MONKEYPOX UPDATE

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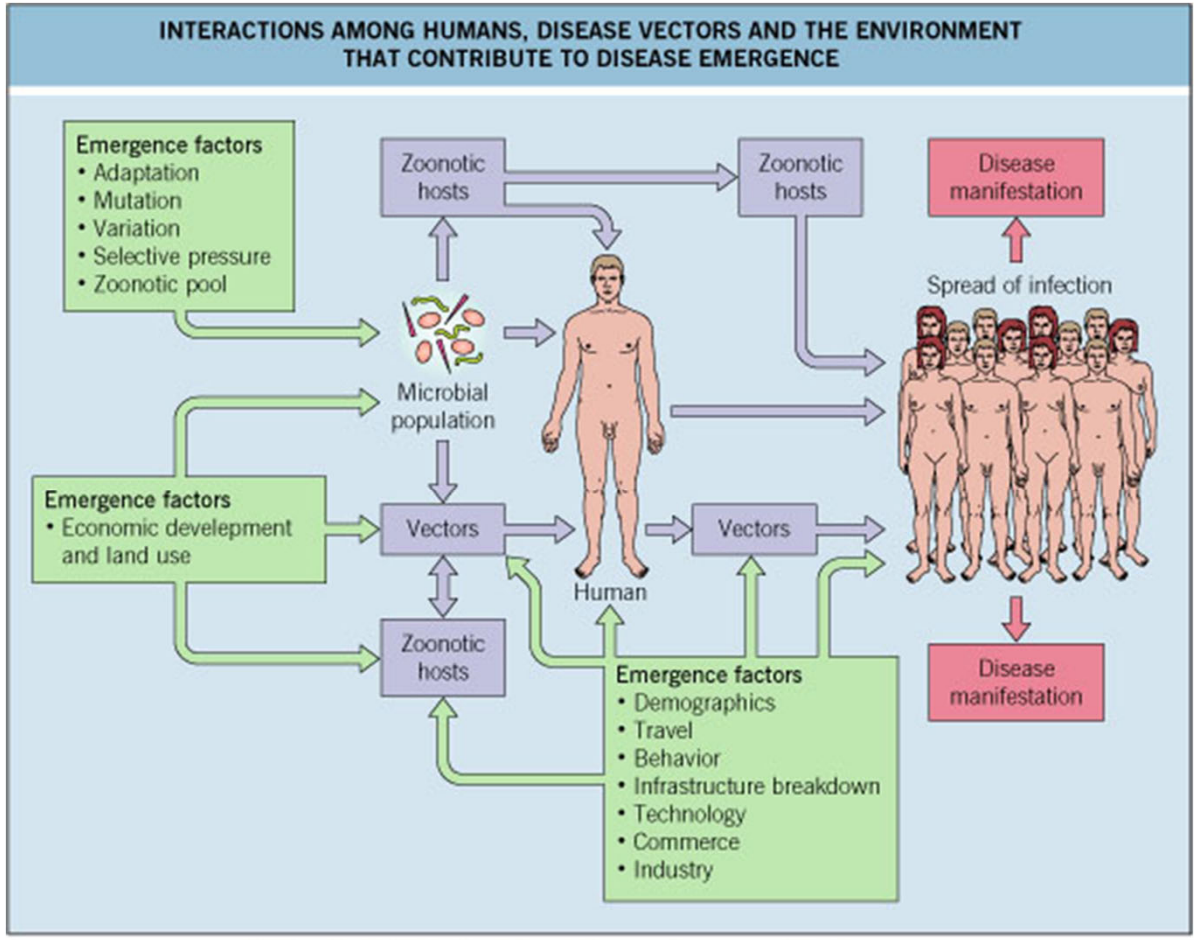
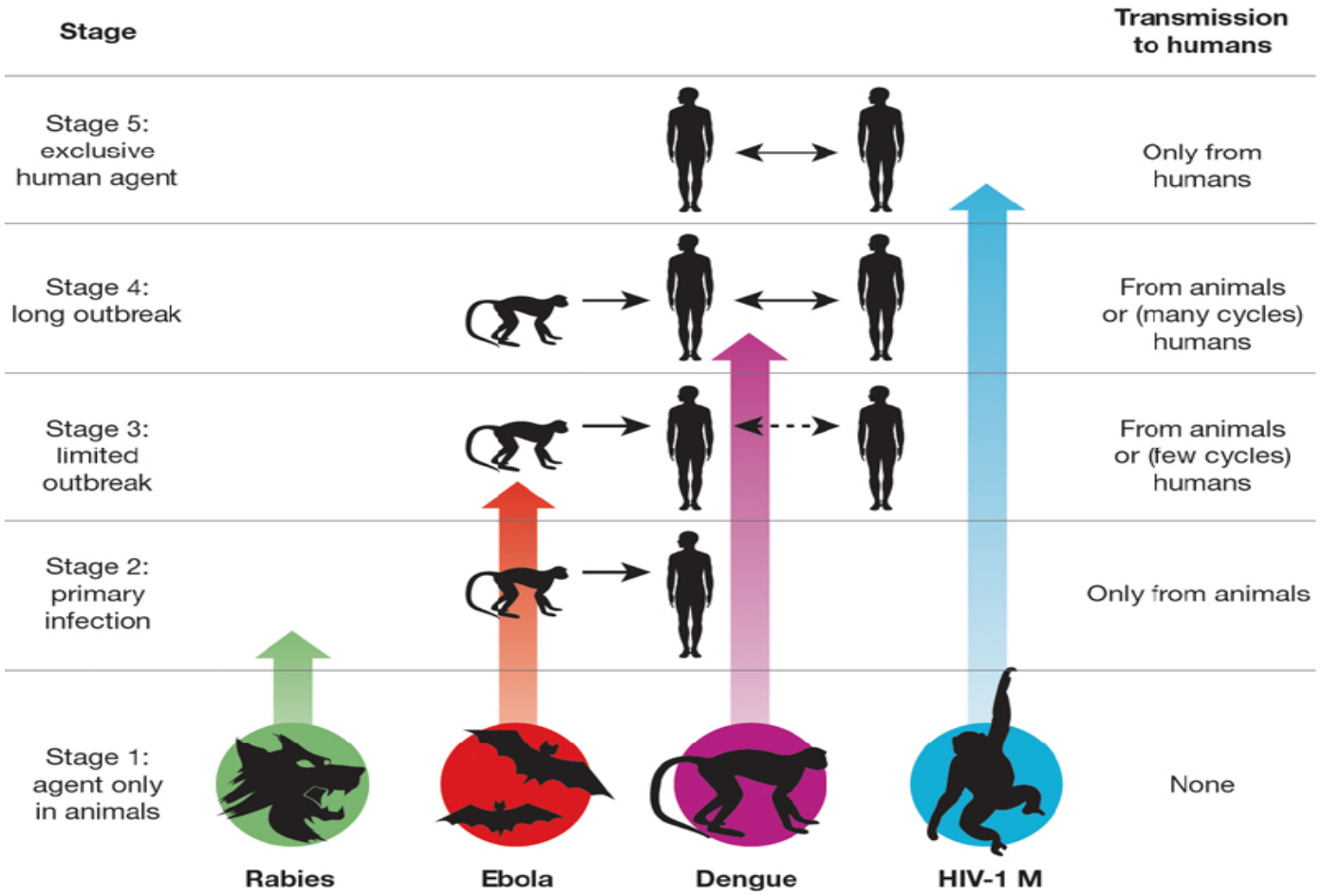
Disclosures: Consultancy; Pfizer, Merck, Sanofi, PDI, Germitec, Wellair
All drugs/vaccines issues discussed consistent with FDA approvals or authorizations
Thanks for Dr. Zack Moore (NC State Epidemiologist) for slides

BASIC CONCEPTS IN DISEASE EMERGENCE

- Emergence of infectious diseases is complex
- Infectious diseases are dynamic
- Most new infections are not caused by genuinely new pathogens
- Agents involved in new and reemergent infections cross taxonomic lines
- The concept of the microbe as *the* cause of disease is inadequate and incomplete
- Human activities are the most potent factors driving disease emergence
- Social, economic, political, climatic, technologic, and environmental factors shape disease patterns and influence emergence
- Understanding and responding to disease emergence require a global prospective, conceptually and geographically
- The current global situation favors disease emergence

Wilson ME. Emerging Infectious Diseases 1995;1:39





http://web.stanford.edu/group/parasites/ParaSites2012/Lassa%20Libby%20Burch

Monkeypox (rodents)

SARS-CoV-2 (bats)

ZOONOTIC DISEASE THREATS

Table 1. Importance of selected zoonotic diseases.

Disease	No. of US[a] cases in 1990–1998	Bioterrorism potential[b]	Infection control concern
Andes virus pulmonary syndrome	Not reportable	+	++
Anthrax	1	+++	+
B virus infection	Not reportable	None	+
Hemorrhagic fever (due to filoviruses and arenaviruses)	Not reportable	+++	+++
Monkeypox	Not reportable	?	++
Plague	80	+++	+++
Q fever	Not reportable	++	+
Rabies	25	None	+

NOTE. +++, high concern; ++, moderate concern; +, low concern; ?, unknown.

[a] Some zoonotic diseases, although not reportable nationally, may be reportable in individual states.

[b] Data are from [5].

Weber DJ, Rutala WA. Clin Infect Dis 2001;32:446

Table 2. Zoonotic diseases: mode(s) of transmission and risk of human-to-human transmission.

Disease	Pathogen	Mode(s) of transmission	Risk of human-to-human transmission
Hantavirus pulmonary syndrome	Andes virus	Inhalation of host rodent feces, urine, or saliva	Undefined; epidemiological and molecular evidence supports hypotheses regarding person-to-person transmission
Anthrax	*Bacillus anthracis*	Direct contact with contaminated animal products (e.g., hides), inhalation of spores, or ingestion of contaminated food	Rare cases of human-to-human transmission via direct contact with cutaneous lesions; risk of infection via inhalation from contaminated clothes and/or patient items
B virus infection	Cercopithecine herpesvirus 1	Direct contact with macaques (e.g., animal bites or scratches, cage scratch, or contaminated sharp injury); direct contact with infected cell culture	Rare; only a single case reported following direct contact with herpetic lesion
Hemorrhagic fever	Multiple agents[a]	Direct contact with potentially infective material (e.g., blood, vomitus, stool, or tissue)	High; person-to-person transmission common; nosocomial transmission frequent
Monkeypox	*Orthopoxvirus*	Contact with lesions; droplet transmission (?)	Attack rate among household contacts (unvaccinated), ~10%
Plague	*Yersinia pestis*	Flea bite; cat scratch; inhalation	High for pneumonic plague; theoretical for cutaneous plague (via inhalation from aspiration or wound irrigation); risk of infection via inhalation from contaminated clothes and/or patient items
Q fever	*Coxiella burnetii*	Contact with products of conception; inhalation	Rare; single case of human-to-human transmission (obstetrician); risk of infection via inhalation from contaminated clothes and/or patient items
Rabies	Rhabdovirus	Animal bites or scratches; rarely, mucous membrane contamination with animal saliva, aerosol transmission while spelunking or in a laboratory, or corneal transplantation; exposure frequently unknown	Animal-to-human transmission via nonintact skin and mucosal contact with saliva is well documented; human-to-human transmission theoretically possible; anecdotal reports of human-to-human transmission; nosocomial transmission not reported

NOTE. ?, unknown.

[a] Including Ebola, Marburg, Lassa, Crimean-Congo hemorrhagic fever, Argentine hemorrhagic fever, and Bolivian hemorrhagic fever viruses.

ORTHOPOXVIRUSES: MONKEYPOX

- Zoonotic Orthopoxvirus disease endemic to West and Central Africa
  - Most important members: Monkeypox, Variola (smallpox), Vaccinia virus (smallpox vaccine)
  - Others: Camelpox, Cowpox, Ectromelia virus, Horsepox virus, Raccoonpox virus, Skunkpox virus, Taterapox virus, Uasin Gishu virus, Volepox virus
- Initially recognized in 1958 a viral eruption in captive primates (reservoir: rodents)
- First human cases observed in Zaire in 1970 and 1971
- Changing epidemiology with time
  - Increasing cases linked to decreasing prevalence of smallpox vaccinees
  - Cases now more likely to be young adults rather than children
- Central African clade (Rho, 0.6-1.0) more virulent than West African clade (Rho, lower)
- Secondary attack rate (households): ~8%; range, 0-11% (unvaccinated)
- Mortality: Central African clade, 1%-10%; West African clade, 1%-3%
  - Current outbreak strain represents a new clade
- Receipt of smallpox vaccine = 85% reduction in infection

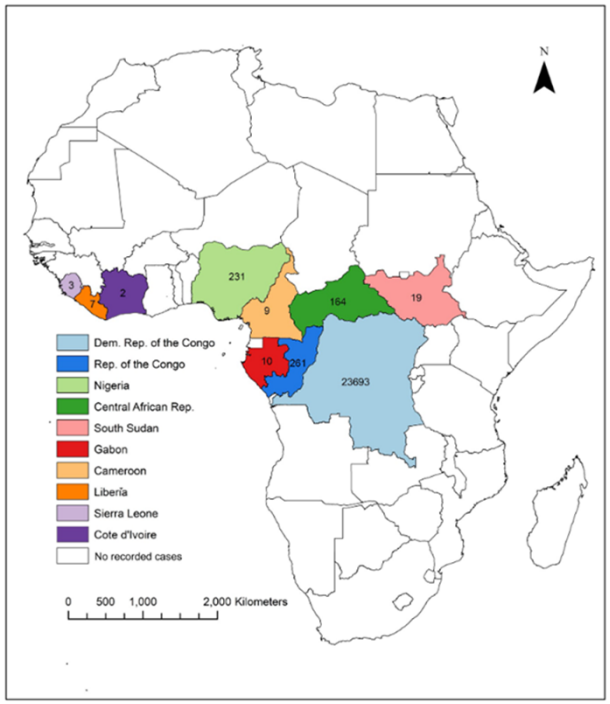


Fig 2. Map of countries and total number of suspected cases identified by this review, 1970-2018*. Created using ArcGIS. *Suspect cases in DRC are reported to exceed 1000 per year[1] and therefore the total reported cases is likely to exceed what was accessible for review.

Alakunle E, et al. Viruses 2020;12:1257

Beer EM, Rao VB. PLOS Neglected Trop Dis 2019; Oct 16

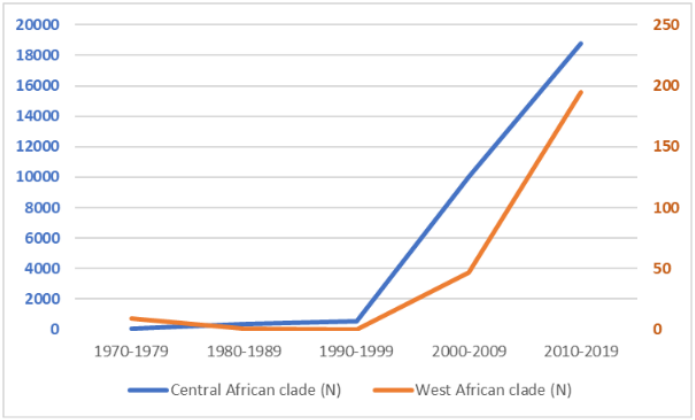
The changing epidemiology of human monkeypox – a potential threat? A systematic review

- The number of human monkeypox cases has been on the rise since the 1970s, with the most dramatic increases occurring in the DRC. The median age at presentation has increased from 4 (1970s) to 21 years (2010–2019). There was an overall case fatality rate of 8.7%, with a significant difference between clades — Central African 10.6% (95% CI: 8.4% – 13.3%) vs. West African 3.6% (95% CI: 1.7% – 6.8%). Since 2003, import- and travel-related spread outside of Africa has occasionally resulted in outbreaks. Interactions/activities with infected animals or individuals are risk behaviors associated with acquiring monkeypox. Our review shows an escalation of monkeypox cases, especially in the highly endemic DRC, a spread to other countries, and a growing median age from young children to young adults. These findings may be related to the cessation of smallpox vaccination, which provided some cross-protection against monkeypox, leading to increased human-to-human transmission.

Burnge EM, et al.
https://www.medrxiv.org/content/10.1101/2021.12.21.21268202v1.full.pdf

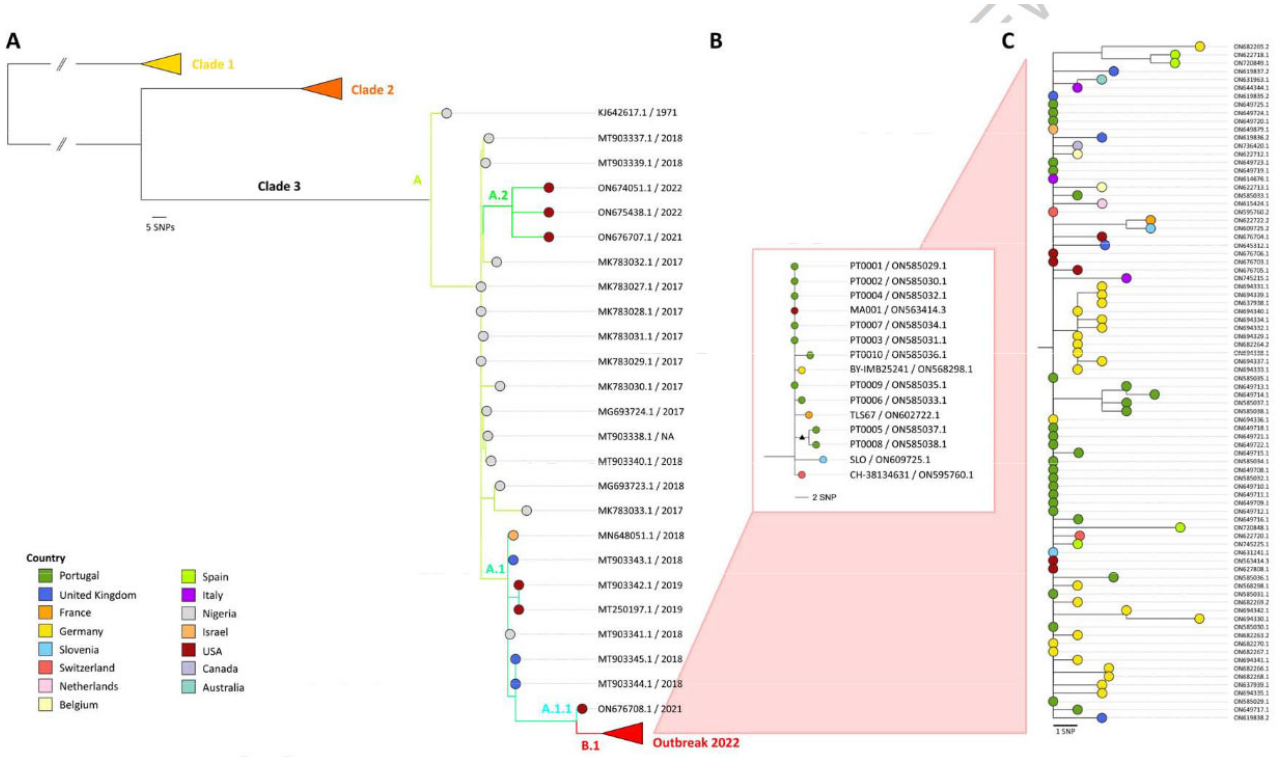
Decade	Central African Clade (N)	West African Clade (N)	Total Cases
1970-1979	38	9	47
1980-1989	355	1	356
1990-1999	520	0	520
2000-2009	92 confirmed 10,027 suspected[2]	47	139 10,027
2009-2019	85 confirmed 18,788 suspected[2]	195	280 18,788

[1] The five cases from Cameroon are not included in this table, as clade was not reported in any of the articles and WHO reported that Cameroon is the only country in which both clades have been detected [12].
[2] Suspected cases are from the Democratic Republic of the Congo, as number of suspected cases rather than confirmed cases were primarily reported. Suspected cases for other countries are not reported since testing of suspected cases was generally undertaken.



