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.

<table>
<thead>
<tr>
<th>Disease</th>
<th>No. of US cases in 1990-1998</th>
<th>Bioterrorism potential</th>
<th>Infection control concern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andes virus pulmonary syndrome</td>
<td>Not reportable</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Anthrax</td>
<td>1</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>B virus infection</td>
<td>Not reportable</td>
<td>None</td>
<td>+</td>
</tr>
<tr>
<td>Hemorrhagic fever (due to filoviruses and arenaviruses)</td>
<td>Not reportable</td>
<td>+++</td>
<td>+ ++</td>
</tr>
<tr>
<td>Monkeypox</td>
<td>Not reportable</td>
<td>?</td>
<td>++</td>
</tr>
<tr>
<td>Plague</td>
<td>80</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Q fever</td>
<td>Not reportable</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Rabies</td>
<td>25</td>
<td>None</td>
<td>+</td>
</tr>
</tbody>
</table>

**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].

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

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pathogen</th>
<th>Mode(s) of transmission</th>
<th>Risk of human-to-human transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hantavirus pulmonary syndrome</td>
<td>Andes virus</td>
<td>Inhalation of host rodent feces, urine, or saliva</td>
<td>Undefined; epidemiological and molecular evidence supports hypotheses regarding person-to-person transmission</td>
</tr>
<tr>
<td>Anthrax</td>
<td>Bacillus anthracis</td>
<td>Direct contact with contaminated animal products (e.g., hides), inhalation of spores, or ingestion of contaminated food</td>
<td>Rare cases of human-to-human transmission via direct contact with cutaneous lesions; risk of infection via inhalation from contaminated clothing and/or patient items</td>
</tr>
<tr>
<td>B virus infection</td>
<td>Coronaviridae</td>
<td>Direct contact with macaques (e.g., animal bites or scratches, cage scratch, or contaminated sharp injury), direct contact with infected cell culture</td>
<td>Rare; only a single case reported following direct contact with herpesvirus lesion</td>
</tr>
<tr>
<td>Hemorrhagic fever</td>
<td>Multiple agents</td>
<td>Direct contact with potentially infective material (e.g., blood, semen, stool, or tissue)</td>
<td>High; person-to-person transmission common; nosocomial transmission frequent</td>
</tr>
</tbody>
</table>

**NOTE:** ? unknown.
a Including Ebola, Marburg, Lassa, Crimean-Congo hemorrhagic fever, Argentine hemorrhagic fever, and Bolivian hemorrhagic fever viruses.

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


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.
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.

MONKEYPOX: CLINICAL COURSE

Siegrist EA, et al. Accepted Clin Infect Dis
Skin and Soft Tissue Manifestations of Monkeypox

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

- 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).

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

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

2022 U.S. Map & Case Count

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
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

<table>
<thead>
<tr>
<th>Devolved administrations</th>
<th>Confirmed cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>England</td>
<td>2,070</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>14</td>
</tr>
<tr>
<td>Scotland</td>
<td>54</td>
</tr>
<tr>
<td>Wales</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>2,162</td>
</tr>
</tbody>
</table>

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

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

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)**

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.

- 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, 2022.

