination findings is beyond the scope of this work (see the work of Blackwell et al¹ for more information), correlating symptom constellations, physical examination findings, mpox lifecycle properties, and mpox epidemiology is vital. Public health clinicians need to recognize the differences between previous outbreaks (eg, 2022 global outbreak with Clade II), current outbreaks (occurring in 2024 with the Clade Ib variant strand), and potential future outbreaks (cf, CDC¹⁸).

Although vaccination as a prevention strategy was discussed in this article, additional and feasible prevention strategies, including contact precautions, isolation procedures, and modification of sexual behaviors, have been detailed elsewhere (see Blackwell et al¹). In addition, vaccine equity—including equity-related issues with the mpox vaccine—persist.²³ In the US, mpox infections have been primarily seen in MSM. Strong and swift action within lesbian, gay, bisexual, transgender, queer, and other (LGBTQ+) communities is credited with the 2022 public health reaction that quickly grew vaccine availability and the government health official response.^{1,24,25}

It is salient to emphasize that modeling suggests that future outbreaks of mpox in the US will continue to disproportionately impact MSM.¹⁸ Thus, public health nurses and other clinicians should continue to serve as major advocates to the LGBTQ+ communities they serve. Encouraging vaccination in eligible individuals and educating the public on the ways in which mpox is communicated and its chain of infection disrupted are essential. Undergraduate and graduate nursing and medical curricula need to include data on mpox; and future research should focus on novel prevention strategies, reduction of vaccine inequity and socioeconomic contributors to infection, and effective public outreach to quickly manage outbreaks.

CRedit authorship contribution statement

Christopher W. Blackwell: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis. **Humberto López**

Castillo: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Conceptualization. **Frances Armstrong:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Conceptualization. **Frank Guido-Sanz:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Conceptualization. **Rodney W. Hicks:** Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Project administration, Methodology, Investigation, Formal analysis.

Declaration of Competing Interest

In compliance with standard ethical guidelines, the authors report no relationships with business or industry that may pose a conflict of interest.

Funding

No external or internal funding was provided.

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