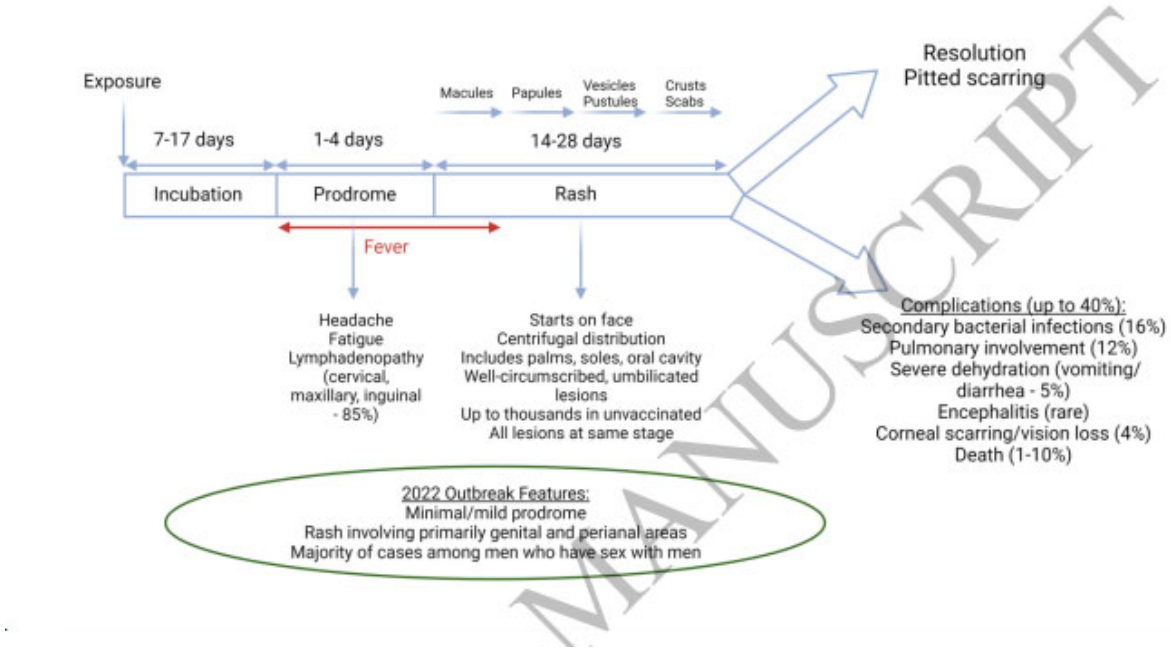
Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus

The largest monkeypox virus (MPXV) outbreak described so far in non-endemic countries was identified in May 2022. Here, shotgun metagenomics allowed the rapid reconstruction and phylogenomic characterization of the first MPXV outbreak genome sequences, showing that this MPXV belongs to clade 3 and that the outbreak most likely has a single origin. Although 2022 MPXV (lineage B.1) clustered with 2018-2019 cases linked to an endemic country, it segregates in a divergent phylogenetic branch, likely reflecting continuous accelerated evolution. An in-depth mutational analysis suggests the action of host APOBEC3 in viral evolution as well as signs of potential MPXV human adaptation in ongoing microevolution. Our findings also indicate that genome sequencing may provide resolution to track the spread and transmission of this presumably slow-evolving dsDNA virus.



Isidro J, et al. Nature Medicine 2022;24 June

MONKEYPOX: CLINICAL COURSE



Siegrist EA, et al. Accepted Clin Infect Dis

	2018			2019	2021		
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Site of HCID unit	London	Liverpool	Newcastle	London	Liverpool	Liverpool	Liverpool
Age range, years*	30–40	30–40	30–40	40–50	30–40	<2	30–40
Sex	Male	Male	Female	Male	Male	Female	Female
Transmission rank	Isolated	Index	Secondary	Isolated	Index	Secondary	Tertiary
Country of acquisition	Nigeria	Nigeria	UK	Nigeria	Nigeria	UK	UK
Smallpox vaccination history	None	None	MVA six days post-exposure or 12 days pre-illness	None	None	None	None
HIV, hepatitis B, and hepatitis C status	Negative	Negative	Negative	Negative	Negative	Not tested (parents negative)	Negative
Prodrome	Fever and night sweats (2 days)	Fever and groin swelling (4 days)	Coryzal illness (1 day)	Fever and headache (2 days)	None	None	None
Lymphadenopathy	Yes	Yes	No	Yes	Yes	Yes	No
Approximate maximum number of concurrent lesions	150	100	32	100	40	30	10
Distribution of lesions	Face, scalp, trunk, limbs, palms, glans penis, and scrotum	Face, trunk, limbs, palms, soles, and scrotum	Face, trunk, hands (including nail bed), and labia majora	Face, scalp, trunk, limbs, penile shaft, palms, and soles	Face, trunk, limbs, palms, and penile shaft	Face, trunk, arms, and legs	Face, trunk, arms, and hands
Complications of illness	Low mood and emotional lability. Ulcerated inguinal lesion with delayed healing	Deep tissue abscesses, severe pain, and low mood	Conjunctivitis, painful disruption of thumbnail from subungual lesion	Ulcerated inguinal lesion with delayed healing	None	Pruritis and contact dermatitis from cleaning products	Low mood
Specific management of complications	Clinical psychology input	Empiric broad-spectrum antibiotics, abscess drainage, and analgesia (including opiate and neuropathic agents)	Antibacterial eye drops	Empiric azithromycin	Nil specific	Calamine lotion and short course of antibiotics at the onset of dermatitis	Nil specific
Monkeypox viral DNA detected							
Blood	Yes	Yes	Yes	Yes	No	Yes	Yes
Nose or throat swab	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Urine	Yes	Yes	Yes	Yes	No	No	No
Antivirals received	Brincidofovir 200 mg (one dose) orally	Brincidofovir 200 mg (two doses) orally	Brincidofovir 200 mg (two doses) orally	None	None	None	Tecovirimat 600 mg twice daily for 2 weeks orally
Day of illness treatment commenced†	7	6	7	--	--	--	5
Complications of treatment	Transaminitis (peak ALT 331 U/L)	Transaminitis (peak ALT 550 U/L)	Transaminitis (peak ALT 127 U/L), nausea, and abdominal discomfort	--	--	--	None
Duration of hospitalisation with monkeypox, days	26	27	35	39	13	22	10
Outcome of monkeypox infection	Full recovery	Full recovery	Full recovery	Full recovery	Full recovery	Full recovery	Full recovery

HCID=high consequence infectious disease. MVA=modified vaccinia Ankara. ALT=alanine transaminase. *Age ranges rather than exact ages are given for patient anonymity. †Onset of illness was defined as the first identification of skin lesions by the patient or carers.

Table: Summary of the clinical course and response to treatment in seven patients with monkeypox

Skin and Soft Tissue Manifestations of Monkeypox

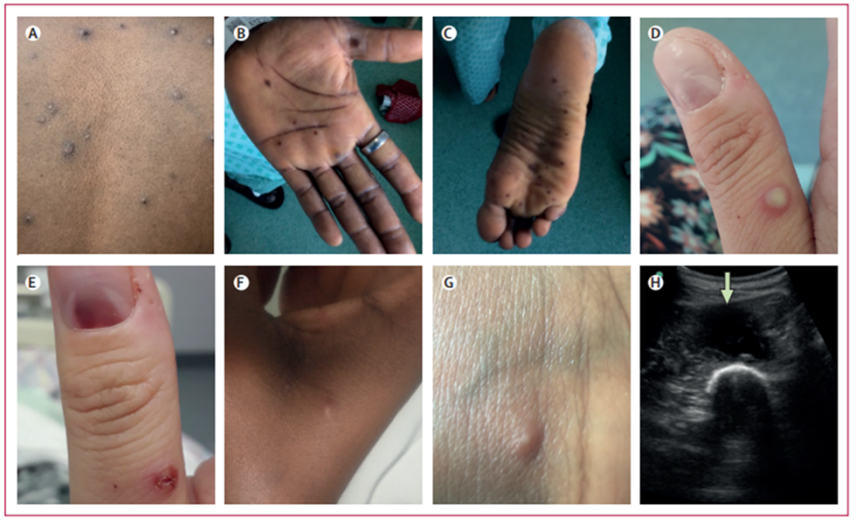
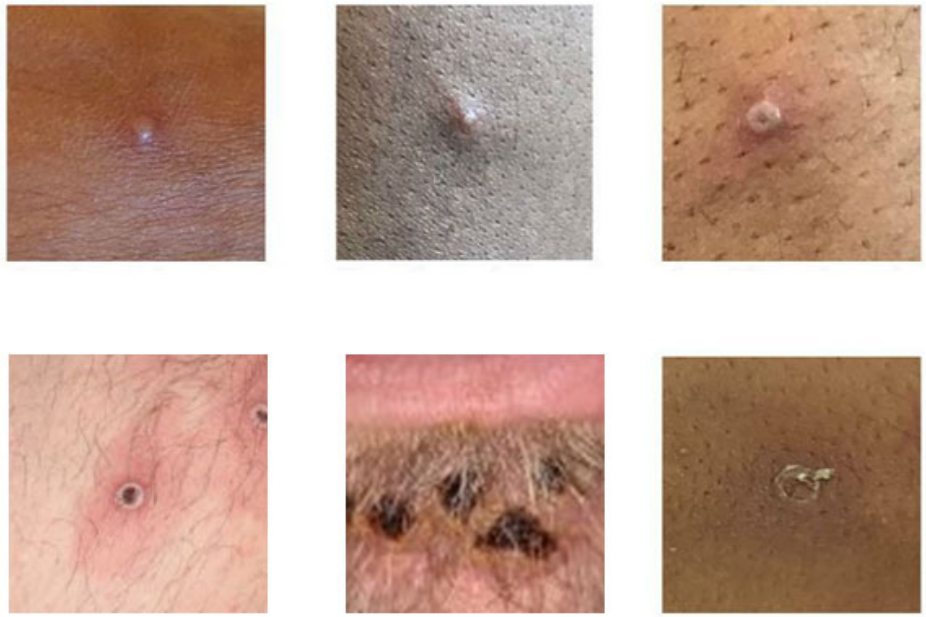


Figure 2: **Skin and soft tissue manifestations of monkeypox**
Skin and soft tissue features included: (A and D) vesicular or pustular lesions; (B and C) macular lesions involving the palms and soles; (D and E) a sub-ungual lesion; (F and G) more subtle papules and smaller vesicles; (H) and a deep abscess (arrow, image obtained during ultrasound-guided drainage).

Adler H, et al. Lancet ID 2022;24 May

Characteristics for Identifying Classic Monkeypox, CDC

- Lesions are well circumscribed, deep seated, and often develop umbilication (resembles a dot on the top of the lesion)
- Lesions are relatively the same size and same stage of development on a single site of the body (ex: pustules on face or vesicles on legs)
- Fever before rash
- Lymphadenopathy common
- Disseminated rash is centrifugal (more lesions on extremities, face)
- Lesions on palms, soles
- Lesions are often described as painful until the healing phase when they become itchy (crusts)

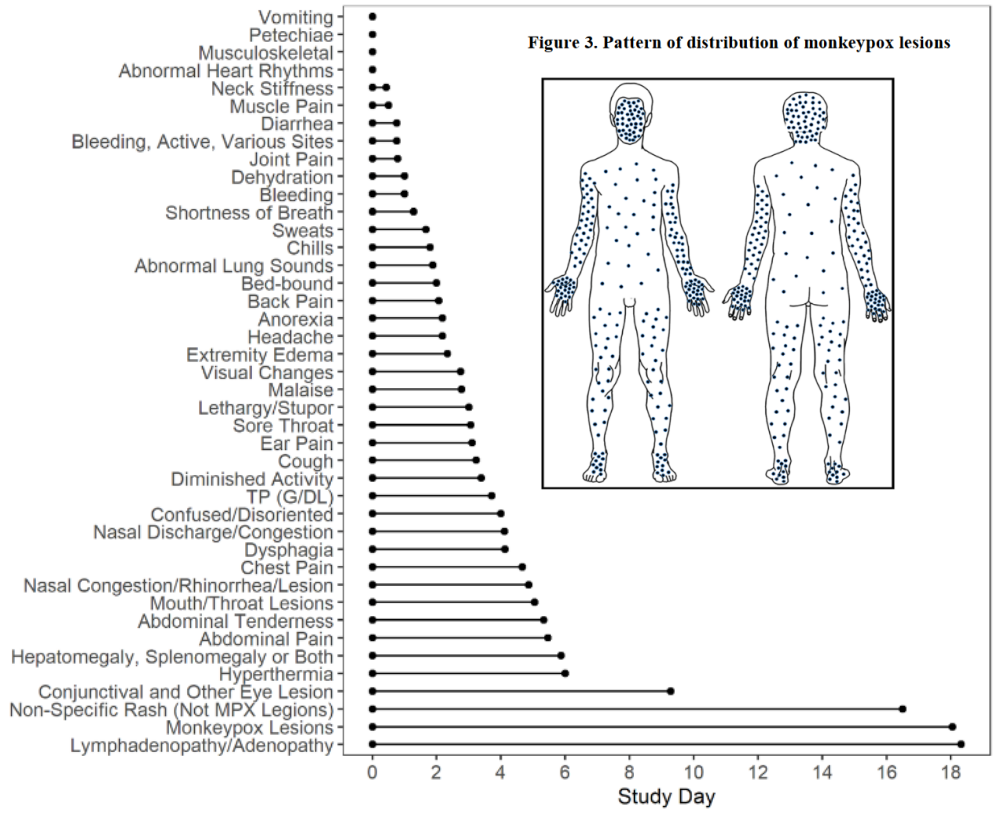


https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html

Clinical characterization of human monkeypox infections in the DRC

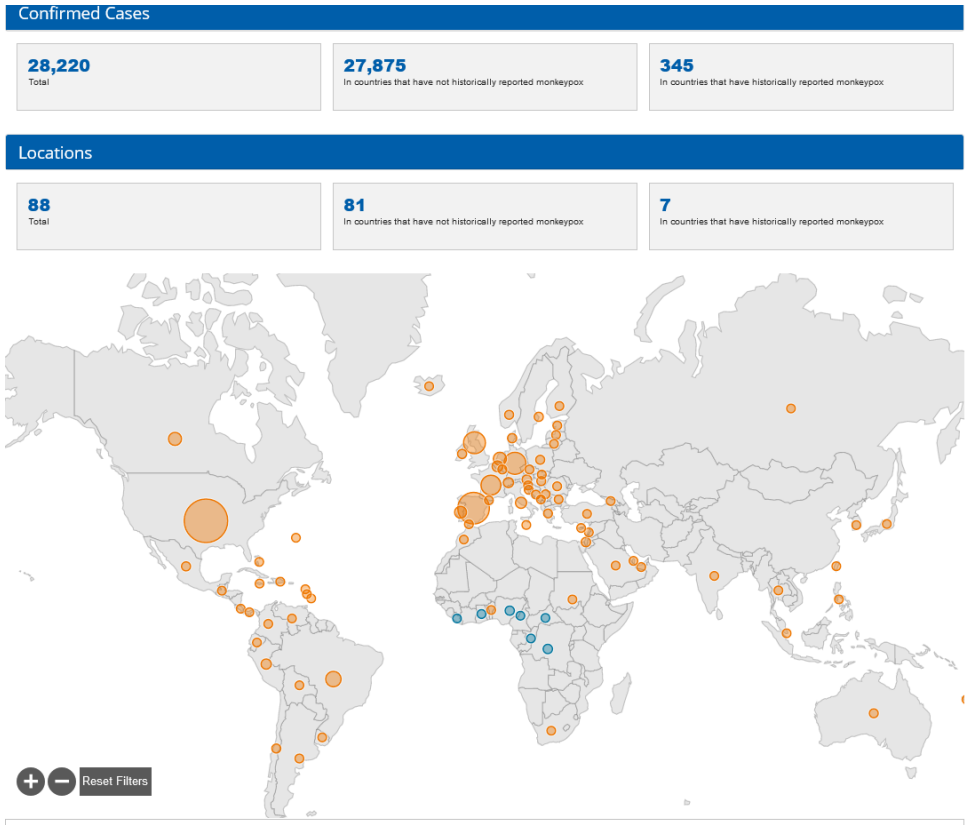
- Site: DRC, 3/2007-8/2011
- The cardinal observations of 216 hospitalized patients are summarized in this report. There were three deaths (3/216) among these hospitalized patients; fetal death occurred in 4 of 5 (80%) patients who were pregnant at admission. The most common complaints were rash (96.8%), malaise (85.2%), sore throat (78.2%), and lymphadenopathy/adenopathy (57.4%). The most common physical exam findings were MPX rash (99.5%) and lymphadenopathy (98.6%). Age group of less than 5 years had the highest lesion count. Patients with fatal disease had significantly higher maximum geometric mean values than survivors for the following variables, respectively: viral DNA in blood (DNAemia, p=0.0072); maximum lesion count (p=0.0025); day of admission mean AST and ALT (p=0.0002 and p = 0.0224, respectively, adjusted p-values).

Figure 1. The duration of clinical symptoms and signs

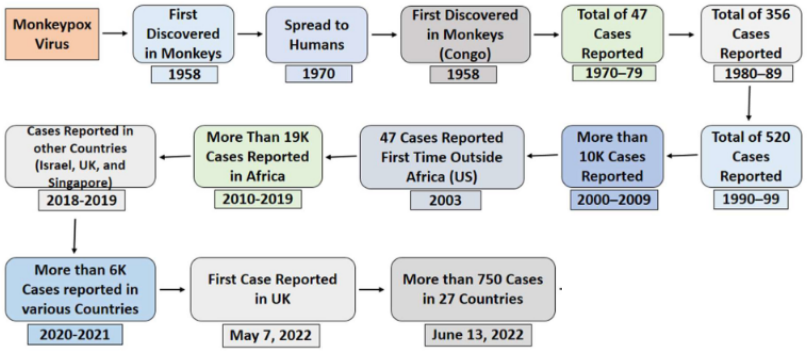


Pittman PR, et.
https://www.medrxiv.org/content/10.1101/2022.05.26.22273379v1.full.pdf

2022 Monkeypox and Orthopoxvirus Outbreak Global Map



https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html



i. 1. Timeline of Monkeypox virus infection.

Anwar F, Waris A. New Microbe and New Infect 2022;48:101004
https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html

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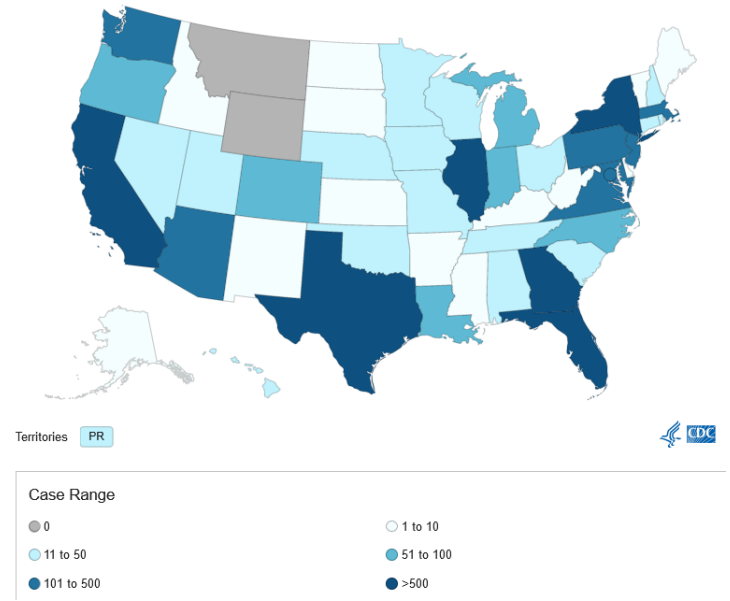
2022 Monkeypox Outbreak US

2022 U.S. Map & Case Count

Updated August 5, 2022 Print

Total confirmed monkeypox/orthopoxvirus cases: **7,510**

*One Florida case is listed here but included in the United Kingdom case counts because the individual was tested while in the UK.