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

<table>
<thead>
<tr>
<th>R0 (median and 95% CrI)</th>
<th>Case number</th>
<th>Period</th>
<th>Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.55 (1.42, 1.73)</td>
<td>2581</td>
<td>2022.5.18-2022.7.22</td>
<td>United States</td>
</tr>
<tr>
<td>1.36 (1.24, 1.60)</td>
<td>1562</td>
<td>2022.5.19-2022.7.22</td>
<td>France</td>
</tr>
<tr>
<td>1.20 (1.17, 1.23)</td>
<td>2268</td>
<td>2022.5.19-2022.7.22</td>
<td>Germany</td>
</tr>
<tr>
<td>1.18 (1.10, 1.31)</td>
<td>3125</td>
<td>2022.5.18-2022.7.22</td>
<td>Spain</td>
</tr>
<tr>
<td>1.13 (1.10, 1.16)</td>
<td>2115</td>
<td>2022.5.6-2022.7.22</td>
<td>England</td>
</tr>
<tr>
<td>1.02 (1.00, 1.04)</td>
<td>588</td>
<td>2022.5.17-2022.7.22</td>
<td>Portugal</td>
</tr>
<tr>
<td>1.29 (1.26, 1.33)</td>
<td>16313</td>
<td>2022.5.6-2022.7.22</td>
<td>All</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Disease</th>
<th>Transmission</th>
<th>$R_0$</th>
<th>HIT[a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>Aerosol</td>
<td>12–19[28,77]</td>
<td>92–94%</td>
</tr>
<tr>
<td>Chickenpox (varicella)</td>
<td>Aerosol</td>
<td>10–12[36]</td>
<td>90–92%</td>
</tr>
<tr>
<td>Mumps</td>
<td>Respiratory droplets</td>
<td>10–12[31]</td>
<td>90–92%</td>
</tr>
<tr>
<td>COVID-19 (Omicron variant)</td>
<td>Respiratory droplets and aerosol</td>
<td>9.5[53]</td>
<td>89%</td>
</tr>
<tr>
<td>Rubella</td>
<td>Respiratory droplets</td>
<td>6–7[84]</td>
<td>83–86%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>Respiratory droplets</td>
<td>5.5[37]</td>
<td>82%</td>
</tr>
<tr>
<td>COVID-19 (Delta variant)</td>
<td>Respiratory droplets and aerosol</td>
<td>5.1[32]</td>
<td>80%</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Respiratory droplets</td>
<td>3.5–6.0[39]</td>
<td>71–83%</td>
</tr>
<tr>
<td>COVID-19 (Alpha variant)</td>
<td>Respiratory droplets and aerosol</td>
<td>4–5[40,41,42]</td>
<td>75–80%</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>Body fluids</td>
<td>2–5[41]</td>
<td>50–80%</td>
</tr>
<tr>
<td>COVID-19 (ancestral strain)</td>
<td>Respiratory droplets and aerosol[42]</td>
<td>2.9 (2.4–3.3)[43]</td>
<td>63% (50–71%)</td>
</tr>
<tr>
<td>SARS</td>
<td>Respiratory droplets</td>
<td>2–4[44]</td>
<td>50–75%</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Saliva</td>
<td>2.6 (1.7–4.3)[45]</td>
<td>62% (41–77%)</td>
</tr>
<tr>
<td>Common cold</td>
<td>Respiratory droplets</td>
<td>2–3[46] [medical citation needed]</td>
<td>50–67%</td>
</tr>
<tr>
<td>Monkeypox</td>
<td>Physical contact, body fluids, respiratory droplets</td>
<td>2.1 (1.5–2.7)[47]</td>
<td>53% (31–63%)</td>
</tr>
<tr>
<td>Influenza (1918 pandemic strain)</td>
<td>Respiratory droplets</td>
<td>2[48]</td>
<td>50%</td>
</tr>
<tr>
<td>Ebola (2014 outbreak)</td>
<td>Body fluids</td>
<td>1.8 (1.4–1.9)[49]</td>
<td>44% (31–44%)</td>
</tr>
<tr>
<td>Influenza (2009 pandemic strain)</td>
<td>Respiratory droplets</td>
<td>1.6 (1.3–2.0)[50]</td>
<td>37% (25–51%)</td>
</tr>
<tr>
<td>Influenza (seasonal strains)</td>
<td>Respiratory droplets</td>
<td>1.3 (1.2–1.4)[50]</td>
<td>23% (17–29%)</td>
</tr>
<tr>
<td>Andes hantavirus</td>
<td>Respiratory droplets and body fluids</td>
<td>1.2 (0.8–1.6)[51]</td>
<td>16% (0–36%)[c]</td>
</tr>
<tr>
<td>Nipah virus</td>
<td>Body fluids</td>
<td>0.5[52]</td>
<td>0%[c]</td>
</tr>
<tr>
<td>MERS</td>
<td>Respiratory droplets</td>
<td>0.5 (0.3–0.8)[53]</td>
<td>0%[c]</td>
</tr>
</tbody>
</table>

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**Comparing Different $R_0$ Values**

$R_0$ (pronounced “$R$-nought”) is the basic reproduction number of infectious agents. It is the average number of people every infected person will transmit the virus to, assuming a completely susceptible population. For example, if $R_0 = 2$, then one case would create two new cases, and each new case would create another two cases. The visual below illustrates this exponential growth across a few different $R_0$ values.