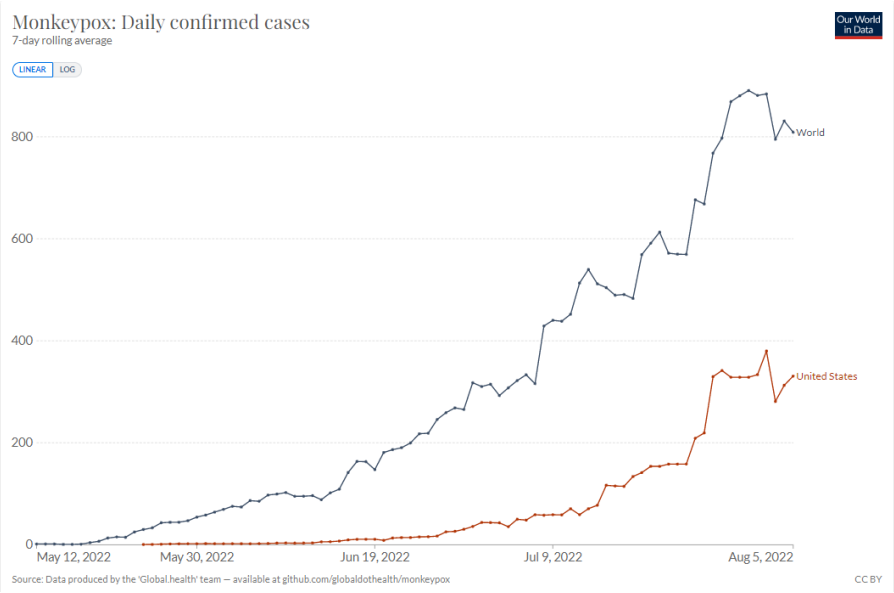


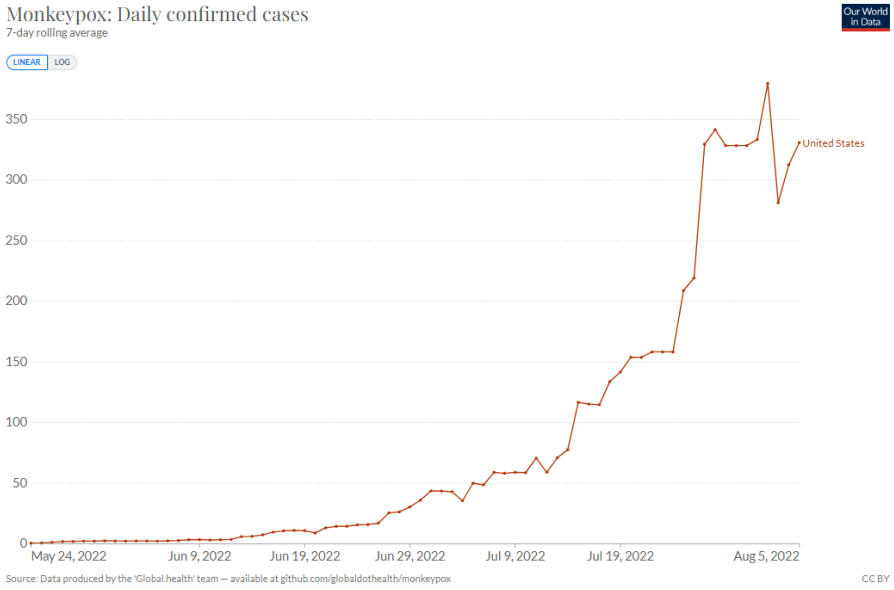
https://www.cdc.gov/poxvirus/monkeypox/response/2022/index.html

Location	Cases
Alabama	19
Alaska	2
Arizona	102
Arkansas	9
California	826
Colorado	78
Connecticut	43
Delaware	6
District Of Columbia	283
Florida	633
Georgia	596
Hawaii	11
Idaho	7
Illinois	602
Indiana	68
Iowa	12
Kansas	1
Kentucky	9
Louisiana	74
Maine	2
Maryland	182
Massachusetts	157
Michigan	70
Minnesota	46
Mississippi	6
Missouri	14
Montana	0
Nebraska	12
Nevada	29
New Hampshire	15
New Jersey	188
New Mexico	10
New York	1,662
North Carolina	95
North Dakota	1
Ohio	45
Oklahoma	11
Oregon	80
Pennsylvania	205
Puerto Rico	19
Rhode Island	29
South Carolina	30
South Dakota	1
Tennessee	42
Texas	606
Utah	46
Vermont	1
Virginia	122
Washington	175
West Virginia	3
Wisconsin	22
Wyoming	0

NC = 95

MONKEYPOX OUTBREAK CURVES: WORLDWIDE & US





Our World in Data - https://ourworldindata.org/monkeypox

MONKEYPOX, UK, 28 July

Table 1. Number of laboratory confirmed cases by devolved administrations, 6 May 2022 to 20 July 2022

Devolved administrations	Confirmed cases
England	2,070
Northern Ireland	14
Scotland	54
Wales	24
Total	2,162

Figure 3. Confirmed monkeypox cases by symptom onset date in England as of 20 July 2022

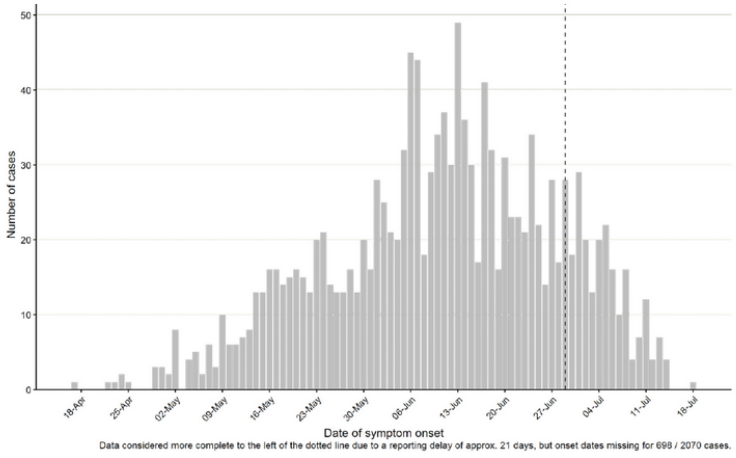


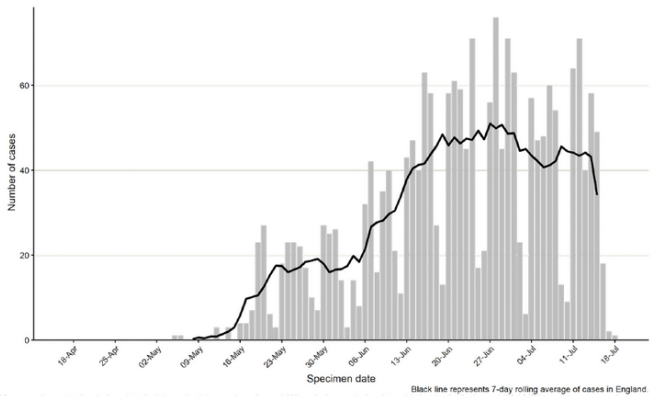
Table 3. Selected epidemiological metrics from enhanced surveillance questionnaires in confirmed monkeypox cases in England as of 19 July 2022

N=576, some metrics have slightly smaller denominators due to missing values

Metric	N (%)
Gay, bisexual, or men who have sex with men*	549 (96.5%)
Travel abroad prior to symptom onset (21 days)	173 (30.3%)
Age below 30 years	98 (22.9%)
History of STI in the last year	313 (55.6%)
One or no sexual partners in last 3 months	82 (14.5%)
10+ sexual partners in last 3 months	176 (31.1%)
Living with HIV	149 (27.7%)
On HIV treatment (among living with HIV)	148 (99.3%)
Ever used PrEP (among HIV negative)	297 (79.2%)

Event type*	% of total (n)
Festival	37% (241)
Sex-on-premise venue	25% (164)
Bar	12% (80)
Nightclub	9% (60)
Gym or swimming pools	7% (44)
Event	4% (27)
Private sex party	4% (26)
Other	2% (12)
Total	100% (654)**

Figure 4. Incidence of confirmed monkeypox cases by specimen date in England as of 20 July 2022



https://www.gov.uk/government/publications/monkeypox-outbreak-technical-briefings/investigation-into-monkeypox-outbreak-in-england-technical-briefing-4

Epidemiologic and Clinical Characteristics of Monkeypox Cases: US, 5/17/22-7/22/22

Assessment of Monkeypox using 1,195 case report forms

Summary

What is already known about this topic?

A global monkeypox outbreak began in 2022.

What is added by this report?

Among U.S. monkeypox cases with available data, 99% occurred in men, 94% of whom reported recent male-to-male sexual or close intimate contact; racial and ethnic minority groups appear to be disproportionately affected. Clinical presentations differed from typical monkeypox, with fewer persons experiencing prodrome and more experiencing genital rashes.

What are the implications for public health practice?

Public health efforts should prioritize gay, bisexual, and other men who have sex with men, who are currently disproportionately affected, for prevention and testing, address equity, and minimize stigma, while maintaining vigilance for transmission in other populations. Clinicians should test persons with rash consistent with monkeypox, regardless of whether the rash is disseminated or was preceded by prodrome.

FIGURE. Monkeypox cases, by report date* — United States, May 17–July 22, 2022

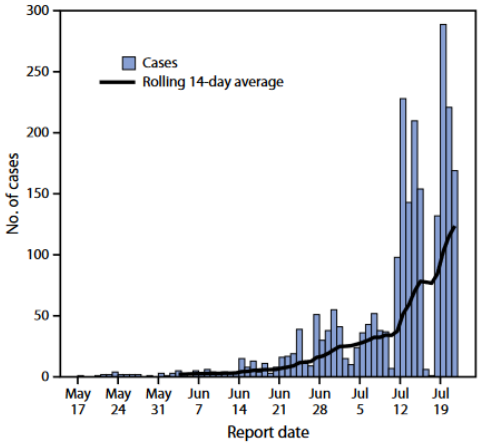


TABLE 1. Characteristics of persons with monkeypox — United States, May 17–July 22, 2022

Characteristic (no. with available information)	No. (%)*
Total	**1,195 (100)**
Gender identity (1,195)	
Man	1,178 (98.7)
Transgender man	3 (0.3)
Woman	5 (0.4)
Transgender woman	5 (0.4)
Prefer not to answer	4 (0.3)
Missing	0 (—)
Race and ethnicity (1,054)	
Asian, non-Hispanic	48 (4.6)
Black, non-Hispanic	276 (26.2)
White, non-Hispanic	428 (40.6)
Hispanic	296 (28.1)
Multiple races, non-Hispanic	6 (0.6)
Missing	141

* Percentages calculated using nonmissing data.

- 42% of persons with monkeypox with available data did not report the typical prodrome as their first symptom, and 46% reported one or more genital lesions during their illness; 41% had HIV infection.
- Among 358 (30%) men (cisgender and transgender) with information on recent sexual behaviors and gender of sex partners available, 337 (94%) reported sex or close intimate contact with a man during the 3 weeks before symptom onset; 16 (4%) reported no such contact. Among 291 men who reported information about their male sexual partners during the 3 weeks preceding symptom onset, 80 (27%) reported one partner, 113 (40%) reported two to four partners, 42 (14%) reported five to nine partners, and 56 (19%) reported 10 or more partners. Among 86 men with information reported, 33 (38%) reported group sex, defined as sex with more than two persons, at a festival, group sex event, or sex party.

Philpott D, et al. MMWR 5 August 2022

Reproduction number of monkeypox in the early stage of the 2022 multi-country outbreak

- Monkeypox, a fast-spreading viral zoonosis outside of Africa in May 2022, has scientists on alert. We estimated the reproduction number to be 1.29 (95% CrI: 1.26, 1.33) by aggregating all cases in 70 countries as of July 22, 2022Monkeypox, a fast-spreading viral zoonosis outside of Africa in May 2022, has scientists on alert. We estimated the reproduction number to be 1.29 (95% CrI: 1.26, 1.33) by aggregating all cases in 70 countries as o.f July 22, 2022

Table 3. The estimated effective reproduction number of monkeypox informed by adjusted daily confirmed cases.

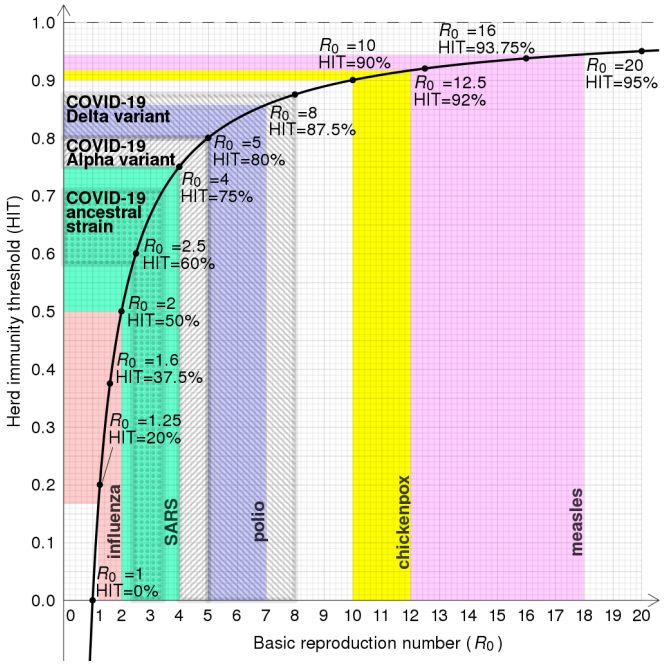
(median and 95% CrI)	Case number	Period	Region
1.55 (1.42, 1.73)	2581	2022.5.18-2022.7.22	United States
1.36 (1.24, 1.60)	1562	2022.5.19-2022.7.22	France
1.20 (1.17, 1.23)	2268	2022.5.19-2022.7.22	Germany
1.18 (1.10, 1.31)	3125	2022.5.18-2022.7.22	Spain
1.13 (1.10, 1.16)	2115	2022.5.6-2022.7.22	England
1.02 (1.00, 1.04)	588	2022.5.17-2022.7.22	Portugal
1.29 (1.26, 1.33)	16313	2022.5.6-2022.7.22	All

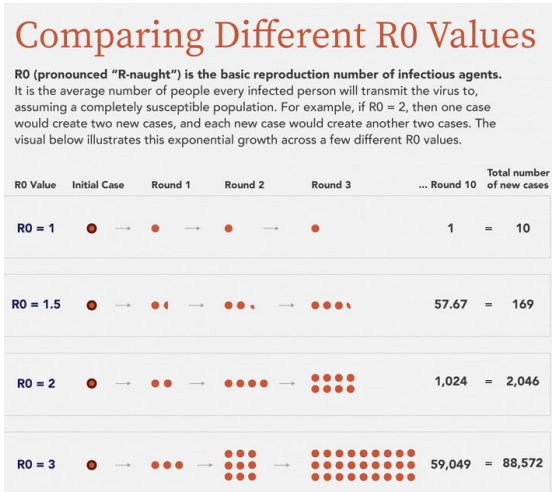
Du Z, et al. https://www.medrxiv.org/content/10.1101/2022.07.26.22278042v1.full.pdf

Values of R_0 and herd immunity thresholds (HITs) of well-known infectious diseases prior to intervention

Disease	Transmission	R_0	HIT[a]
Measles	Aerosol	12–18[29][7]	92–94%
Chickenpox (varicella)	Aerosol	10–12[30]	90–92%
Mumps	Respiratory droplets	10–12[31]	90–92%
COVID-19 (Omicron variant)	Respiratory droplets and aerosol	9.5[32]	89%
Rubella	Respiratory droplets	6–7[b]	83–86%
Polio	Fecal–oral route	5–7[b]	80–86%
Pertussis	Respiratory droplets	5.5[37]	82%
COVID-19 (Delta variant)	Respiratory droplets and aerosol	5.1[38]	80%
Smallpox	Respiratory droplets	3.5–6.0[39]	71–83%
COVID-19 (Alpha variant)	Respiratory droplets and aerosol	4–5[40][*medical citation needed*]	75–80%
HIV/AIDS	Body fluids	2–5[41]	50–80%
COVID-19 (ancestral strain)	Respiratory droplets and aerosol[42]	2.9 (2.4–3.4)[43]	65% (58–71%)
SARS	Respiratory droplets	2–4[44]	50–75%
Diphtheria	Saliva	2.6 (1.7–4.3)[45]	62% (41–77%)
Common cold	Respiratory droplets	2–3[46][*medical citation needed*]	50–67%
Monkeypox	Physical contact, body fluids, respiratory droplets	2.1 (1.5–2.7)[47]	53% (31–63%)
Influenza (1918 pandemic strain)	Respiratory droplets	2[48]	50%
Ebola (2014 outbreak)	Body fluids	1.8 (1.4–1.8)[49]	44% (31–44%)
Influenza (2009 pandemic strain)	Respiratory droplets	1.6 (1.3–2.0)[2]	37% (25–51%)
Influenza (seasonal strains)	Respiratory droplets	1.3 (1.2–1.4)[50]	23% (17–29%)
Andes hantavirus	Respiratory droplets and body fluids	1.2 (0.8–1.6)[51]	16% (0–36%)[c]
Nipah virus	Body fluids	0.5[52]	0%[c]
MERS	Respiratory droplets	0.5 (0.3–0.8)[53]	0%[c]

Wikipedia https://en.wikipedia.org/wiki/Basic_reproduction_number
https://www.mastersindatascience.org/resources/r0-infectious-diseases/





Estimating the incubation period of monkeypox virus during the 2022 multi-national outbreak, US

- Study population: From May 17, 2022 to June 6, 2022, 30 probable and confirmed cases of monkeypox were reported in the US. Data from 8 patients were excluded. Data from 22 probable (N=1) and confirmed (N=21) caes included in this analysis.
- Period: For time from exposure to first symptom onset, we estimated a mean incubation period of 7.6 days (95% credible interval (CrI): 6.2–9.7) (median 6.4, 95% CrI: 5.1 – 7.9) and a standard deviation of 1.8 days (95% CrI: 1.6–2.2) (Figure 1). The 95th percentile was 17.1 days (95% CrI:12.7–24.3) after exposure. For time from exposure to rash onset, we estimated a mean incubation period of 8.7 days (95% CrI: 6.9–11.7) (median 7.8 days, 95% CrI: 5.9 – 10.0) and a standard deviation of 1.6 days (95% CrI: 1.4–2.1) (Figure 2). The 95th percentile was 17.7 days (95% CrI 12.4–28.1) after exposure

Chaarniga K, et al.

Figure 1. Monkeypox virus incubation period (exposure to **first symptom onset**), United States and the Netherlands, May 2020 – June 2022. Blue shaded area represents 95% credible intervals.

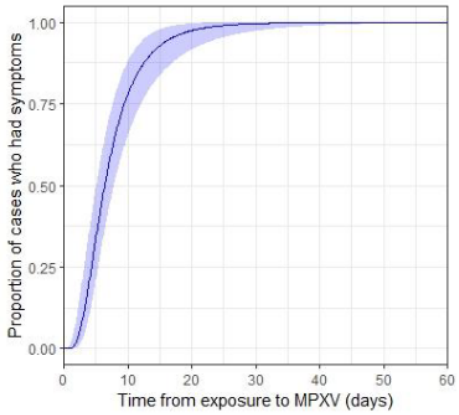
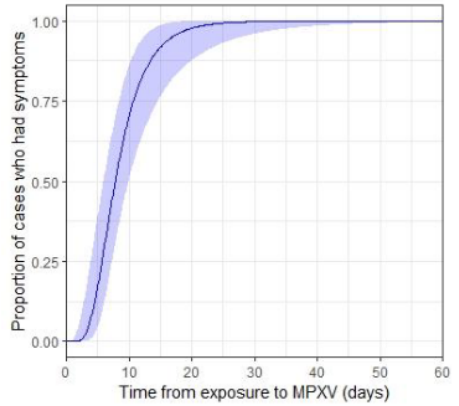


Figure 2. Monkeypox virus incubation period (exposure to **rash onset**), United States, May 2020 – June 2022. Blue shaded area represents 95% credible intervals.



The incubation period for monkeypox cases confirmed in the Netherlands, May 2022

ABSTRACT

n May 2022 outbreaks of monkeypox have been reported in countries where the monkeypox virus is not endemic. We estimate the incubation period for monkeypox, using the reported time of exposure and symptom onset for 18 confirmed cases detected in the Netherlands up to 31st May 2022. The mean incubation period was 8.5 days, ranging from 4.2 to 17.3 days (5th to 95th percentiles). These findings underpin 21 days for monitoring or quarantining of case contacts.

Miura F, et al
https://www.medrxiv.org/content/10.1101/2022.06.09.22276068v1.full.pdf

Table 1. Estimated mean of incubation period for different parametric distributions and computed goodness-of-fit.

	Mean (days)	WAIC*	LOOIC†
Lognormal	8.5 [95%CI‡: 6.6–10.9]	77.1	77.5
Gamma	9.1 [95%CI: 7.5–11.3]	79.5	79.7
Weibull	9.6 [95%CI: 7.4–12.4]	81.2	81.6

*WAIC: Widely applicable information criterion. †LOOIC: Leave-One-Out Information Criterion; these values indicate the goodness-of-fit, where lower values indicate a better fit. ‡CI, credible interval.

Table 2. Estimated percentiles of the incubation period for monkeypox, using different parametric distributions.