### Table: Comparing Different $R_0$ Values

<table>
<thead>
<tr>
<th>$R_0$ Value</th>
<th>Initial Case</th>
<th>Round 1</th>
<th>Round 2</th>
<th>Round 3</th>
<th>Round 4</th>
<th>Round 5</th>
<th>Round 6</th>
<th>Round 7</th>
<th>Round 8</th>
<th>Round 9</th>
<th>Round 10</th>
<th>Total number of new cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R_0 = 1$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>$R_0 = 1.5$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>57.47</td>
</tr>
<tr>
<td>$R_0 = 2$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1,026</td>
</tr>
<tr>
<td>$R_0 = 3$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>99,049</td>
</tr>
</tbody>
</table>

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

ABSTRACT

In 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/10.1101/2022.06.09.2276068v1.full.pdf
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.

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.

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

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
# MONKEYPOX: SKIN LESIONS

## Enanthem Through the Scab Stage

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

## Key Characteristics of Monkeypox Rash

[Image of Monkeypox Rash]

## More Monkeypox Rash Photos

[Image of Monkeypox Rash Photos]

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**Clinical Recognition | Monkeypox | Poxvirus | CDC**
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)

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 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 differentiate 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 be done 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)

ACIP, 17 June
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

<table>
<thead>
<tr>
<th>Case</th>
<th>Sample type</th>
<th>Symptoms compatible with MPX at time of sampling</th>
<th>MPXV PCR result on remnant DNA extract (Ct value)</th>
<th>MPXV PCR result on original sample (Ct value)</th>
<th>Timing of follow-up sample with respect to original sample</th>
<th>MPXV PCR result on follow-up sample (Ct value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pooled sample</td>
<td>None</td>
<td>Positive (27.63)</td>
<td>Anorectal swab: Positive (26.69); oropharyngeal swab: Negative</td>
<td>+37 days</td>
<td>Negative</td>
</tr>
<tr>
<td>2</td>
<td>Anorectal swab</td>
<td>None</td>
<td>Positive (22.15)</td>
<td>Positive (20.06)</td>
<td>+21 days</td>
<td>Negative</td>
</tr>
<tr>
<td>3</td>
<td>Anorectal swab</td>
<td>None</td>
<td>Positive (19.19)</td>
<td>Positive (17.16)</td>
<td>+24 days</td>
<td>Negative</td>
</tr>
<tr>
<td>4</td>
<td>Anorectal swab</td>
<td>Painful vesicular perianal rash</td>
<td>Positive (29.06)</td>
<td>Positive (27.38)</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Ct = cycle threshold; NA = not applicable
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

Titanji BK, et al. Open Forum Infectious Diseases 2022;21 June
Bunge EM, et al. PLOS Neglected Tropical Diseases 2022;11 February;
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

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.
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)
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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.
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\textsuperscript{1,4}
  - Eating utensils\textsuperscript{2}

- Nosocomial transmission to HCP has been reported\textsuperscript{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\textsuperscript{7}; survival in cotton may be as long as 18 months\textsuperscript{8}

- Smallpox, disinfectant susceptibility: Ethanol, isopropanol, 60-95\% ≤1min; 1\% benzalkonium Chloride ≤1min\textsuperscript{9}

- Vaccinia: Sodium hypochlorite, QAUT plus CHG inactivating virus at all concentrations tested\textsuperscript{10}


Fig. 1. Fall in log titre of variola virus with time under different environmental conditions.
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/cm$^2$) 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)

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](https://www.medrxiv.org/content/10.1101/2022.07.21.22277864v1)
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
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
• 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
Evaluating Patients for Monkeypox (5/24/2022)

Individual presents with a macular or popular rash (generalized or localized)

Close contact* with a person who received a diagnosis of confirmed or probable monkeypox within 21 days of illness onset

*Close contact defined as prolonged face-to-face contact (within a few feet), direct contact with body fluids, lesion material, or contaminated clothing or linens

NO

YES

High risk - Initiate isolation precautions including gown, gloves, eye protection, and N95 or higher-level respirator immediately.
1) Call Epi On-call to discuss (919-733-3419)
2) Collect specimens for concurrent monkeypox, syphilis, & molecular VZV/HSV testing
3) Notify BTEP (919-807-8600) if testing approved (approval is REDCap) to arrange BTEP Dash transport

Meets at least one (1) of the below epidemiologic criteria within the 21 days prior to symptom onset:
- Traveled to a country where monkeypox is endemic (central or west African countries), OR
- Is a man who has had close or intimate contact with another man (MSM)

AND

Onset of 2 of 3 below symptoms (with or without fever) within the 21 days of epi-exposure risk:
- Chills and/or sweats, OR
- New lymphadenopathy (periauricular, axillary, cervical, or inguinal)

Low risk
Work up for other more likely causes like syphilis and VZV/HSV (VZV/HSV testing should be molecular testing, not serology)

NO

YES

Moderate risk - Initiate isolation precautions including gown, gloves, eye protection, and N95 or higher-level respirator immediately.
1) Call Epi On-call to discuss (919-733-3419)
2) Rule-out more likely causes of rash (i.e. syphilis, molecular VZV/HSV testing) but collect specimens for monkeypox testing**
3) Notify BTEP (919-807-8600) if testing approved (approval is REDCap) to arrange BTEP Dash transport
**Monkeypox testing to be done if other testing is negative or rash progression w/ monkeypox

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 McLeod 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 McLeod 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 the UNC McLeod lab in which case red cap swab is sufficient for MPX and HSV and VZV testing
- Alcohol wipes
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.unccmedicalcenter.org/app/files/public/2b768a6.d854-4b5a-439c-1e133572eac4dd/pdf/mclendon-labo-memo-micro2208-jul22-2022.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 the patient lives: https://www.ncdhis.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-DHIS (state) lab**

Prior to collecting specimens:

9. Contact the NC DHIS 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 DHIS Epidemiologist On-Call, collect the specimen per the procedure below.

11. Print and complete the NC DHIS BTEP form to include with specimens (the ICD-10 for Monkeypox is B04): https://dhph.ncdhhs.gov/Forms/2010-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://unc.edu/healthcare/about/Documents/202207/July/Monkeypox_Whatyoushoulddowhileyouwaitforresults.pdf
# MEDICAL COUNTERMEASURES: VACCINE OPTIONS

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

<table>
<thead>
<tr>
<th>Name</th>
<th>Indication</th>
<th>Dosing &amp; Administration</th>
<th>Availability</th>
<th>Storage and Handling</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>JYNNEOS</strong></td>
<td>FDA approved for prevention of smallpox &amp; monkeypox in adults 18+</td>
<td>2 doses (0.5 mL each) administered 4 weeks apart. Subcutaneous injection</td>
<td>SNS request; ~ 72,000 doses in SNS and growing</td>
<td>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</td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>Individuals &lt;18 can be treated under expanded access IND.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ACAM2000</strong></td>
<td>FDA approved for smallpox prevention in adults and pediatrics &gt;1 y.o.</td>
<td>1 drop of vaccine suspension via scarification using bifurcated needle. CDC Training Videos for ACAM2000 administration</td>
<td>SNS Request; &gt; 100 Million doses in SNS</td>
<td>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).</td>
<td>Live vaccinia virus Myocarditis risk Contraindications for severe immunocompromise and peds &lt;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.</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ACAM2000*</th>
<th>JYNNEOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine virus</td>
<td>Replication-competent vaccinia virus</td>
<td>Replication-deficient modified vaccinia Ankara</td>
</tr>
<tr>
<td>“Take” following vaccination†</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Risk for inadvertent inoculation and autoinoculation</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Risk for serious adverse event</td>
<td>Myopericarditis in 5.7 per 1,000 primary vaccines</td>
<td>No significant events identified during clinical trials</td>
</tr>
<tr>
<td>Risk for cardiac adverse events</td>
<td>FDA assessed by comparing immunologic response and take rates to Dryvax*</td>
<td>Clinical trial data limited in evaluating this outcome; however, no significant events in data abstracted from single study arms³</td>
</tr>
<tr>
<td>Assessment of effectiveness</td>
<td>Percutaneously using a bifurcated needle by multiple puncture (scarification) technique, ¹, single dose</td>
<td>FDA assessed by comparing immunologic response to ACAM2000 and animal studies</td>
</tr>
<tr>
<td>Administration</td>
<td>Subcutaneously, 2 doses 28 days apart</td>
<td></td>
</tr>
</tbody>
</table>

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.
³ 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.
¹ https://www.fda.gov/media/75/92/download

Contraindication to JYNNEOS = serious vaccine component allergy
MMWR 2022;71:3 June
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 $1 \times 10^8$ 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% ($2\times10^7$ 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 $\geq 6$ 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.