	Lognormal		Gamma		Weibull	
Percentile	Estimate	95% CI*	Estimate	95% CI	Estimate	95% CI
2.5th	3.6	2.0–5.0	3.8	2.0–5.2	2.3	0.9–4.1
5th	4.2	2.5–5.5	4.4	2.6–5.8	3.1	1.4–5.0
50th	8.5	6.6–10.9	8.7	7.0–10.7	9.2	6.9–11.8
95th	17.3	13.0–29.0	15.3	12.5–20.7	16.9	13.7–23.9
97.5th	19.9	14.4–35.7	16.9	13.6–23.3	18.5	14.9–26.9
99th	23.3	16.3–45.8	18.8	14.9–26.7	20.3	16.1–30.6

*CI, credible interval.

Estimated Monkeypox Susceptible MSM Population in North Carolina

ABSTRACT

Using NHANES survey data we estimate that there are nearly 65,100 North Carolina residents who identify as men who have sex with men (MSM). Among those men, it is estimated nearly 15,700 have had at least one new sexual partner in the last year and represent the highest risk for infection and onward transmission of monkeypox. Vaccination strategies should consider vaccinating with highest priority those who are highly sexually active men who have sex with men as these sexual networks have the capacity to drive the monkeypox epidemic. Estimates of the number of MSM by county as well as the estimates of highly sexually active MSM are provided by North Carolina county in order to inform vaccination quantities and priorities given the current limited supply of vaccines.

DeWitt ME, et al. https://doi.org/10.1101/2022.07.21.22277860

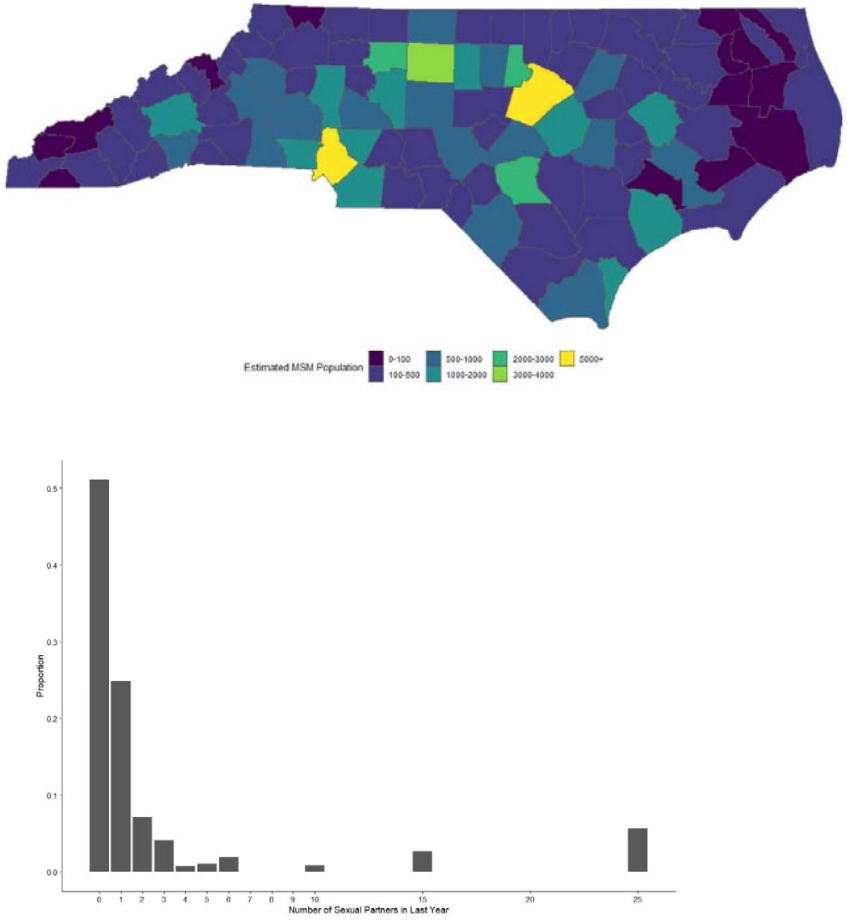


Figure 2: Distribution of the Reported Number of Male Sexual Partners in the Last Year Among MSM Respondents in NHANES

CURRENT MONKEYPOX SYMPTOMS

Atypical features of current outbreak

- Presentation of only a few or even just a single lesion
- Absence of skin lesions in some cases, with anal pain and bleeding
- Lesions in the genital or perineal/perianal area which do not spread further
- Lesions appearing at different (asynchronous) stages of development
- The appearance of lesions before the onset of fever, malaise and other constitutional symptoms (absence of prodromal period).

- Novel manifestations of monkeypox are clearly linked to the location of mucocutaneous monkeypox lesions. Nearly all patients reporting peri-anal or rectal lesions reported pain and hospital admission has been required for patients with severe rectal pain with some having radiologically evident proctitis.
- Oropharyngeal symptoms (for example, tonsillitis, peritonsillar cellulitis or peritonsillar abscess or neck lymphadenopathy) have developed in some individuals causing pain or difficulty swallowing. Monkeypox lesions on external genitalia have caused severe swelling and pain and, in some cases, led to the development of paraphimoses. Cutaneous lesions have resulted in secondary bacterial infections of skin and soft tissues (cellulitis).
- Systemic symptoms including fever, lymphadenopathy and myalgia are common but in contrast to current understanding do not always precede mucocutaneous manifestations of monkeypox and approximately 10% of patients did not exhibit any systemic symptoms. Furthermore, 15 individuals (11.3%) have presented with a solitary cutaneous lesion with no subsequent skin lesions.

https://www.gov.uk/government/publications/monkeypox-outbreak-technical-briefings/investigation-into-monkeypox-outbreak-in-england-technical-briefing-3

MONKEYPOX: CLINICAL RECOGNITION

- Lesions are firm or rubbery, well-circumscribed, deep-seated, and often develop umbilication (resembles a dot on the top of the lesion)
- During the current global outbreak:
  - Lesions often occur in the genital and anorectal areas or in the mouth
  - Rash is not always disseminated across many sites on the body
  - Rash may be confined to only a few lesions or only a single lesion
  - Rash does not always appear on palms and soles
- Rectal symptoms (e.g., purulent or bloody stools, rectal pain, or rectal bleeding) have been frequently reported in the current outbreak
- Lesions are often described as painful until the healing phase when they become itchy (crusts)
- Fever and other prodromal symptoms (e.g., chills, lymphadenopathy, malaise, myalgias, or headache) can occur before rash but may occur after rash or not be present at all
- Respiratory symptoms (e.g. sore throat, nasal congestion, or cough) can occur

Lesions typically develop simultaneously and evolve together on any given part of the body. The evolution of lesions progresses through four stages—macular, papular, vesicular, to pustular—before scabbing over and desquamation.

The incubation period is 3-17 days (median, 9.5 days). During this time, a person does not have symptoms and may feel fine.

The illness typically lasts 2-4 weeks.

The severity of illness can depend upon the initial health of the individual and the route of exposure.

Clinical Recognition | Monkeypox | Poxvirus | CDC

Epidemiologic and Clinical Characteristics of Monkeypox Cases: US, May 17–July 22, 2022, CDC

TABLE 2. Symptoms and rash among persons with monkeypox — United States, May 17–July 22, 2022

Characteristic	Ever experienced during illness* (N = 1,007) No. (%)§ Yes	No	No. missing	Initially experienced† (N = 461) No. (%)§ Yes	No	No. missing
Symptoms						
Rash¶	1,004 (100.0)	0 (—)	3	121 (41.6)	170 (58.4)	170
Fever	596 (63.3)	345 (36.7)	66	120 (41.2)	171 (58.8)	170
Chills	550 (59.1)	381 (40.9)	76	48 (16.5)	243 (83.5)	170
Lymphadenopathy	545 (58.5)	387 (41.5)	75	23 (7.9)	268 (92.1)	170
Malaise	531 (57.1)	399 (42.9)	77	24 (8.2)	267 (91.8)	170
Myalgia	507 (55)	415 (45)	85	13 (4.5)	278 (95.5)	170
Headache	469 (50.8)	454 (49.2)	84	27 (9.3)	264 (90.7)	170
Rectal pain	201 (21.9)	715 (78.1)	91	0 (—)	291 (100.0)	170
Pus or blood in stools	184 (20.5)	713 (79.5)	110	0 (—)	291 (100.0)	170
Abdominal pain	96 (11.5)	742 (88.5)	169	1 (0.3)	290 (99.7)	170
Rectal bleeding	90 (10.0)	810 (90.0)	107	0 (—)	291 (100.0)	170
Tenesmus	90 (10.0)	809 (90.0)	108	2 (0.7)	289 (99.3)	170
Vomiting or nausea	83 (9.2)	817 (90.8)	107	0 (—)	291 (100.0)	170
Rash sites						
Genitals	333 (46.4)	385 (53.6)	289	214 (55.7)	170 (44.3)	77
Arms	284 (39.6)	434 (60.4)	289	20 (5.2)	364 (94.8)	77
Face	276 (38.4)	442 (61.6)	289	94 (24.5)	290 (75.5)	77
Legs	265 (36.9)	453 (63.1)	289	18 (4.7)	366 (95.3)	77
Perianal	225 (31.3)	493 (68.7)	289	86 (22.4)	298 (77.6)	77
Mouth, lips, or oral mucosa	179 (24.9)	539 (75.1)	289	99 (25.8)	285 (74.2)	77
Palms of hands	157 (21.9)	561 (78.1)	289	13 (3.4)	371 (96.6)	77
Trunk	156 (21.7)	562 (78.3)	289	14 (3.6)	370 (96.4)	77
Neck	130 (18.1)	588 (81.9)	289	33 (8.6)	351 (91.4)	77
Head	97 (13.5)	621 (86.5)	289	8 (2.1)	376 (97.9)	77
Soles of feet	77 (10.7)	641 (89.3)	289	1 (0.3)	383 (99.7)	77

* Symptoms experienced up until the time of interview.
† Symptoms reported by persons with monkeypox as their first symptoms during their illness or the body location where rash first appeared.
§ Percentages calculated using nonmissing data.
¶ Rash includes at least one lesion affecting the skin or mucous membranes.

- The most frequently reported signs and symptoms included rash (100%), fever (63%), chills (59%), & lymphadenopathy (59%)
- Among 291 persons with available information about their first symptoms, 58% reported at least one prodromal symptom; for the 42% of patients without prodromal symptoms, illness began with a rash.
- Among 104 persons with information on the number of lesions, 88% of cases involved fewer than 50 lesions.
- Among 339 persons with vaccination status available, 48 (14%) reported previous receipt of smallpox vaccine, including 11 (23%) who received 1 of 2 JYNNEOS doses during the current outbreak (one received 1 vaccine dose >3 weeks prior to symptom onset

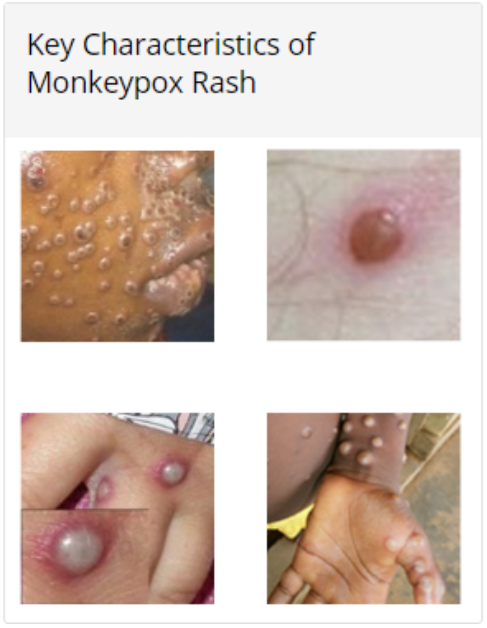
Philpott D, et al. MMWR 5 August 2022

UNC SCHOOL OF MEDICINE

MONKEYPOX: SKIN LESIONS

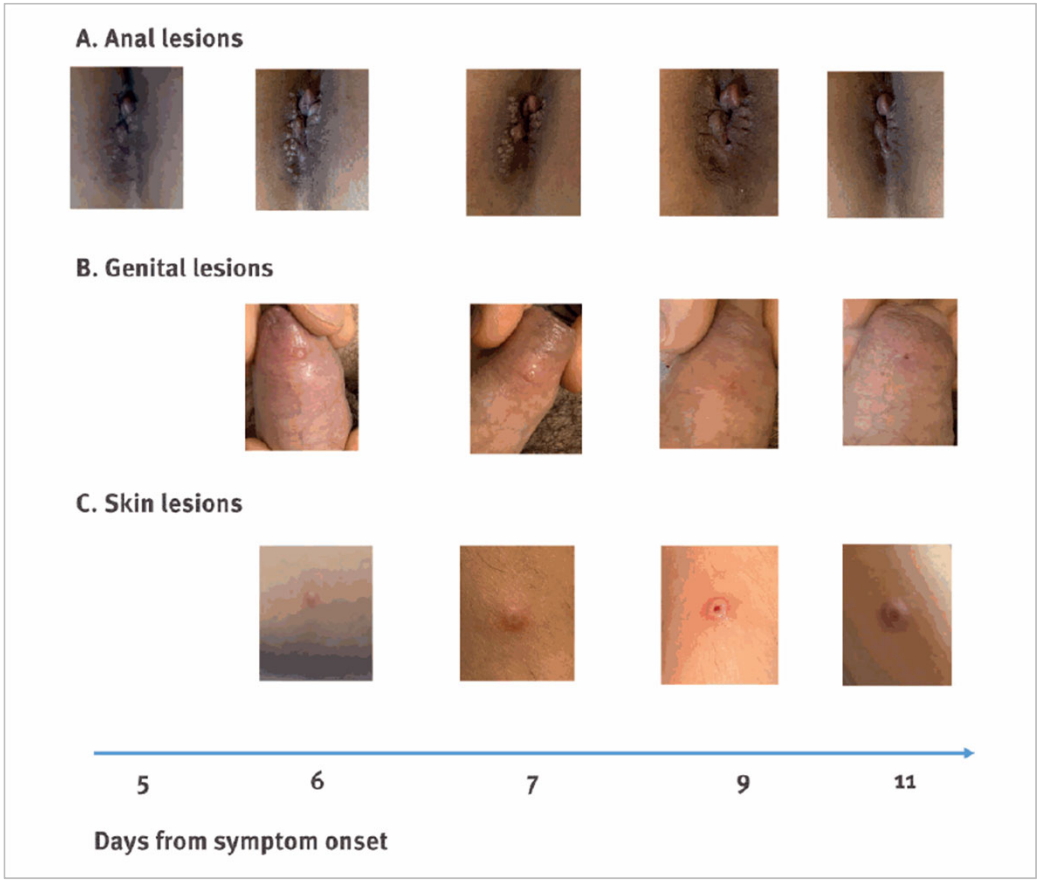
Enanthem Through the Scab Stage

Stage	Stage Duration	Characteristics
Enanthem		• Sometimes, lesions first form on the tongue and in the mouth.
Macules	1–2 days	• Macular lesions appear.
Papules	1–2 days	• Lesions typically progress from macular (flat) to papular (raised).
Vesicles	1–2 days	• Lesions then typically become vesicular (raised and filled with clear fluid).
Pustules	5–7 days	• Lesions then typically become pustular (filled with opaque fluid) – sharply raised, usually round, and firm to the touch (deep seated). • Finally, lesions typically develop a depression in the center (umbilication). • The pustules will remain for approximately 5 to 7 days before beginning to crust.
Scabs	7–14 days	• By the end of the second week, pustules have crusted and scabbed over. • Scabs will remain for about a week before beginning to fall off.

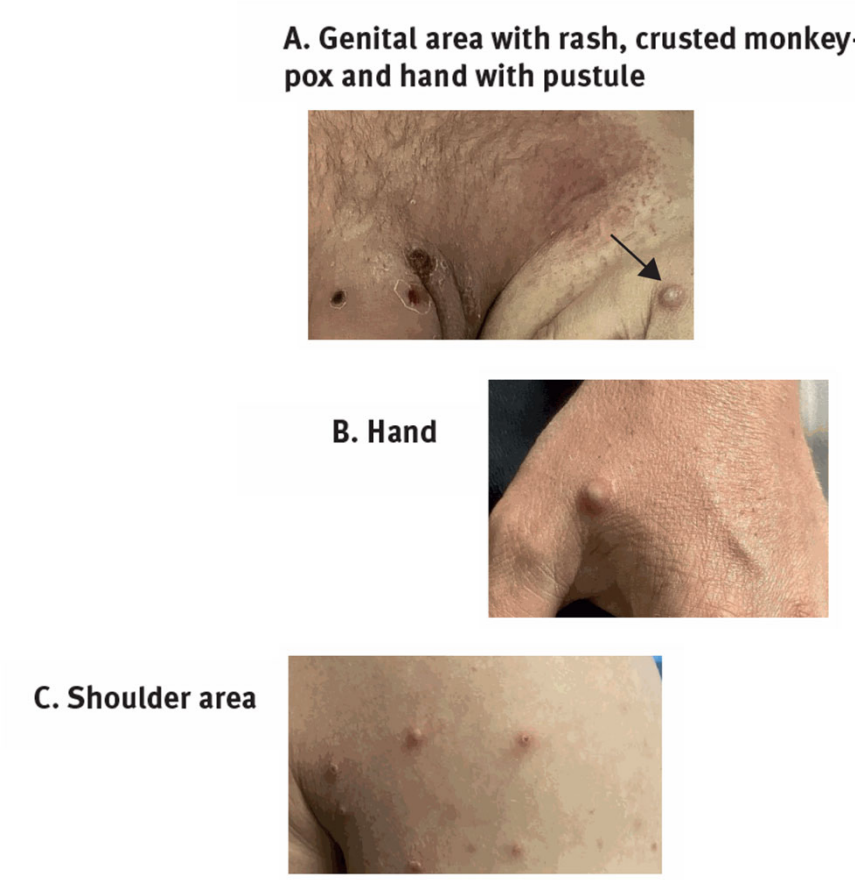


Clinical Recognition | Monkeypox | Poxvirus | CDC

Monkeypox skin lesions from current outbreak



Antinori A, et al. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. Euro Surveill 2022 Jun;27(22)



Hammerschlag Y, et al. Monkeypox infection presenting as genital rash, Australia, May 2022. Euro Surveill 2022 Jun;27(22)

MONKEYPOX: CLINICAL ISSUES

Differential diagnosis

- Varicella: Difference in VZV lesions vs Monkeypox – 1) Lymphadenopathy often present in Monkeypox but not in varicella; 2) Lesions in Monkeypox are generally in the same stage vs varicella where where vesicular lesions are characteristically in different stages of development and healing
- Herpes simplex: HSV can present with both oral and genital lesions similar to Monkeypox. PCR of lesions can differential HSV from Monkeypox
- Others STIs: Since Monkeypox can present with genital ulcers or a macular rash on palms or soles, other STIs must be considered including secondary syphilis, chancroid and lymphagranuloma venereum
- Other poxviruses: Similar lesions can be caused by tanapox, Orf, and bovine stomatitis – all are uncommon. Other novel orthopoxviruses include Alaskapoxvirus, Orthopoxvirus Abatino, and Akhmeta virus

Guidance for clinicians

- Observation of classic monkeypox rash OR
- Observation of rash that could be consistent with monkeypox in persons with epidemiologic risk factors:
  - Contact with a person or people a) with similar appearing rash or b)diagnosed with monkeypox
  - Close or intimate in-person contact with people in a social network experiencing monkeypox activity (e.g., men who have sex with men who meet partners through an online website, digital app or social event)
  - History of recent international travel to country currently reporting cases
- When lesions are not consistent with classic lesions, full body skin exam should bedone to evaluate whether some classic lesions are observed
- Diagnosis of STI does not rule-out co-infection with monkeypox (co-infection may occur with STIs and Monkeypox)

Asymptomatic monkeypox virus infections among male sexual health clinic attendees in Belgium

- Background: Monkeypox is transmitted by close contact with symptomatic cases, and those infected are assumed to be uniformly symptomatic. Evidence of subclinical monkeypox infection is limited to a few immunological studies which found evidence of immunity against orthopoxviruses in asymptomatic individuals who were exposed to monkeypox cases. We aimed to assess whether asymptomatic infections occurred among individuals who underwent sexually transmitted infection (STI) screening in a large Belgian STI clinic around the start of the 2022 monkeypox epidemic in Belgium
- Methods: Anorectal and oropharyngeal swabs collected for gonorrhoea/chlamydia screening from May 1 until May 31, 2022 were retrospectively tested by a monkeypox-specific PCR.
- Results: In stored samples from 224 men, we identified three cases with a positive anorectal monkeypox PCR. All three men denied having had any symptoms in the weeks before and after the sample was taken. None of them reported exposure to a diagnosed monkeypox case, nor did any of their contacts develop clinical monkeypox.

Table 1: Characteristics of MPXV-positive samples

Case	Sample type	Symptoms compatible with MPX at time of sampling	MPXV-PCR result on remnant DNA extract (Ct value)	MPXV-PCR result on original sample (Ct value)	Timing of follow-up sample with respect to original sample	MPXV-PCR result on follow-up sample (Ct value)
1	Pooled sample	None	Positive (27·63)	Anorectal swab: Positive (26·69); oropharyngeal swab: Negative	+37 days	Negative
2	Anorectal swab	None	Positive (22·15)	Positive (20·05)	+21 days	Negative
3	Anorectal swab	None	Positive (19·19)	Positive (17·16)	+24 days	Negative
4	Anorectal swab	Painful vesicular perianal rash	Positive (29·06)	Positive (27·38)	NA	NA

Ct = cycle threshold; NA = not applicable

De Baetselier I, et al
https://www.medrxiv.org/content/10.1101/2022.07.04.22277226v1.full.pdf

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MONKEYPOX: ROUTES OF TRANSMISSION

- Animal-to-human via bite/scratch, direct contact, and indirect contact (cleaning cages, animal products)
- Human-to-human
  - Respiratory secretions (droplet transmission) – prolonged face-to-face contact (no data regarding risk from patients with pneumonia)
  - Direct contact (skin-to-skin) with body fluids or body lesions
  - Indirect contact/fomites (drinking or eating from same dish, contact with contaminated linens)
  - Sexual: Direct contact, unknown if via semen or vaginal fluids
  - Vertical (transplacental) or at deliver: May lead to fetal demise
- Mortality: The case fatality rate for the Central African clade is 1-10% versus <3% for the West African clade
  - Likely an overestimate (biased by severity)
  - Currently outbreak expected mortality <1%; highest risk immunocompromised, pregnant women, young children
- UK Health Authority, 28 July 2022
  - Daily case growth rate has slowed
  - No confirmed cases of airborne transmission; Limited household transmission
  - Hospitalizations for severe pain, secondary bacterial infections
  - No deaths

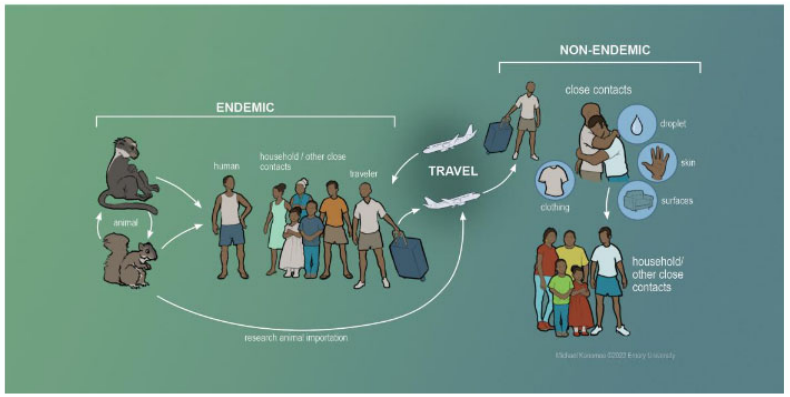


Figure 1. Transmission of human monkeypox. In endemic countries, spillover events occur from zoonotic animal reservoirs into humans, potentially leading to limited outbreaks usually facilitated by close human contact. Outbreaks can also occur in nonendemic regions through introduction of the virus via human travel or importation of animals harboring the virus. Subsequent human-to-human transmission can then occur via household contacts and via other close contacts.

Titanji BK, et al. Open Forum Infectious Diseases 2022;21 June
Bunge EM, et al. PLOS Neglected Tropical Diseases 2022:11 February;
Reynolds MG, et al. Curr Opin Virology 2018;28:108-115; CDC
Khalil A, et al. Ultrasound Obstet Gynecol 2022;2 June

MONKEYPOX INFECTION IN PREGNANCY

- 5 lab-confirmed cases (all in Africa) with outcomes:
  - 3 pregnancy losses
  - 1 livebirth of healthy term neonate
  - 1 preterm delivery of neonate with generalized rash consistent with congenital monkeypox infection

Table 1. Cases of Monkeypox Virus Infection During Pregnancy

Author, Year, Location	Laboratory Test (PCR)	No. of Monkeypox Virus Lesions	Pregnancy Outcome	Gestational Age at Diagnosis; Time from Illness Onset to Pregnancy Outcome	Other Clinical Findings
Jezek and Fenner, 1983, North Zaire	Monkeypox virus isolated from maternal vesicle fluid	n/a	Preterm birth of female neonate "at the beginning of 7th month"; neonatal rash clinically consistent with congenital monkeypox virus infection; neonatal death at 6.5 wk of age from "malnutrition"	Approximately 5.5 mo; 6 wk	Maternal: initially presented with fever followed by rash the next day; serum test negative for syphilis Neonate: birth weight less than 1,500 g; laboratory samples lost; scabs reported on skin 2 wk after birth
Mbala et al, 2017, Democratic Republic of the Congo	Yes	76	Spontaneous abortion	1st trimester; 14 d	Congo Basin strain
	Yes	1,135	Spontaneous abortion	1st trimester; 24 d	Congo Basin strain
	Yes	113	Stillbirth; congenital monkeypox virus infection	18 wk; 21 d	Congo Basin strain; viral load increased with onset of fever and lack of fetal movement; co-infection with malaria; virus isolated in fetal tissue and placenta
	Yes	16	Full-term live birth	14 wk; 6 mo	Congo Basin strain

PCR, polymerase chain reaction; n/a, not available

Meaney-Delman DM, et al. Obstet Gynecol 2022;00:1-7

MONKEYPOX INFECTION IN PREGNANCY

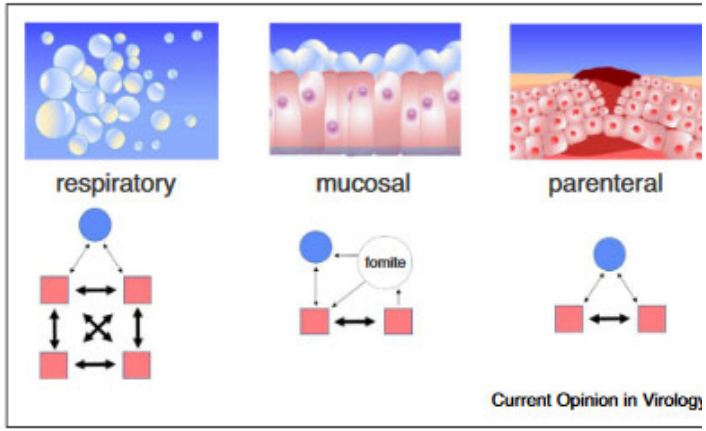
- Degree of susceptibility during pregnancy and severity of monkeypox infection in pregnancy unknown
- Smallpox in pregnancy
  - More severe illness
  - Higher case fatality rate
  - Greater risk of hemorrhagic complications
- Adverse pregnancy outcomes with Orthopoxviruses, including monkeypox
  - Pregnancy loss
  - Congenital infection
  - Preterm birth

- The signs and symptoms of monkeypox virus infection in people who are pregnant appear similar to those in non-pregnant people with monkeypox virus infection, including prodromal symptoms (e.g., fever, headache, lymphadenopathy, malaise, sore throat and cough) and rash.
- During pregnancy, the cause of fever may be difficult to differentiate from other infections, such as intraamniotic infection (chorioamnionitis), until the rash appears. Rash in a person who is pregnant with risk factors for monkeypox virus infection needs to be differentiated from dermatoses of pregnancy, including polymorphic eruption of pregnancy (also known as pruritic urticarial papules and plaques of pregnancy). In addition, monkeypox lesions can mimic those in other infections. Patients with rashes initially considered characteristic of more common infections (e.g., varicella zoster or sexually transmitted infections) should be carefully evaluated for a characteristic monkeypox rash, and diagnostic testing should be considered, especially if the person has epidemiologic risk factors for monkeypox virus infection. Co-infections with monkeypox virus and sexually transmitted infections (STIs) have been reported and the presence of an STI does not rule out monkeypox, so a broad approach to testing is encouraged.

Clinical Considerations for Monkeypox in People Who are Pregnant or Breastfeeding | Monkeypox | Poxvirus | CDC

MONKEYPOX: ROUTES OF TRANSMISSION

- Animal-to-human via bite/scratch, direct contact, and indirect contact (cleaning cages, animal products)
- Human-to-human
  - Respiratory secretions (droplet transmission) – prolonged face-to-face contact (no data regarding risk from patients with pneumonia)
  - Direct contact (skin-to-skin) with body fluids or body lesions
  - Indirect contact/fomites (drinking or eating from same dish, contact with contaminated linens)
  - Sexual: Direct contact, unknown if via semen or vaginal fluids
  - Vertical (transplacental) or at deliver: May lead to fetal demise
- Mortality: The case fatality rate for the Central African clade is 1-10% versus <3% for the West African clade
  - Likely an overestimate (biased by severity)
  - Currently outbreak expected mortality <1%; highest risk immunocompromised, pregnant women, young children
- UK Health Authority, 28 July 2022
  - Daily case growth rate has slowed
  - No confirmed cases of airborne transmission; Limited household transmission
  - Hospitalizations for severe pain, secondary bacterial infections
  - No deaths



Transmission routes of orthopoxviruses (OPXVs). OPXVs can be transmitted through respiratory, mucosal, or parenteral routes. Blue circles and red squares represent a distinct host species; arrows symbolize potential transmission between and within species. Intraspecific transmission (respiratory, mucosal, or parenteral) may become intensified at higher host densities (represented by darker arrows). Mucosal transmission can occur via fomites or environmenta contamination, facilitating opportunities for both interspecific and intraspecific transmission. Parenteral infection occurs when virus is introduced through breaches in the skin.

Bunge EM, et al. PLOS Neglected Tropical Diseases 2022:11 February;
Reynolds MG, et al. Curr Opin Virology 2018;28:108-115; CDC
Khalil A, et al. Ultrasound Obstet Gynecol 2022;2 June

MONKEYPOX TRANSMISSION: UNKNOWNS

- To what extent children, people with specific underlying conditions (including those that may cause immunocompromise, eczema or atopic dermatitis), or pregnant people are at risk of severe disease, as they have been with previous outbreaks of monkeypox.
- Whether people with immunosuppression have more Monkeypox virus present in body fluids.
- How often Monkeypox virus may be spread from respiratory secretions, or at what point during infection a person with monkeypox symptoms might be more likely to spread Monkeypox virus through respiratory secretions. As stated above, transmission during brief interactions has not been reported.
- If Monkeypox virus may be present in body fluids, including oral and respiratory secretions, urine, feces, and semen.
- Whether Monkeypox virus can be spread through semen or vaginal fluids. Viral DNA has been detected in semen.

Isolation and Prevention Practices for People with Monkeypox | Monkeypox | Poxvirus | CDC

MONKEYPOX: TRANSMISSION & VIRAL SURVIVAL

- Transmission: 1) Direct contact with body fluids or lesions; 2) Respiratory (droplet transmission) - no data on risk if patient has pneumonia; 3) Sexual? (unknown if via semen or vaginal fluids); 4) Vertical (transplacental; mother-to-fetus); 5) Indirect (via fomites)
  - Bedding & clothes[1,4]
  - Eating utensils[2]
- Nosocomial transmission to HCP has been reported[3,4,5,6]
- Smallpox virus (Monkeypox surrogate) environmental survival: At the ambient temperature of 25.8-26.4°C and 85-90° relative humidity, the virus in crusts survived only 8 weeks but at lower temperatures and relative humidities the survival time was considerably prolonged[7]; survival in cotton may be as long as 18 months[8]
- Smallpox, disinfectant susceptibility: Ethanol, isopropanol, 60-95% ≤1min; 1% benzalkonium Chloride ≤1min[9]
- Vaccinia: Sodium hypochlorite, QAUT plus CHG inactivating virus at all concentrations tested[10]

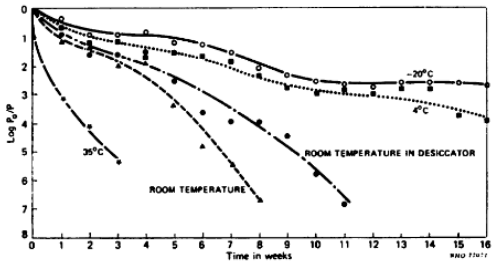


Fig. 1. Fall in log titre of variola virus with time under different environmental conditions.

[1]Harris E. JAMA 2022 27 May; [2]Nolen LD, et al. Am J Trop Med Hyg 2015;93:410; [3]Adler H, et al. Lancet ID 2022;24 May; [4]Vaughan A, et al. EID 2020;26:782; [5]Learned LA, et al. Am J Trop Med Hyg 2005;73:428; [6]Yinka-Ogunleye A, et al. Lancet ID 2019;19:872; [7]Huq F. Bull WHO 1976;54:3571; [8]MacCallum FO, McDonald JR. Bull WHO 1957;16:247; [9]Tanabe I et al. Appl Environ Microbiol 1976;32:209; [10]de Oliveira TML, Rehfeld LS, et al. Am J Trop Med 2011;85:152

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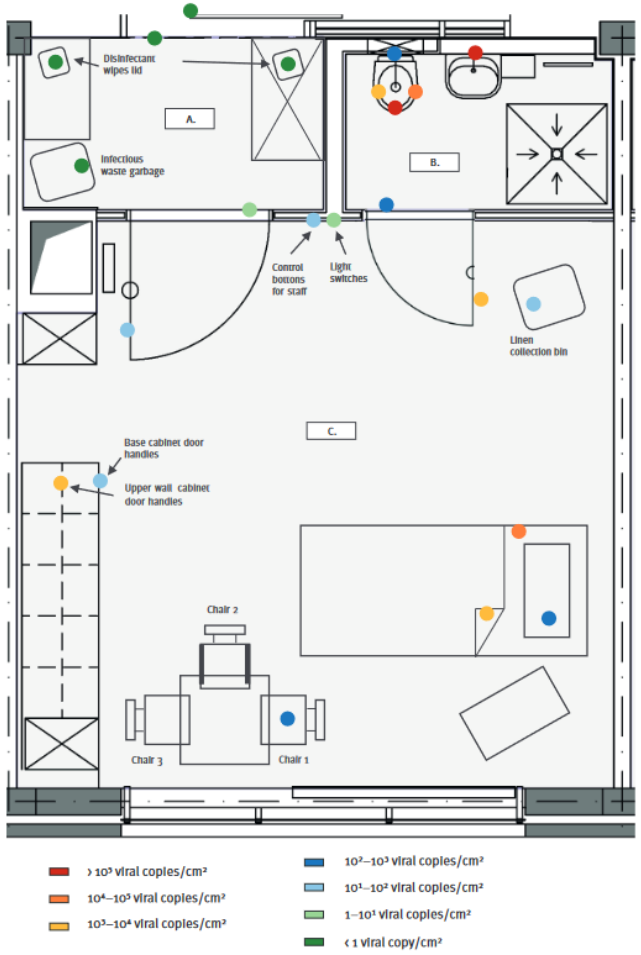
Evidence of surface contamination in hospital rooms occupied by patients infected with monkeypox, Germany, June 2022

- The extent of monkeypox virus environmental contamination of surfaces is unclear. We examined surfaces in rooms occupied by two monkeypox patients on their fourth hospitalisation day. Contamination with up to 10^5 viral copies/cm^2 on inanimate surfaces was estimated by PCR and the virus was successfully isolated from surfaces with more than 10 6 copies. These data highlight the importance of strict adherence of hospital staff to recommended protective measures. If appropriate, pre-exposure or early post-exposure vaccination should be considered for individuals at risk.
- In the anteroom, all hand-contact points examined yielded positive PCR results. However, only traces of viral DNA (maximum = 3 cp/cm2) were detected on the handle of the door leading to the patient's room. Traces of viral DNA were identified on the handle of both anteroom doors located in the ward corridor, outside the anteroom.
- Limitations: 1) DNA environmentally stable; 2) small sample size; 3) does not provide evidence of transmission (high infectious dose required)

FIGURE

Outline map of the (A) anteroom (B) bathroom and (C) room of a hospitalised patient[a] infected with monkeypox virus, with various sampled-surface locations and measured monkeypox virus contamination levels, Germany, June 2022

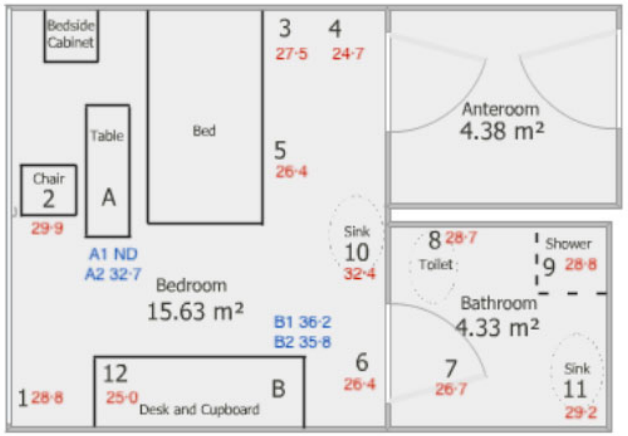


Norz D, et al. Eurosurveillance 2022;30 June

Air and surface sampling for monkeypox virus in UK hospital

- Goal: Assess environmental contamination with Monkeypox virus in 5 inpatient room.
- **Results**: We identified widespread surface contamination (66 positive out of 73 samples) in occupied patient rooms (MPXV DNA Ct values 24·7-38·6), on HCP protective equipment after use, and in doffing areas (Ct 26·3-34·3). Five out of fifteen air samples taken were positive. Significantly, three of four air samples collected during a bed linen change in one patient's room were positive (Ct 32·7-35·8). Replication-competent virus was identified in two of four samples selected for viral isolation, including from air samples collected during the bed linen change.

Gould S, et al
https://www.medrxiv.org/content/10.1101/2022.07.21.22277864v1



*Air samples collected over 10 minutes at at a rate of 50L/minutes (500L)

Table 1: Clinical characteristics and results of surface and air environmental sampling in patients' rooms.

	Room A (P1)*	Room A (P2)	Room C (P2)	Room D*	Room E*
Background information					
Date of sampling	*24th May*	*17th June*	*16th June*	*17th June*	*16th June*
Days since onset	*9*	*30*	*6*	*26*	*7*
Days since admission	*2*	*7*	*7*	*18*	*3*
Throat Ct at admission	*27*	*Negative*	*22*	*37*	*30*
Lesion Ct at admission	*22*	*23*	*28*	*23*	*31*
Plasma Ct at admission	*32*	*34*	*35*	*Negative*	*31*
Days on tecovirimat	*2*	*4*	*NR*	*NR*	*3*
Patient Room Ct values					
Floor	NA	26.9	30.9	34.9	32.5
Call button	27.5	29.4	32.4	Negative	26.1
Light switch	24.7	31.6	34.5	36.3	30.2
TV remote control	25.0	28.9	37.4	32.2	28.2
Observation machine	26.4	NA	NA	NA	NA
Tap handle (bedroom)	32.4	34.2	35.6	36.7	27.1
Window ledge	28.8	29.7	Negative	35.6	35.5
Chair – arm rest	29.9	33.5	33.8	31.6	24.9
Door handle (room to bathroom)	26.7	33.3	32.6	Negative	28.1
Bathroom Ct values					
Vent/grille (room to bathroom)	26.4	25.9	27.9	33.3	33.6
Toilet flush handle	28.7	32.6	31.8	34.8	26.4
Shower handle	28.8	33.5	34.0	33.8	32.7
Tap handle (bathroom)	29.2	29.3	32.8	Negative	25.9
Anteroom Ct values					
Floor: toxic side	26.3	28.7	33.2	32.9	30.6
Floor: non-toxic side	NA	33.6	Negative	36.8	36.8
Ward Ct values					
Corridor	NA	Negative	37.5	Negative	36.7
Air sampling Ct values					
Pre bed change near	Negative	Negative	Negative	Negative	Negative
Pre bed change far	36.2	36.5	Negative	Negative	Negative
During bed change near	32.7	36.2	Negative	Negative	Negative
During bed change far	35.8	Negative	Negative	Negative	Negative

Table 1: Details of environmental sampling performed in five patient rooms at the Royal Free Hospital May-June 2022. P1/P2 = Rooms A was sampled on two occasions with different patients occupying this room on each visit; rooms were decontaminated every 12hrs during occupancy using 5,000ppm available chlorine sodium hypochlorite on all surfaces and 10,000 ppm available chlorine sodium hypochlorite for toilet, shower, wash basins and floors with a full room clean after patient discharge, followed by decontamination using vapourised hydrogen peroxide. *Denotes occupant of this room was the first patient admitted into this room with monkeypox Ct = qPCR crossing threshold value of MPXV DNA detected. NA = Not applicable (sample not taken for this room). NR = Tecovirimat not received.