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. 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).

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

<table>
<thead>
<tr>
<th>Study visit-day</th>
<th>Group</th>
<th>Lyophilized SC</th>
<th>Liquid SC</th>
<th>Liquid ID</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Serumcreation, aN (%) [95% CI]</td>
<td>GMT [95% CI]</td>
<td>GMT [95% CI]</td>
<td>GMT [95% CI]</td>
</tr>
<tr>
<td>Day 0*</td>
<td>0/145 (80.0%) [0.0, 2.5]</td>
<td>2/149 (1.3%) [0.2, 4.8]</td>
<td>2/146 (1.3%) [0.2, 4.9]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7/2 [7.4, 60]</td>
<td>7/2 [7.4, 60]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 14</td>
<td>6/145 (4.1%) [3.3, 49.8]</td>
<td>4/149 (28.5%) [22.3, 37.5]</td>
<td>5/146 (35.8%) [30.4, 46.4]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(10/55, 12.0)</td>
<td>(10/55, 11.1)</td>
<td>(10/55, 11.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1/149 (0.5%) [0.3, 4.2]</td>
<td>1/149 (0.5%) [0.3, 4.2]</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>(1/55, 0.9)</td>
<td>(1/55, 0.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 28*</td>
<td>6/145 (4.1%) [3.3, 49.8]</td>
<td>0/149 (0.0%) [0.0, 2.5]</td>
<td>6/146 (4.2%) [0.3, 5.0]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(10/55, 12.0)</td>
<td>(10/55, 11.1)</td>
<td>(10/55, 11.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0/149 (0.0%) [0.0, 2.5]</td>
<td>0/149 (0.0%) [0.0, 2.5]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1/55, 0.9)</td>
<td>(1/55, 0.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 42</td>
<td>13/145 (9.0%) [8.0, 97.6]</td>
<td>4/149 (28.5%) [22.3, 37.5]</td>
<td>13/146 (56.1%) [46.1, 65.7]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(10/55, 12.0)</td>
<td>(10/55, 11.1)</td>
<td>(10/55, 11.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3/149 (2.0%) [0.3, 4.2]</td>
<td>3/149 (2.0%) [0.3, 4.2]</td>
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<tr>
<td></td>
<td>(1/55, 0.9)</td>
<td>(1/55, 0.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 56</td>
<td>13/145 (9.0%) [8.0, 97.6]</td>
<td>11/149 (76.3%) [71.6, 85.1]</td>
<td>13/146 (56.1%) [46.1, 65.7]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(10/55, 12.0)</td>
<td>(10/55, 11.1)</td>
<td>(10/55, 11.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3/149 (2.0%) [0.3, 4.2]</td>
<td>3/149 (2.0%) [0.3, 4.2]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1/55, 0.9)</td>
<td>(1/55, 0.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 208</td>
<td>7/138 (5.8%) [4.7, 62.0]</td>
<td>1/149 (0.5%) [0.3, 4.2]</td>
<td>7/146 (4.9%) [0.3, 6.0]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(7/138, 5.8)</td>
<td>(1/149, 0.5)</td>
<td>(7/138, 5.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0/149 (0.0%) [0.0, 2.5]</td>
<td>0/149 (0.0%) [0.0, 2.5]</td>
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<tr>
<td></td>
<td>(1/55, 0.9)</td>
<td>(1/55, 0.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak post vaccination 2</td>
<td>14/145 (9.9%) [8.0, 97.6]</td>
<td>14/149 (95.3%) [90.6, 98.1]</td>
<td>13/146 (56.1%) [46.1, 65.7]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(10/55, 12.0)</td>
<td>(10/55, 11.1)</td>
<td>(10/55, 11.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1/149 (0.5%) [0.3, 4.2]</td>
<td>1/149 (0.5%) [0.3, 4.2]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1/55, 0.9)</td>
<td>(1/55, 0.9)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Half Life (days)* 69 92 77

Note: non-inferiority established. (95% CI) titer ≥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 analytic Serconcentration was defined as PINT value ≥15.
* First vaccination.
* Second vaccination.
* Based on Day 42, 56, and 208. Accuracy of these 3-point estimates was compromised as many Day 208 observations for EN-PINT were found below the lower limit of detection.