Infection-competent monkeypox virus contamination identified in domestic settings following an imported case of monkeypox into the UK.

ABSTRACT

An imported case of monkeypox was diagnosed in December 2019 in a traveler returning from Nigeria to the UK. Subsequently, environmental sampling was performed at two adjoining single room residences occupied by the patient and their sibling. Monkeypox virus DNA was identified in multiple locations throughout both properties, and monkeypox virus was isolated from several samples three days after the patient was last in these locations. Positive samples were identified following use of both vacuum and surface sampling techniques; these methodologies allowed for environmental analysis of potentially contaminated porous and non-porous surfaces via real-time quantitative PCR analysis in addition to viral isolation to confirm the presence of infection-competent virus.

Atkinson B et al. https://www.medrxiv.org/content/10.1101/2022.06.27.22276202v1

Room	Item sampled	Sample method	Ct value	Viral isolation	NGS data
Patient's residence	Mattress and sheet	Vacuum	22.6	✓	NA
Patient's residence	Towel (left on top of bed)	Vacuum	22.7	✓	✓
Patient's residence	Bedding (duvet and pillows)	Vacuum	23.7	NA	NA
Patient's residence	iPad	Swab	25.2	✓	✓
Patient's residence	Door handle to landing	Swab	25.4	NA	NA
Patient's residence	Watch	Swab	25.8	NA	NA
Patient's residence	Corner taps of wash basin	Swab	25.9	NA	NA
Patient's residence	Fridge	Swab	26.9	NA	NA
Patient's residence	Passport/holder/wallet	Swab	27.2	NA	NA
Patient's residence	Small towel and cushions	Vacuum	27.7	NA	NA
Landing	Handle to patient's residence	Swab	28.1	✓	✓
Patient's residence	Kitchenette cupboard handles	Swab	28.2	NA	NA
Patient's residence	TV remote	Swab	28.5	NA	NA
Patient's residence	Large suitcase handle	Swab	28.6	NA	NA
Patient's residence	Toothbrush blue (in residence)	Swab	28.6	NA	NA
Main bathroom	Toilet flush	Swab	29.9	NA	NA
Main bathroom	Sink taps	Swab	29.9	×	NA
Landing	Handle to main bathroom	Swab	30.0	NA	NA
Patient's residence	Light switch	Swab	30.0	NA	NA
Patient's residence	Toothbrush pink (in residence)	Swab	30.5	NA	NA
Sibling's residence	Duvet	Vacuum	30.5	✓	NA
Patient's residence	Standalone tall light switch	Swab	30.7	NA	NA
Sibling's residence	Towel	Vacuum	31.1	NA	NA
Landing	Handle to utility room	Swab	31.3	NA	NA
Patient's residence	Intercom phone to front door	Swab	31.4	NA	NA
Landing	Bannister	Swab	31.4	×	NA
Patient's residence	Sofa	Vacuum	31.6	✓	NA
Landing	Hall Light Switch	Swab	32.0	×	NA
Patient's residence	Wardrobe handles	Swab	32.0	NA	NA
Main bathroom	Toilet seat	Swab	32.1	NA	NA
Patient's residence	Electronic remote	Swab	32.2	NA	NA
Sibling's residence	Pillows	Vacuum	32.2	NA	NA
Small shower room	Sink taps	Swab	32.5	NA	NA
Main bathroom	Inner door handle	Swab	33.5	NA	NA
Sibling's residence	Mattress and sheet	Vacuum	34.3	×	NA
Sibling's residence	Towel (left on top of bed)	Vacuum	35.3	NA	NA
Landing	Bedding (duvet and pillows)	Swab	38.1	NA	NA
Landing	iPad	Swab	ND	NA	NA
Sibling's residence	Door handle to landing	Swab	ND	NA	NA
Small shower room	Watch	Swab	ND	NA	NA
Small shower room	Corner taps of wash basin	Swab	Invalid	NA	NA
Small shower room	Fridge	Swab	Invalid	NA	NA

Table: RT-qPCR crossing threshold (Ct) values for environmental samples collected at the patient's residence including the adjoining residence occupied by their sibling and shared bathrooms. Results have been ordered by Ct value to allow assessment of contamination level (lower Ct value indicates greater contamination with MPXV DNA). NA = not attempted. ND = not detected. Invalid = internal extraction control outside of defined parameters; negative result from these samples cannot be considered as accurate. NB Ct values for samples collected from the bus are not shown - all samples were negative for MPXV DNA.

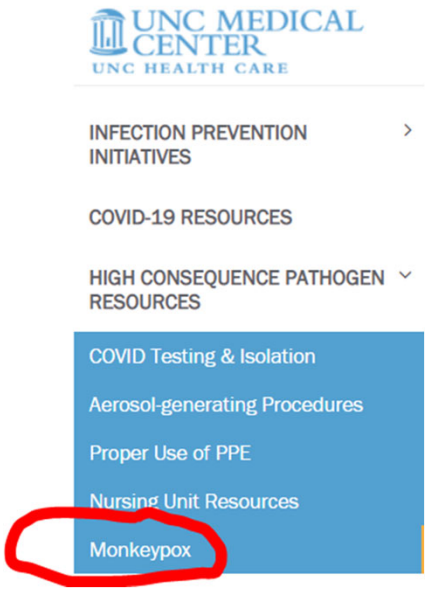
MONKEYPOX (enveloped virus): INFECTION PREVENTION, CDC

- Isolation precautions: Standard Precautions should be applied for all patient care, including for patients with suspected monkeypox. If a patient seeking care is suspected to have monkeypox, infection prevention personnel should be notified immediately.
- Patient placement: A patient with suspected or confirmed monkeypox infection should be placed in a single-person room; special air handling is not required. The door should be kept closed (if safe to do so). The patient should have a dedicated bathroom. Transport and movement of the patient outside of the room should be limited to medically essential purposes. If the patient is transported outside of their room, they should use well-fitting source control (e.g., medical mask) and have any exposed skin lesions covered with a sheet or gown.
  - UNC, we are planning to use Special Airborne/Contact precautions (i.e., placement in an All room or private room with HEPA filter plus PPE as below) – same as COVID-19 (for simplicity)
- PPE: Gown, gloves, eye protection, and N95 or higher-level respirator
- Waste management: Waste management (i.e., handling, storage, treatment, and disposal of soiled PPE, patient dressings, etc.) should be performed in accordance with U.S. Department of Transportation (DOT) Hazardous Materials Regulations (HMR; 49 CFR, Parts 171-180.). Required waste management practices and category designation can differ depending on the monkeypox virus clade (Any clade(s) except West African, category A, always –until inactivate; West African clade, regulated medical waste)
  - Treat materials in contact with lesions as regulated medical waste
- Linens, eating utensils: Manage per usual hospital policy (avoid shaking)
- Antiseptics (hand hygiene): Alcohol (60-90% waterless product), or soap/CHG plus water
- Surface disinfection: EPA list Q agents (emerging infectious disease claim)
- Activities such as dry dusting, sweeping, or vacuuming should be avoided. Wet cleaning methods are preferred.
- Duration of precautions: Until all lesions have resolved, the scabs have fallen off, and a fresh layer of intact skin has formed.

https://www.cdc.gov/poxvirus/monkeypox/clinicians/infection-control-healthcare.html

INFECTION PREVENTION, UNC-MC

- Isolation: Special Airborne-Contact precautions: Gown, Gloves, and eye protection or PAPR
- Patients do not need to be escorted into clinic
- Patient should immediately be brought back to a room and not wait in the waiting area
- Airborne Infection Isolation Room (AIIR) if available
- No AIIR? Private room with door closed, use a HEPA if available



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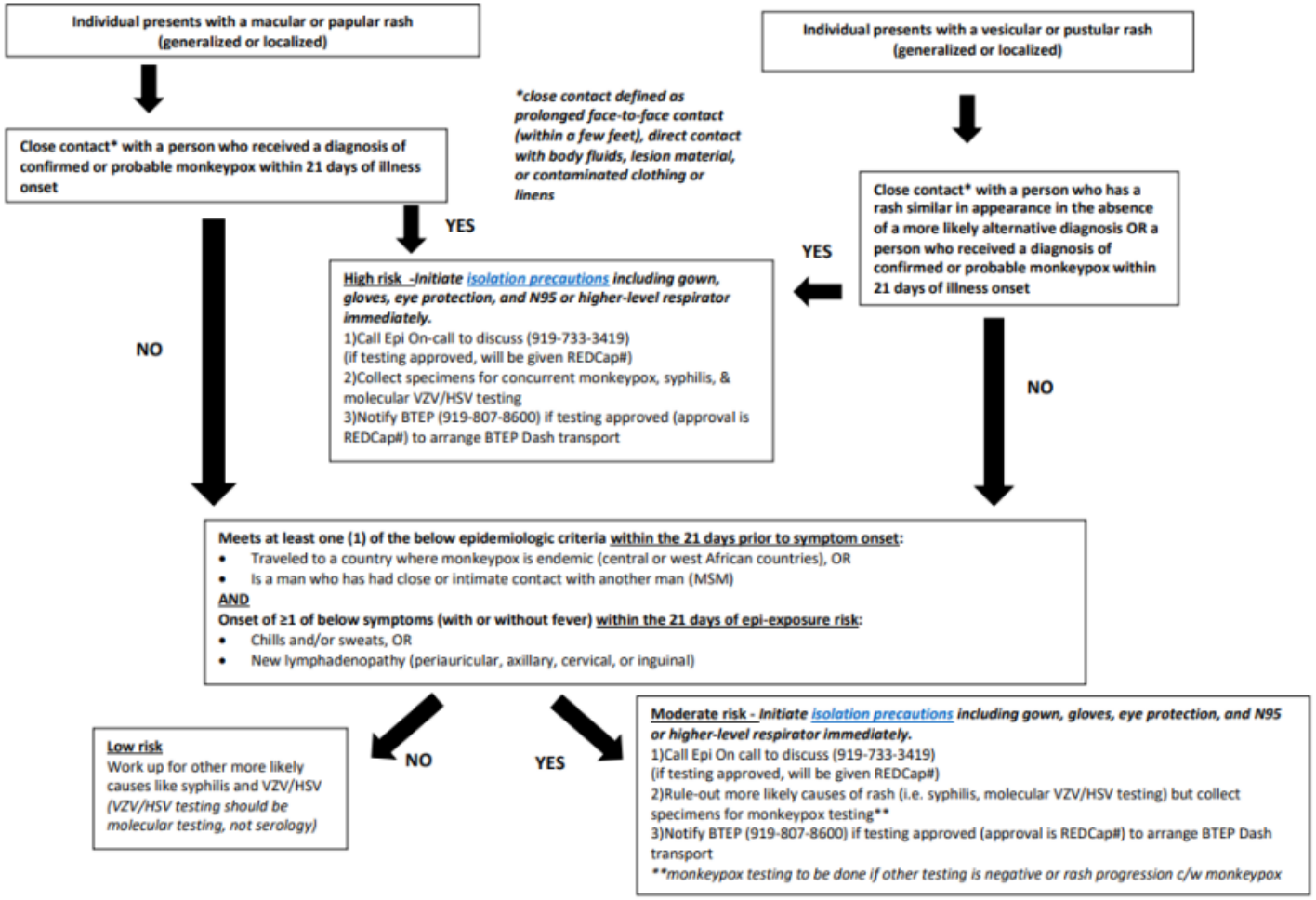
Evaluating Patients for Monkeypox (5/24/2022)



NC Health Dept.

Although a prodromal illness (i.e. flu-like illness) commonly presents 1-3 days before rash onset with monkeypox, there have been reports of several cases presenting with perianal or genital lesions in the absence of subjective fever. Providers are encouraged to contact the epidemiologist on call to discuss any concerns or complicated situations not covered by this algorithm.

MONKEYPOX TESTING, UNC-MC

How to Collect a Specimen for MPX Testing

Options for laboratory testing at present include the **UNC Medical Center McLendon Laboratory**, the **NC Department of Health and Human Services (DHHS)** lab, and commercial labs including **Mayo Clinic Lab** and **Labcorp**. Collection procedures are generally the same and are described below but may change on request of the laboratory receiving the sample or due to supply issues. Healthcare staff should follow specimen collection procedures operative at their facility. Note that approval by the NC DHHS is required prior to specimen collection only if testing is to be performed by the NC DHHS lab, as detailed below. Approval from the NC DHHS is not needed when specimens are to be tested at the UNC McLendon or a commercial lab.

Personal Protective Equipment

- All persons entering the room of a patient with possible MPX (including any persons obtaining specimens) should follow Special Airborne Contact Precautions which entails: respiratory protection (N95 respirator plus eye protection or PAPR, gloves, and gown).

Materials Needed

- Red cap swabs (double swabs)—these are sterile synthetic swabs

- A separate swab for **HSV and VZV** DNA PCR testing, unless using UNC McLendon lab in which case red cap swab is sufficient for MPX and HSV and VZV testing
- Alcohol wipes

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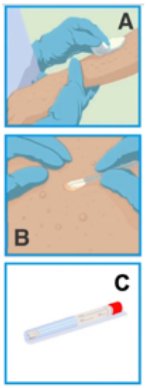
MONKEYPOX TESTING, UNC-MC

Procedure

1. Select lesion for specimen collection and pre-label the specimen collection tube with patient identifiers.
2. If the lesion is dry and will be unroofed, gently sanitize the lesion with an alcohol wipe and let dry (Panel A). Otherwise, swab lesions that are open and wet without first wiping with alcohol. Lesions on sensitive areas should not be wiped with alcohol.
3. Vigorously swab the base of the lesion with both of the swab tips in the red capped transport device (Panel B). *Do not remove the swabs from the cap.* When rectal or vaginal lesions are suspected, swabs can be inserted into the orifice.
4. Put the double headed swab back into the clear transport tube (Panel C). DO NOT PUT THE SWABS INTO ANY TRANSPORT MEDIA, if sending to McLendon Laboratory at UNC Medical Center.
5. Repeat the above procedures using a different red cap double swab for a second lesion, from a separate body site, if present.
6. When sending to McLendon Lab at UNC Medical Center: For each lesion sampled (i.e., one order per lesion), use Epic "LAB192403" to find the MONKEYPOX PCR order. Specimen type should be "Swab, Lesion" and specimen source should be the anatomic location sampled. *Remember to place separate orders for each lesion sampled.* See:

   https://www.uncmedicalcenter.org/app/files/public/2b7688a6-d854-4b5a-a39c-1a36672cac4d/pdf-mclendon-labs-memo-micro208-jul29-2022.pdf



7. All suspect cases, regardless of which lab the specimen is sent to, must be reported to NC Division of Public Health (919-733-3419) or the local health department in the county where live patient lives: https://www.ncdhhs.gov/divisions/public-health/county-health-departments
8. Additional testing is typically needed for **HSV and/or VZV** and separate appropriate swabs should be obtained for these tests, unless testing will be done at the McLendon Lab at UNC Medical Center. In addition, blood may need to be drawn for **syphilis** testing.

ONLY if sending to the NC DHHS (state) lab

Prior to collecting specimens:

9. Contact the NC DHHS Epidemiologist On-Call to approve specimen collection: **919-733-3419**. You may receive a recording and be asked to leave a message. The Epidemiologist will return calls within 1 hour. As above, for patients not present at a UNC facility (e.g., at home) the Epidemiologist can assist with identifying a location for testing.
10. Following approval by the NC DHHS Epidemiologist On-Call, collect the specimen per the procedure below.
11. Print and complete the NC DHHS BTEP form to include with specimens (the ICD-10 for Monkeypox is B04): https://slph.dph.ncdhhs.gov/Forms/5010-BT-and-Emerging-Pathogens.pdf

Notes

- Waste including PPE can be disposed of using standard hazardous medical waste procedures.
- Hand deliver to the microbiology laboratory. Offsite locations should use their regular workflow for getting specimens to McLendon Laboratories or to a commercial lab, if appropriate.
- Patients who are tested for MPX should be instructed on recommendations for isolation procedures. A UNC Health hand-out for patients awaiting test results can be found at https://unchcs.intranet.unchealthcare.org/Documents/2022/07-July/Monkeypox_Whatyoushoulddowhileyouwaitforresults.pdf

MEDICAL COUNTERMEASURES: VACCINE OPTIONS

Both options thought to be ~85% effective at preventing monkeypox.

Name	Indication	Dosing & Administration	Availability	Storage and Handling	Notes
★ **JYNNEOS** Also known as: Imvamune Imvanex	FDA approved for prevention of smallpox & monkeypox in **adults 18+** **Individuals <18 can be treated under expanded access IND.**	2 doses (0.5 mL each) administered 4 weeks apart. **Subcutaneous injection**	SNS request; **~ 72,000 doses in SNS and growing**	**Keep frozen** at -25°C to -15°C (-13°F to +5°F). Once thawed, the vaccine may be kept at +2°C to +8°C (+36°F to +46°F) for **8 weeks**	Live attenuated virus vaccine; **non-replicating** modified vaccinia Ankara-Bavarian Nordic (MVA-BN) **Ships frozen from SNS** Can transport refrigerated for immediate/short term use **Single dose vials;** SNS does not provide ancillary supplies
ACAM2000	FDA approved for smallpox prevention in **adults and pediatrics >1 y.o.** **Expanded access IND for monkeypox**	1 drop of vaccine suspension via scarification using bifurcated needle. CDC Training Videos for ACAM2000 administration	SNS Request; **> 100 Million doses in SNS**	Prior to reconstitution, **store frozen** at -15°C to -25°C (5°F to -13°F); may also be stored refrigerated at 2°C to 8°C (36°F to 46°F) for up to 18 months. Diluent stored at room temperature of 15°C to 30°C (59°F to 86°F).	Live vaccinia virus Myocarditis risk Contraindications for severe immunocompromise and peds <1. Only administered by trained individuals; previous vaccination recommended Counseling on covering wound and handling bandages **100 doses per vial; comes with diluent and 100 bifurcated needles; transfer syringes not included.**

★ Denotes preferred MCM

JYNNEOS VACCINE
(approved for Monkeypox)

TABLE 2. Distinctions between ACAM2000 and JYNNEOS that might facilitate decision-making among vaccinees at risk for orthopoxvirus infections — United States, 2022

Characteristic	Vaccine product	
	ACAM2000*	JYNNEOS
Vaccine virus	Replication-competent vaccinia virus	Replication-deficient modified vaccinia Ankara
"Take" following vaccination†	Yes	No
Risk for inadvertent inoculation and autoinoculation	Yes	No
Risk for serious adverse event	Yes	No significant events identified during clinical trials
Risk for cardiac adverse events	Myopericarditis in 5.7 per 1,000 primary vaccinees	Clinical trial data limited in evaluating this outcome; however, no significant events in data abstracted from single study arms§
Assessment of effectiveness	FDA assessed by comparing immunologic response and take rates to Dryvax*	FDA assessed by comparing immunologic response to ACAM2000 and animal studies
Administration	Percutaneously using a bifurcated needle by multiple puncture (scarification) technique,¶ single dose	Subcutaneously, 2 doses 28 days apart

Abbreviation: FDA = Food and Drug Administration.

* Both ACAM2000 and Dryvax are derived from the New York City Board of Health strain of vaccinia; ACAM2000 is a second generation smallpox vaccine derived from a clone of Dryvax, purified, and produced using modern cell culture technology.

† A "take" is postvaccination lesion often used as a marker of successful vaccination after ACAM2000.

§ Because JYNNEOS is a replication-deficient virus vaccine, serious adverse events are believed to be fewer. However, the mechanism of myopericarditis in persons who receive ACAM2000 is poorly understood; for this reason, it is unknown whether persons who receive JYNNEOS might experience myopericarditis.

¶ https://www.fda.gov/media/75792/download

Contraindication to JYNNEOS = serious vaccine component allergy

MMWR 2022;71:3 June

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HHS ENHANCED VACCINATION STRATEGY

- **On 6/28, US HHS announced a new strategy to broaden access to vaccine in response to the growing outbreak**
  - Transitioned from pull to push model
  - Phased approach delivering ~1.6M doses of JYNNEOS to states by the end of 2022
    - Phase 1 – 56,000 doses (week of July 4th)
    - Phase 2A – 144,000 doses (week of July 11th)
    - Phase 2B – 131,000 doses (week of July 18th)
    - Phase 3 - ~800,000 doses (timing TBD)
  - Vaccine allocations to states based on at risk populations and current case counts
  - An additional 2.2 million doses of JYNNEOS expected to be available in 2023
  - ACAM2000 is available in more plentiful supply
    - However, this product carries greater risk of certain serious side effects and cannot be given to individuals who are immunocompromised or have heart disease.
    - Can be requested from the strategic national stockpile if necessary
  - For more information: Fact Sheet: Biden-Harris Administration's Monkeypox Outbreak Response

NC VACCINATION RESPONSE - DISTRIBUTION

Phase I

- NC allocation = 444 doses (arrived 7/6)
  - Seven local health departments chosen to serve as hubs
    - Buncombe, Durham, Forsyth, Mecklenburg, New Hanover, Pitt, Wake
    - Note: Haywood and Mecklenburg Counties received small amounts of vaccine prior to Phase 1 due to response operations

Phase 2A

- NC allocation = 2,365 doses (arrived 7/14)
  - Distributed to the same seven LHDs
  - Seven HIV clinic partners identified to pair with LHD hubs to receive vaccine to expand access
    - Atrium Health, Duke, ECU Health, Southern Region Area Health Education Center (SRAHEC), UNC Health, Wake Forest Baptist Health, Western North Carolina Community Health Services (WNCCHS)

Phase 2B

- NC allocation = 1,739 doses (will arrive this week)
  - Distributions in progress to the following LHDs
    - Mecklenburg (720)
    - Wake (359)
    - Durham (300 – Transfer from Wake)
    - Cumberland (160)
    - Guilford (140)
    - Buncombe (60)

By Friday July 22nd, NC will have received a total of 4,548 doses of JYNNEOS

Enough to vaccinate ~2,300 individuals

NC VACCINATION RESPONSE - ELIGIBILITY

Current Monkeypox Vaccine Eligibility

- PEP: People who have been in close contact with someone diagnosed with monkeypox
- "PEP ++": Men who have sex with men or transgender individuals who have had multiple or anonymous sex partners in the last 14 days
- PrEP: Available for certain healthcare and public health response team members designated by public health authorities

At this time, most clinicians in the United States and laboratorians not performing the orthopoxvirus generic test to diagnose orthopoxviruses, including monkeypox, are not advised to receive orthopoxvirus PrEP

Comparison of lyophilized versus liquid modified vaccinia Ankara (MVA) formulations and SC versus ID routes of administration in healthy vaccinia-naïve subjects

- Background: Modified vaccinia Ankara (MVA) is being developed as a safer smallpox vaccine and is being placed in the US Strategic National Stockpile (SNS) as a liquid formulation for subcutaneous (SC) administration at a dose of 1 × 10 8 TCID 50 in a volume of 0.5 mL. This study compared the safety and immunogenicity of the standard formulation, dose and route with both a more stable, lyophilized formulation and with an antigen-sparing intradermal (ID) route of administration.
- Methods: 524 subjects were randomized to receive either a full dose of Lyophilized-SC, a full dose of Liquid-SC or 20% (2×10^7 TCID 50 in 0.1 mL) of a full dose Liquid-ID MVA on Days 0 and 28. Safety and immunogenicity were followed through 180 days post 2nd vaccination.
- Results: Among the 3 groups, the proportion of subjects with moderate/severe functional local reactions was significantly different (P = 0.0013) between the Lyophilized-SC group (30.3%), the Liquid-SC group (13.8%) and Liquid-ID group (22.0%) only after first vaccination; and for moderate/severe measured erythema and/or induration after any vaccination (P = 0.0001) between the Lyophilized-SC group (58.2%), the Liquid-SC group (58.1%) and the Liquid-ID group (94.8%) and the reactions lasted longer in the Liquid-ID group. In the ID Group, 36.1% of subjects had mild injection site skin discoloration lasting ≥6 months.
- After second vaccination Day (42–208), geometric mean of peak neutralization titers were 87.8, 49.5 and 59.5 for the Lyophilized-SC, Liquid-SC and Liquid-ID groups, respectively, and the maximum number of responders based on peak titer in each group was 142/145 (97.9%), 142/149 (95.3%) and 138/146 (94.5%), respectively. At 180 days after the 2nd vaccination, geometric mean neutralization titers declined to 11.7, 10.2 and 10.4 with only 54.3%, 39.2% and 35.2% of subjects remaining seropositive for the Lyophilized-SC, Liquid-SC and Liquid-ID groups, respectively. Both the Lyophilized-SC and Liquid-ID groups were considered non-inferior (primary objective) to the Liquid-SC group

Frey SE, et al. Vaccine 2015;33:5225-5234

UNC SCHOOL OF MEDICINE

Comparison of lyophilized versus liquid modified vaccinia Ankara (MVA) formulations and SC versus ID routes of administration in healthy vaccinia-naïve subjects

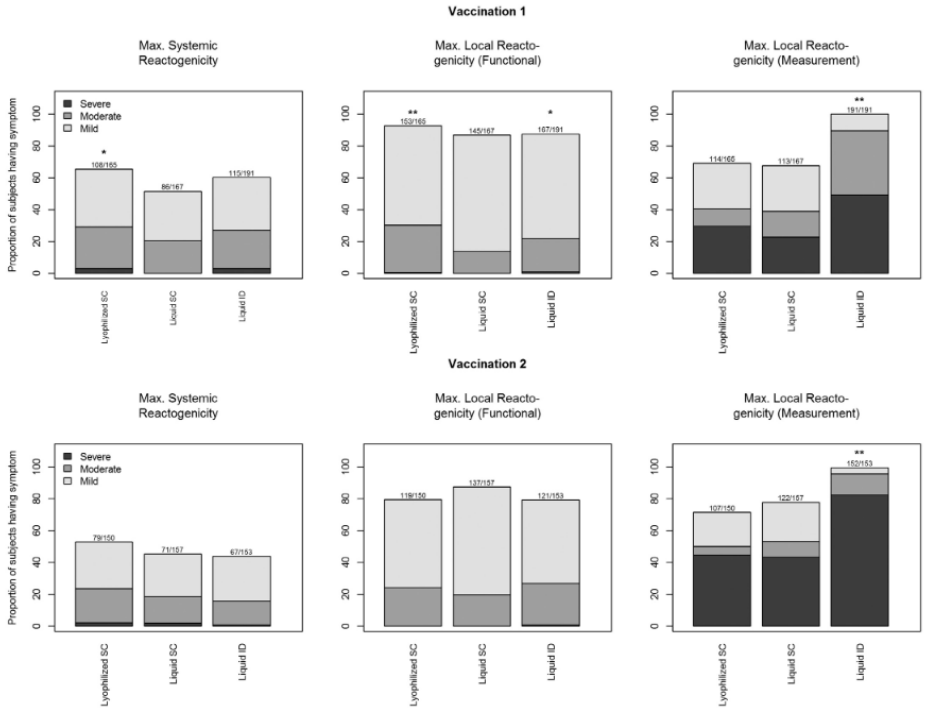

Fig. 2. Maximum severity grade for reactogenicity collected by subjects in the Lyophilized-SC, Liquid SC and Liquid-ID groups for 15 days (Days 0–14) after each vaccination. Systemic reactogenicity events were graded using a functional scale of mild (present but easily tolerated), moderate (able to tolerate routine activity with effort), and severe (unable to continue routine activity). Fever grading scale for oral temperature was mild ≥37.8–<38 °C, moderate ≥38–<39 °C, and severe ≥39 °C; fever is included in the systemic reactogenicity. Local injection site reactogenicity events other than erythema and induration were graded using a functional scale of mild (present but easily tolerated), moderate (able to tolerate routine activity with effort), and severe (unable to continue routine activity). Local injection site erythema and induration were measured and graded as mild (<15 mm), moderate (15–30 mm) or severe (>30 mm). * $P<0.05$, ** $P<0.01$.

Table 1a
BN PRNT per protocol population analysis: summary of number and proportion of responders with titers ≥ 15, peak geometric mean titers (GMT), and number of subjects with ≥4-fold rise by vaccination and visit.

Study visit day	Group		
	Lyophilized SC Seroconversion, n/N (%) [95% CI] GMT [95% CI] ≥4-fold rise n/N (%) [95% CI]	Liquid SC Seroconversion, n/N (%) [95% CI] GMT [95% CI] ≥4-fold rise n/N (%) [95% CI]	Liquid ID Seroconversion, n/N (%) [95% CI] GMT [95% CI] ≥4-fold rise n/N (%) [95% CI]
Day 0[a]	0/145 (0.0) [0.0, 2.5] 7.5 [,] NA	2/149 (1.3) [0.2, 4.8] 7.7 [7.4, 8.0] NA	2/146 (1.4) [0.2, 4.9] 7.7 [7.4, 7.9] NA
Day 14	60/145 (41.4) [33.3, 49.8]* 10.9 [9.9, 12.0][NIE] 6/145 (4.1) [1.5, 8.8]	44/149 (29.5) [22.3, 37.5] 10.0 [9.0, 11.1] 3/149 (2.0) [0.4, 5.8]	56/146 (38.4) [30.4, 46.8] 10.3 [9.3, 11.3][NIE] 2/146 (1.4) [0.2, 4.9]
Day 28[b]	61/145 (42.1) [33.9, 50.5]** 10.8 [9.9, 11.9][NIE] 6/145 (4.1) [1.5, 8.8]	39/149 (26.2) [19.3, 34.0] 9.6 [8.7, 10.6] 3/149 (2.0) [0.4, 5.8]	68/146 (46.6) [38.3, 55.0]*** 10.8 [9.9, 11.9][NIE] 2/146 (1.4) [0.2, 4.9]
Day 42	137/145 (94.5) [89.4, 97.6] 77.6 [62.3, 96.7][NIE] 100/145 (69.0) [60.8, 76.4]	137/148 (92.6) [87.1, 96.2] 45.2 [36.4, 56.2] 70/148 (47.3) [39.0, 55.7]	134/146 (91.8) [86.1, 95.7] 54.4 [43.7, 67.8][NIE] 82/146 (56.2) [47.7, 64.4]
Day 56	132/144 (91.7) [85.9, 95.6]** 39.4 [31.9, 48.6][NIE] 63/144 (43.8) [35.5, 52.3]	117/148 (79.1) [71.6, 85.3] 23.4 [19.4, 28.3] 37/148 (25.0) [18.3, 32.8]	124/146 (84.9) [78.1, 90.3] 33.4 [27.2, 41.0][NIE] 59/146 (40.4) [32.4, 48.8]
Day 208	75/138 (54.3) [45.7, 62.8]* 11.7 [10.7, 12.8][NIE] 5/138 (3.6) [1.2, 8.3]	56/143 (39.2) [31.1, 47.7] 10.2 [9.4, 11.0] 1/143 (0.7) [0.0, 3.8]	50/142 (35.2) [27.4, 43.7] 10.4 [9.4, 11.5][NIE] 5/142 (3.5) [1.2, 8.0]
Peak post vaccination 2	142/145 (97.9) [94.1, 99.6] 87.8 [71.2, 108.3][NIE] 105/145 (72.4) [64.4, 79.5]	142/149 (95.3) [90.6, 98.1] 49.5 [40.0, 61.3] 75/149 (50.3) [42.0, 58.6]	138/146 (94.5) [89.5, 97.6] 59.6 [48.1, 74.0][NIE] 86/146 (58.9) [50.5, 67.0]
Half Life [days][c]	69	92	77

NIE: non-inferiority established. PRNT titers ≥15 and <75 were designated a titer of 15 by BN. Titer values of <15 (below limit of detection) were replaced by 7.5 (half the lower limit of detection) for analysis. Seroconversion was defined as PRNT value ≥15.

[a] First vaccination.
[b] Second vaccination.
[c] Based on Day 42, 56, and 208. Accuracy of these 3-point estimates was compromised as many Day 208 observations for BN-PRNT were found below the lower limit of detection.

* $P<0.05$.
** $P<0.01$.
*** $P<0.001$.

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The effects of PEP smallpox vaccination on clinical disease presentation

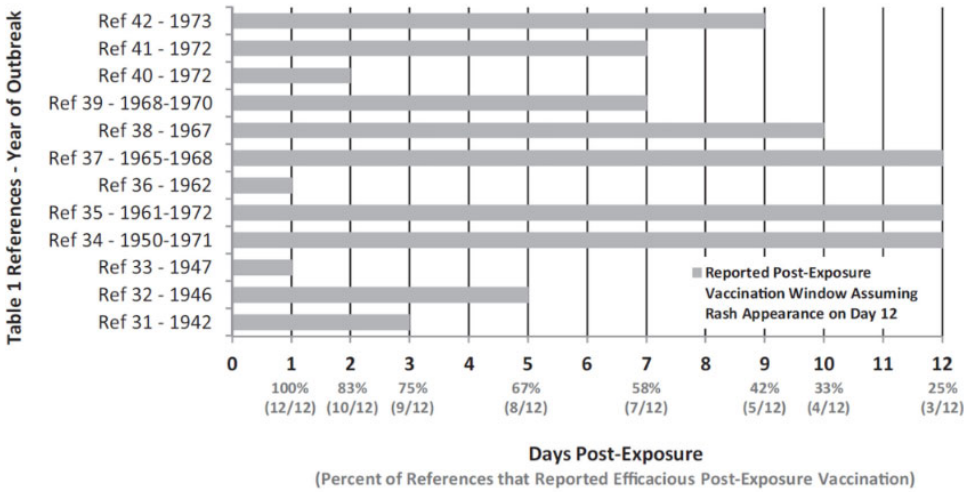
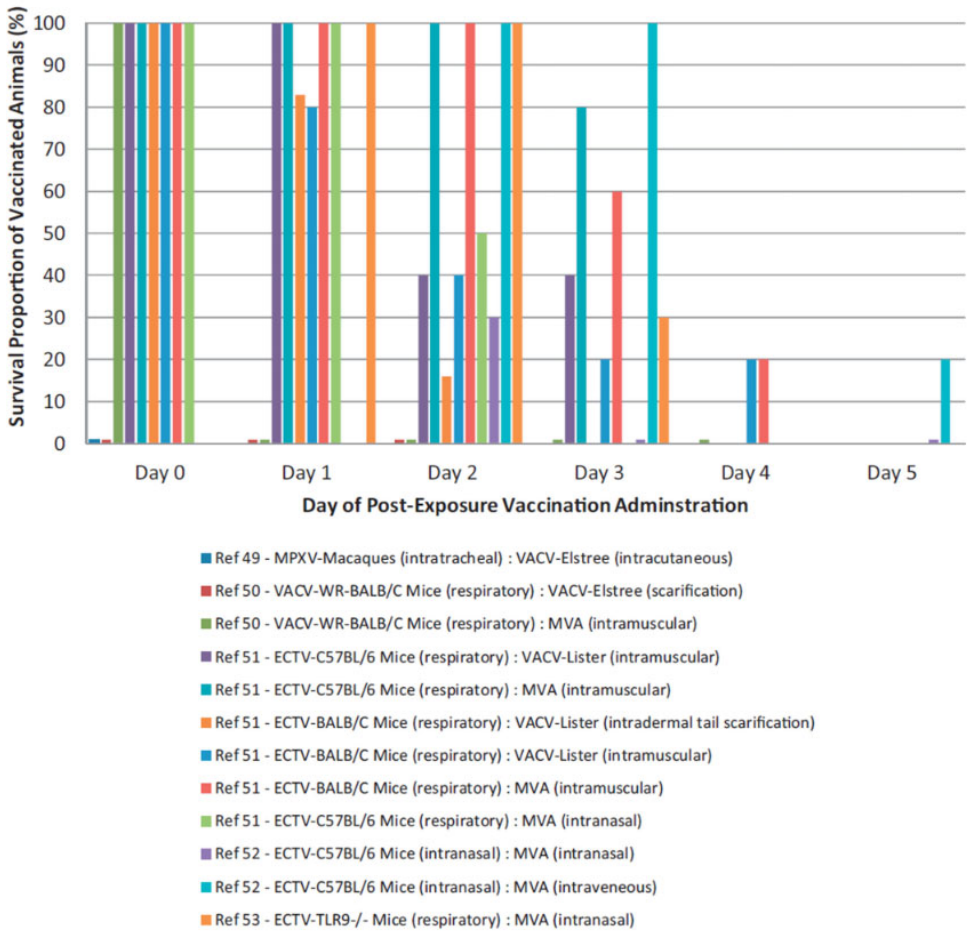


Fig. 1.
Post-exposure vaccination window extrapolated from historical epidemiology reports. A review of references that described post-exposure vaccination as providing partial or complete protection from, or attenuation of, smallpox symptoms during disease outbreaks was accomplished. The reported post-exposure vaccination windows were charted (gray bars) by the days post-exposure that efficacious vaccination was administered (black horizontal axis text). The percentage of references that indicated a benefit to post-exposure vaccination prior to each day post-exposure (gray horizontal axis text) were determined.



Keckler MS, et al. Vaccine 2013;31:5192

MONKEYPOX IN PREGNANCY: TREATMENT

- Pregnant and breastfeeding people should be prioritized for medical treatment
- Contact health department to facilitate request through CDC and the Strategic National Stockpile for access to treatment options
- Breastfeeding
  - Delay breastfeeding until patient meets criteria for discontinuing isolation (i.e., all lesions have resolved, scabs have fallen off, and a fresh layer of intact skin has formed) •
  - Consider support from lactation provider to initiate and maintain milk production •
  - Unknown if Monkeypox virus is present in breast milk
  - Expressed breast milk from patient with symptomatic monkeypox infection or in isolation should be discarded

Available Treatment Options

- Tecovirimat (TPOXX or ST-246)
  - No human data of treatment during pregnancy
  - No fetal toxic effects in animal studies
  - First-line antiviral for pregnant/breastfeeding people
- Cidofovir and Brincidofovir
  - Embryotoxic and teratogenic in animal models
  - No adequate human studies
  - Avoid in 1st trimester and while breastfeeding
- Vaccinia immune globulin intravenous (VIGIV)
  - No human or animal data during pregnancy
  - Breast milk excretion unknown
  - Other immunoglobulins used safely and widely in pregnancy, but use caution in breastfeeding people

Clinical Considerations for Monkeypox in People Who are Pregnant or Breastfeeding | Monkeypox | Poxvirus | CDC

Guidelines for pregnant individuals with monkeypox virus exposure

On May 21, 2022, WHO reported an emerging global outbreak of monkeypox virus infection, with documented community transmission among people in contact with symptomatic cases in non-endemic countries.

The likelihood of infection in pregnant women is high because of post-COVID-19 border reopening and travel among countries presently experiencing an outbreak.

Human infections with monkeypox and smallpox (a closely related orthopoxvirus) can carry a high risk of severe congenital infection, pregnancy loss, and maternal morbidity and mortality.[1] Of four pregnant women from the Democratic Republic of the Congo infected with monkeypox virus (probably with the central African clade of the virus) between 2007 and 2011, two had spontaneous early miscarriages, and one had a second-trimester loss at 18 weeks' gestation.[2] The stillborn fetus had a generalised skin rash, and monkeypox virus DNA detected in fetal tissue, umbilical cord, and placenta, confirming vertical transmission of monkeypox virus. Genomic sequencing data suggest the west African clade of monkeypox virus is responsible for the current outbreak; although it is associated with milder disease and a lower case fatality rate in

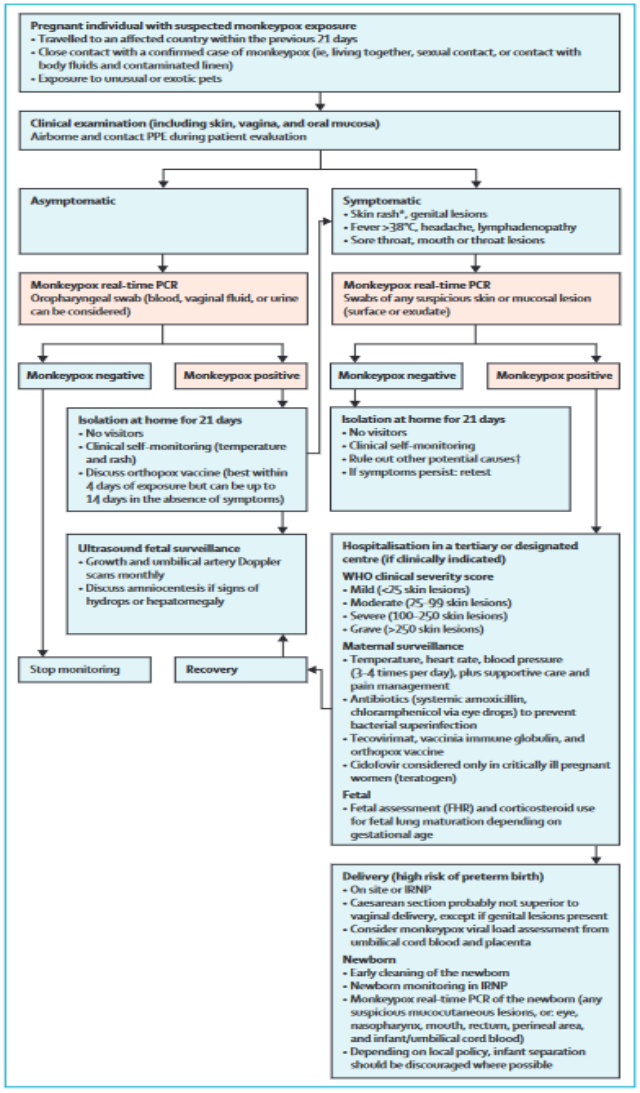


Figure: Clinical management algorithm for suspected monkeypox virus exposure during pregnancy
FHR=fetal heart rate. IRNP=isolation room with negative pressure. PPE=personal protective equipment. *Higher suspicion if skin rash is concentrated over the genitals, face, and extremities. †PCR should be done from a vesicle or genital lesion. We also suggest PCR for herpes simplex virus, varicella zoster virus, and syphilis to rule out other causes of vesiculopustular rash in pregnancy.