P < 0.05.
P < 0.01.
The effects of PEP smallpox vaccination on clinical disease presentation

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 orthopoxivirus) can carry a high risk of severe congenital infection, pregnancy loss, and maternal morbidity and mortality. 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. 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 pregnancy.

Figure: Clinical management algorithm for suspected monkeypox virus exposure during pregnancy

Clinical management algorithm for suspected monkeypox virus exposure during pregnancy

- Pregnant individual with suspected monkeypox exposure
  - Isolated from others in the country within 24 hours
  - Clinical contact with a confirmed case of monkeypox (i.e., living together, sexual contact, or contact with body fluids and contaminated items)
  - Exposure to unvaccinated or unvaccinated

Clinical examination (including skin, vaginal, and rectal Lauren)

- Asymptomatic
  - Monkeypox real-time PCR (molecular test) (blood, vesicular fluid, or skin can be considered)

- Symptomatic
  - Monkeypox real-time PCR (molecular test) (blood, vesicular fluid, or skin can be considered)

- Monkeypox-negative
  - Monitor for 21 days
  - No treatment
  - Clinical monitoring
  - Rule out other potential causes
  - If symptoms persist

- Monkeypox-positive
  - Isolation at home for 21 days
  - Medication
  - Clinical monitoring
  - Rule out other potential causes
  - If symptoms persist

- Ultrasonography findings
  - Growth and ultrasound of offspring scan monthly
  - Delay in medical examination of signs of hepatitis or jaundice

- Hospitalisation in a tertiary or designated centre (if clinically indicated)
  - WHO: Clinical criteria
  - MDM: CD5+, CD4+, CD8+
  - Moderate (5%–9% skin lesions)
  - Severe (10%–15% skin lesions)
  - Critical (>15% skin lesions)

- Mortality surveillance:
  - Temperature, heart rate, blood pressure
  - 3.4 (Hepatitis B, 3.4 (Hepatitis C, 3.4 (Hepatitis D, 3.4 (Hepatitis E, 3.4 (Hepatitis F, 3.4 (Hepatitis G)

- Radiological: chest X-ray, and chest CT scan

- Considered as critical if pregnant women (neonatal)

- Fetal
  - Fetal assessment (EEG) and corticosteroids for fetal termination depending on gestational age

- Recovery

- Discharged (no signs of infection)
  - On site of diagnosis
  - Exceptions: contact therapy
  - Considered as complete if no new lesions or previous lesions are resolved

- Enhanced monitoring
  - Delay in medical examination of signs of hepatitis or jaundice
  - Post-PHP monitoring

- Pregnancy
  - Early therapy of the mother
  - Enhanced monitoring in HBV
  - Monitor and report PHE of the newborn: any suspicious development of fever, rash, maculopapular rash, eczema, nystagmus, nausea, vomiting, pruritus, and jaundice

- Prevention
  - Continuous monitoring of the mother
  - Enhanced monitoring in HBV
  - Monitor and report PHE of the newborn: any suspicious development of fever, rash, maculopapular rash, eczema, nystagmus, nausea, vomiting, pruritus, and jaundice

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
## 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