Published Online
June 21, 2022
https://doi.org/10.1016/
S0140-6736(22)01063-7

For more on the 2022 **monkeypox outbreak** see https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON385

Submissions should be made via our electronic submission system at http://ees.elsevier.com/thelancet/

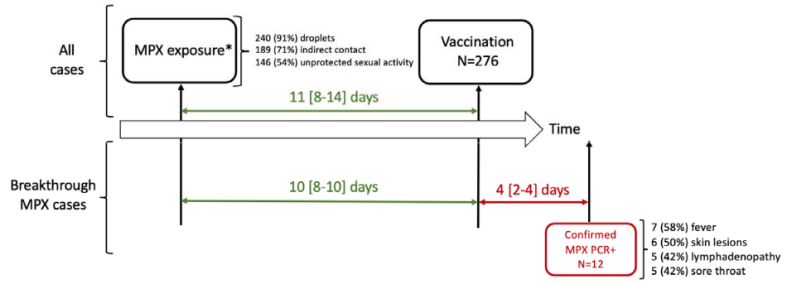
Dashraath P, et al. Lancet 2022;2 July

Breakthrough infections after post-exposure vaccination against Monkeypox

- Study: Observational analysis of all consecutive individuals vaccinated with IMVANEX® vaccine after a high-risk contact defined as close skin-to-skin or mucosal contact and/or indirect contact on textile or surface and/or droplets exposure defined by a contact at less than 2 meters during at least 3 hours with a PCR-confirmed Monkeypox patient.
- Most of the patients were men (91%, n=250) and men who have sex with men (88%, n=233). The vaccine was well tolerated with no severe adverse event. Among the 276 vaccinated individuals, 12 (4%) had a confirmed Monkeypox breakthrough infection with no severe infection. Ten out of 12 patients developed a Monkeypox infection in the five days following vaccination and two had a breakthrough infection at 22 and 25 days.

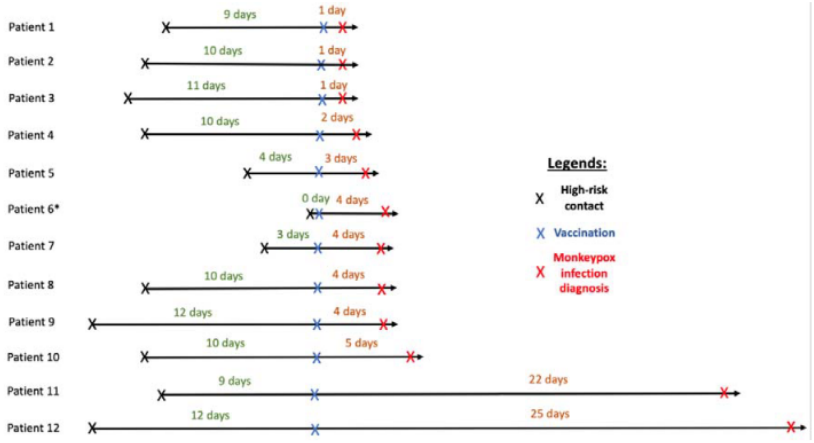
Thy M, et al. https://doi.org/10.1101/2022.08.03.22278233

Figure 1: Flow chart of early post-exposure vaccination against Monkeypox



Legends:
MPX: Monkeypox
*MPX exposure: direct skin-to-skin or mucosal contact including sexual intercourse with a -confirmed monkeypox patient, indirect contact with a confirmed monkeypox patient through fomites (textiles or surfaces) and/or droplets exposure defined by a contact at less than 2 meters during at least 3 hours with a confirmed monkeypox patient

Figure 2: Delay between exposure, vaccination and confirmed Monkeypox infection in the 12 breakthrough infections



Legend: *Patient 6: Direct inoculation with a percutaneous needlestick

Breakthrough infections after post-exposure vaccination against Monkeypox

Table 1: Main characteristics of the early post-exposure ring vaccinated population and comparison between who developed symptoms or not after vaccination

	Total	Breakthrough Monkeypox infections*
n	276	12
Age (median [IQR])	19.0 [14.0-25.0]	24.0 [15.8-26.8]
Male (%)	250 (90.6)	11 (91.7)
Born in France (%)	177 (87.2)	8 (88.9)
MSM (%)	233 (88.3)	11 (91.7)
Number of sexual partners during past month (median [IQR])	8.0 [3-13]	11.0 [4-12.5]
Number of STIs during past year (median [IQR])	1.5 [1-2]	1.5 [1-2]
Chemsex user (%)	75 (28.6)	4 (33.3)
Domestic animal (%)	57 (21.0)	2 (18.2)
Past medical history (%)	73 (26.7)	3 (25.0)
Cancer or blood disease (%)	2 (0.7)	0 (0.0)
HIV (%)	38 (13.9)	4 (33.3)
Immunodepressed (%)	3 (1.1)	0 (0.0)
Past history of STIs (%)	144 (61.5)	8 (72.7)
PreP user (%)	138 (51.3)	5 (41.7)
Past history of smallpox vaccination (%)	29 (10.5)	2 (16.7)
Symptomatic before vaccination (%)	23 (8.3)	0 (0.0)
Fever before vaccination (%)	4 (1.4)	0 (0.0)
Skin lesions before vaccination (%)	16 (5.8)	0 (0.0)
Healthcare worker (%)	30 (10.9)	2 (16.7)
Travel during past month (%)	96 (35.8)	3 (25.0)
Exposure with confirmed Monkeypox by PCR (%)	259 (98.5)	7 (100.0)
Relationship with confirmed Monkeypox (%)		
Occasionnal partner	132 (53.2)	3 (42.9)
Friend	46 (18.5)	3 (42.9)
Permanent partner	17 (6.9)	0 (0.0)
Patient	14 (5.6)	1 (14.3)
Room mate	10 (4.0)	0 (0.0)
Family	11 (4.4)	0 (0.0)
Droplets exposure (%)	240 (90.6)	11 (91.7)
Indirect exposure (%)	189 (71.1)	10 (83.3)
Unprotected sexual intercourse (%)	146 (53.7)	5 (41.7)

Legends: * confirmed with PCR
MSM: men having sex with men; STIs: sexually transmitted infections; HIV: human immunodeficiency virus; PreP : HIV pre-exposure prophylaxis

Table 2: Details of side effects and symptoms after early post-exposure ring vaccination

	Total	Breakthrough Monkeypox infections*
n	276	12
Side effects of vaccination (%)	**49 (50.0)**	**0 (0.0)**
Local pain (%)	43 (46.2)	0 (0.0)
Fatigue (%)	13 (15.5)	0 (0.0)
Delay between exposure and symptoms (median [IQR])		12.0 [9.3-15.3]
Delay between vaccination and symptoms (median [IQR])		4.0 [1.8-4.3]
Positive Monkeypox PCR (%)	**12 (54.5)**	**12 (100.0)**
Symptoms		
Fever after vaccination (%)	11 (4.7)	7 (58.3)
Body aches after vaccination (%)	4 (1.7)	2 (16.7)
Lymphadenopathy after vaccination (%)	5 (2.1)	5 (41.7)
Sore throat after vaccination (%)	6 (2.6)	5 (41.7)
Cough after vaccination (%)	1 (0.4)	1 (8.3)
Headaches after vaccination (%)	1 (0.4)	0 (0.0)
Skin lesions		
Anal lesions (%)	6 (2.6)	5 (41.7)
Rectitis (%)	3 (1.3)	2 (16.7)
Face lesions (%)	3 (1.3)	2 (16.7)
Trunk lesions (%)	6 (2.6)	4 (33.3)
Limbs lesions (%)	2 (0.9)	2 (16.7)
Genital lesions (%)	2 (0.9)	1 (8.3)
Associated STI (%)	4 (1.6)	1 (8.3)
Length of follow-up after vaccination (median [IQR])	**5.5 [1.0-20.0]**	**13.5 [5.8-19.3]**

Legends: * confirmed with PCR
STI: sexually transmitted infection

Thy M, et al. https://doi.org/10.1101/2022.08.03.22278233

MEDICAL COUNTERMEASURES: TREATMENT OPTIONS

Currently no proven, safe, and effective treatments for Monkeypox. Animal data suggests smallpox treatments could be used in severe cases.

Name	Indication	Dosing & Administration	Availability	Storage and Handling	Notes
★ TPOXX tecovirimat	FDA approved for treatment of smallpox in adults and pediatric patients weighing at least 3kg. **Expanded access protocol for monkeypox**	Oral and IV formulations Weight based dosing 14 day course of therapy	**SNS request**	Oral: 200mg capsules; 42 caps/bottle Stored at controlled room temp (>13kg) IV: 200mg/20mL vial Store refrigerated @ 2-8°C (>3kg)	TPOXX IV contraindicated in those with serve renal impairment TPOXX oral must be taken within 30 minutes after moderate/high fat meal No human data on use in pregnancy; no toxicity in animal reproductive studies
Vistide cidofovir	FDA approved for treatment of CMV retinitis in AIDS patients **Expanded access protocol for monkeypox**	5mg/kg IV once weekly x 2 weeks Must be administered with fluids and probenecid	**Commercially & SNS Request**	75 mg/mL in clear glass, single use vial Store at controlled room temperature 20-25°C	Causes severe nephrotoxicity Renal function monitored within 48 hours prior to administration No human data on use in pregnancy; embryotoxic in rats
Vaccinia Immune Globulin VIGIV CNJ-016	FDA approved for the treatment of complications associated with vaccinia vaccination **Expanded access protocol for Monkeypox**	6,000 U/kg IV x 1 dose Higher doses can be given if patient does not respond	**SNS Request**	15mL vial containing > 50,000 U/vial Product may be stored frozen at or below 5°F (≤ -15°C) or refrigerated at 36 to 46°F (2 to 8°C)	No animal or human pregnancy data; Other immune globulins used in pregnancy w/o negative effects

Note: CDC is currently developing a expanded access protocol for a fourth treatment; Tembexa (brincidovofir). However it is currently not available commercially or through SNS request

★ Denotes preferred MCM

Table 2 Summary of therapies for the management of monkeypox

Treatments	Route	Dosing	Mode of action	Common adverse events	Contraindications (US labeling)	Major drug interactions	Use in specific populations
Tecovirimat	PO, IV (approved in May 2022)	Adults: 600 mg twice daily for 14 days; pediatrics (13 kg or more), if 13 kg to less than 25 kg: 200 mg BID for 14 days, if 25 kg to less than 40 kg: 400 mg twice daily for 14 days, if 40 kg or more: 600 mg twice daily for 14 days	Orthopoxvirus VP37 envelope wrapping protein inhibitor	Headache, nausea, abdominal pain, vomiting. Infusion-site reactions may occur with IV form	None	Repaglinide (hypoglycemia), Midazolam (decreased effectiveness of midazolam) Note: Co-adminstration with repaglinide may cause hypoglycemia. Monitor blood glucose and monitor for hypoglycemic symptoms during co-administration	PO: Hepatic/renal adjustment not required. IV: should not be administered to patients with severe renal impairment
Brincidofovir	PO (tablets, oral suspension)	Adults weighing ≥ 48 kg: 200 mg once weekly for two doses; adults and pediatric patients weighing ≥10 kg to less than 48 kg: 4 mg/kg of the oral suspension once weekly for two doses; pediatrics weighing less than 10 kg, the dose is 6 mg/kg of the oral suspension once weekly for 2 doses	Phosphorylated to active metabolite, cidofovir diphosphate, which selectively inhibits orthopoxvirus DNA polymerase-mediated viral DNA synthesis	Diarrhea, nausea, vomiting, and abdominal pain	None	OATP1B1 and 1B3 inhibitors increase Brincidofovir exposure which may increase Brincidofovir -associated adverse reactions. Consider alternative medication that are not OATP1B1 or 1B3 inhibitors	Not recommended in pregnant and breast-feeding women (perform pregnancy test in women of childbearing potential before treatment). Perform liver function tests before and during treatment as brincidofovir may cause increases in serum transaminases and serum bilirubin
Cidofovir	IV	5 mg/kg once weekly for 2 weeks, followed by 5 mg/kg IV once every other week	Undergoes cellular phosphorylation, then selectively inhibits orthopoxvirus DNA polymerase-mediated viral DNA synthesis	Decreased serum bicarbonate, proteinuria, neutropenia, infection, hypotony of eye, iritis, uveitis, nephrotoxicity, fever	Hypersensitivity to cidofovir or any component of the formulation; history of clinically-severe hypersensitivity to probenecid or other sulfa-containing medications; serum creatinine > 1.5 mg/dL; CrCl ≤ 55 mL/minute; urine protein ≥ 100 mg/dL (≥ 2+ proteinuria); use with or within 7 days of nephrotoxic agents; direct intraocular injection	Probenecid, agents of nephrotoxic potential	Dose adjustment based on renal function is necessary: Serum creatinine > 1.5 mg/dL, CrCl ≤ 55 mL/minute, or urine protein ≥ 100 mg/dL (≥ 2+ proteinuria)

Rizk JG, et al
Drugs 2022;82:957-963

CDC GUIDANCE FOR TREATMENT OF MONKEYPOX: PATIENTS FOR WHOM THERAPY MAY BE INDICATGED

- Many individuals infected with monkeypox virus have a mild, self-limiting disease course in the absence of specific therapy. However, the prognosis for monkeypox depends on multiple factors such as previous vaccination status, initial health status, concurrent illnesses, and comorbidities among others. People who should be considered for treatment following consultation with CDC might include:
- People with severe disease (e.g., hemorrhagic disease, confluent lesions, sepsis, encephalitis, or other conditions requiring hospitalization)
- People who may be at high risk of severe disease:
  - People with immunocompromise (e.g., AIDS/acquired immune deficiency syndrome infection, leukemia, lymphoma, generalized malignancy, solid organ transplantation, therapy with alkylating agents, antimetabolites, radiation, tumor necrosis factor inhibitors, high-dose corticosteroids, being a recipient with hematopoietic stem cell transplant <24 months post-transplant or ≥24 months but with graft-versus-host disease or disease relapse, or having autoimmune disease with immunodeficiency as a clinical component)[1]
  - Pediatric populations, particularly patients younger than 8 years of age
  - Pregnant or breastfeeding women
  - People with a history or presence of atopic dermatitis, people with other active exfoliative skin conditions (e.g., eczema, burns, impetigo, varicella zoster virus infection, herpes simplex virus infection, severe acne, severe diaper dermatitis with extensive areas of denuded skin, psoriasis, or Darier disease [keratosis follicularis])
  - People with one or more complications (e.g., secondary bacterial skin infection; gastroenteritis with severe nausea/vomiting, diarrhea, or dehydration; bronchopneumonia; concurrent disease or other comorbidities)[4]
- People with monkeypox virus aberrant infections that include its accidental implantation in eyes, mouth, or other anatomical areas where monkeypox virus infection might constitute a special hazard (e.g., the genitals or anus)

FACTORS MITIGATING AGAINST A PANDEMIC

- Monkeypox is less infectious that current SARS-CoV-2 variants
- Only rare descriptions of transmission prior to onset of symptoms
- Easier identification than COVID-19 (i.e., rash/skin lesions usually present)
- Diagnostic tests available from CDC/State HDs and commercial labs (e.g., LabCorp, Quest, Aegis plus Mayo Clinics): test capacity ~80,000 per week by end of July – UNC Microbiology lab processing Monkeypox tests as of today
- Same PPE as currently used for COVID-19; readily available in medical facilities
- JYNNEOS vaccine available for pre- and post-exposure prophylaxis. Based on smallpox vaccine in the past, pre-exposure prophylaxis should be ~85% effective. For PEP, provide within 4 days of exposure; if given between days 4-14, may reduce sx but not prevent disease. Expected substantial expansion of dose available for PrEP (e.g., NYC, Montreal) and PEP
- FDA approved therapies available for smallpox (IND required for Monkeypox)
  - Tecovirimat Idrug of choice (PO and IV formulations available)
  - Others: Cidofovir, Brincidofovir, vaccinia immune globulin (VIGIV)
  - Consider for treatment: 1) Immunocompromised persons; 2) Children (esp. <8 years of age); 3) Pregnant or breastfeeding; 4) Persons with one or more complications (e.g., comorbidities, secondary bacterial infections, severe N/V, dehydration, pneumonia)
- Vaccine and antivirals available via CDC (strategic government stockpile)
- Concerns: Endemicity - 1) transmission to natural hosts (rodents); 2) continued human-to-human transmission

MONKEYPOX, PUBLIC MEASURES

- 1) isolate ill persons from uninfected persons; 2) practice good hand hygiene and use appropriate personal protective equipment to protect household members if ill or caring for ill persons at home (e.g., a surgical mask, long sleeves and pants, and disposable gloves); 3) use an EPA–registered disinfectant with an emerging viral pathogens claim that is found on EPA's List Q for disinfection of surfaces (https://www.epa.gov/pesticide-registration/disinfectants-emerging-viral-pathogens-evps-list-q). Patients should also avoid contact with pets and other animals while infectious, because some mammals might be susceptible to monkeypox. Persons with symptoms of monkeypox, including unexplained lesions, should contact their health care provider for an evaluation and should avoid close contact with others, including intimate or sexual contact, until they are evaluated or receive testing.
- Anyone with a rash that looks like monkeypox should talk to their healthcare provider, even if they don't think they had contact with someone who has monkeypox. People who may be at higher risk might include but are not limited to those who:
  - Had contact with someone who had a rash that looks like monkeypox or someone who was diagnosed with confirmed or probable monkeypox
  - Had skin-to-skin contact with someone in a social network experiencing monkeypox activity, this includes men who have sex with men who meet partners through an online website, digital application ("app"), or social event (e.g., a bar or party)
  - Traveled outside the US to a country with confirmed cases of monkeypox or where monkeypox activity has been ongoing
  - Had contact with a dead or live wild animal or exotic pet that exists only in Africa or used a product derived from such animals (e.g., game meat, creams, lotions, powders, etc.)

https://www.cdc.gov/mmwr/volumes/71/wr/pdfs/mm7123e1-H.pdf; https://www.cdc.gov/poxvirus/monkeypox/response/2022/index.html

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KEY LINKS

- UNC-MC Monkeypox policies and guidelines: https://uncmedicalcenter.intranet.unchealthcare.org/dept/Epidemiology/Pages/Monkeypox.aspx
- UNC-Health Monkeypox guidelines: https://unchcs.intranet.unchealthcare.org/Pages/Monkeypox.aspx
- CDC. Isolation and Prevention Practices for People with Monkeypox. https://www.cdc.gov/poxvirus/monkeypox/clinicians/isolation-procedures.html
- CDC. Clinical Recognition. https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html
- CDC. Guidance for Tecovirimat Use Under Expanded Access Investigational New Drug Protocol during 2022 U.S. Monkeypox Cases. https://www.cdc.gov/poxvirus/monkeypox/clinicians/Tecovirimat.html
- CDC. Safer Sex, Social Gatherings, and Monkeypox. https://www.cdc.gov/poxvirus/monkeypox/sexualhealth/index.html
- CDC. Clinical Considerations for Monkeypox in People Who are Pregnant or Breastfeeding. https://www.cdc.gov/poxvirus/monkeypox/clinicians/pregnancy.html
- NC DHHS Monkeypox in NC. https://epi.dph.ncdhhs.gov/cd/diseases/monkeypox.html

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