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Breakthrough Monkeypox infections*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>276</td>
<td>32</td>
</tr>
<tr>
<td>Age (median [IQR])</td>
<td>19.0 [14.0–25.0]</td>
<td>24.0 [15.8–26.8]</td>
</tr>
<tr>
<td>Male (%)</td>
<td>250 (91.7)</td>
<td>11 (91.7)</td>
</tr>
<tr>
<td>MSM (%)</td>
<td>177 (62.7)</td>
<td>8 (65.6)</td>
</tr>
<tr>
<td>Number of sexual partners during past month (median [IQR])</td>
<td>8.0 [3–13]</td>
<td>13.0 [4–12.5]</td>
</tr>
<tr>
<td>Number of STIs during past year (median [IQR])</td>
<td>1.5 [0–3]</td>
<td>1.5 [0–2]</td>
</tr>
<tr>
<td>Chemsex (%)</td>
<td>75 (26.6)</td>
<td>4 (33.3)</td>
</tr>
<tr>
<td>Domestic animal (%)</td>
<td>57 (21.0)</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>Past medical history (%)</td>
<td>73 (26.7)</td>
<td>3 (25.0)</td>
</tr>
<tr>
<td>Cancer or blood disease (%)</td>
<td>7 (2.6)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>HIV (%)</td>
<td>38 (13.9)</td>
<td>4 (33.3)</td>
</tr>
<tr>
<td>Immunodeficient (%)</td>
<td>3 (1.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Past history of STIs (%)</td>
<td>144 (63.5)</td>
<td>8 (66.7)</td>
</tr>
<tr>
<td>PreP user (%)</td>
<td>128 (53.1)</td>
<td>5 (41.7)</td>
</tr>
<tr>
<td>Past history of smallpox vaccination (%)</td>
<td>89 (33.3)</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>Symptomatic before vaccination (%)</td>
<td>23 (8.6)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Fever before vaccination (%)</td>
<td>4 (1.4)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Skin lesions before vaccination (%)</td>
<td>14 (5.2)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Healthcare worker (%)</td>
<td>80 (29.5)</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>Travel during past month (%)</td>
<td>96 (35.8)</td>
<td>3 (25.0)</td>
</tr>
<tr>
<td>Exposure with confirmed Monkeypox by PCR (%)</td>
<td>259 (96.5)</td>
<td>7 (100.0)</td>
</tr>
<tr>
<td>Relationship with confirmed Monkeypox (%)</td>
<td>3 (1.3)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Occasional partner (%)</td>
<td>132 (52.5)</td>
<td>3 (24.2)</td>
</tr>
<tr>
<td>Friend (%)</td>
<td>46 (18.5)</td>
<td>3 (24.2)</td>
</tr>
<tr>
<td>Permanent partner (%)</td>
<td>17 (6.9)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Patient (%)</td>
<td>10 (4.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Room mate (%)</td>
<td>9 (3.5)</td>
<td>1 (100.0)</td>
</tr>
<tr>
<td>Family (%)</td>
<td>11 (4.4)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Indirect exposure (%)</td>
<td>3 (1.2)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Unprotected sexual intercourse (%)</td>
<td>180 (67.1)</td>
<td>10 (83.3)</td>
</tr>
<tr>
<td><strong>n</strong></td>
<td>276</td>
<td>32</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Breakthrough Monkeypox infections*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>276</td>
<td>32</td>
</tr>
<tr>
<td>Side effects of vaccination (%)</td>
<td>49 (50.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Local pain (%)</td>
<td>49 (46.7)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Fatigue (%)</td>
<td>13 (15.5)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Delay between exposure and symptoms (median [IQR])</td>
<td>12.0 [6.0–15.5]</td>
<td>4.0 [3.8–4.8]</td>
</tr>
<tr>
<td>Positive Monkeypox PCR (%)</td>
<td>12 (54.5)</td>
<td>12 (100.0)</td>
</tr>
</tbody>
</table>

### Symptoms
- Fever after vaccination (%) | 11 (4.7) | 7 (56.0) |
- 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) |
- Rectal lesions (%) | 3 (1.3) | 2 (16.7) |
- Face lesions (%) | 3 (1.3) | 2 (16.7) |
- Trunk lesions (%) | 8 (3.6) | 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 [3.0–20.0] | 13.5 [5.5–19.3]

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

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

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

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

Denotes preferred MCM
<table>
<thead>
<tr>
<th>Treatments</th>
<th>Route</th>
<th>Dosing</th>
<th>Mode of action</th>
<th>Common adverse events</th>
<th>Contraindications (US labeling)</th>
<th>Major drug interactions</th>
<th>Use in specific populations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecovirimat</td>
<td>PO, IV (approved in May 2022)</td>
<td>Adults: 600 mg twice daily for 14 days; pediatric (13 kg or more), if 13 kg in 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</td>
<td>Orthopoxvirus VP37 envelope wrapping protein inhibitor</td>
<td>Headache, nausea, abdominal pain, vomiting. Infusion-site reactions may occur with IV form</td>
<td>None</td>
<td>Repaglinide (hypoglycemia), Midazolam (decreased effectiveness of midazolam)</td>
<td>PO: Hypotensive adjustment not required. IV: should not be administered to patients with severe renal impairment</td>
</tr>
<tr>
<td>Brincidofovir</td>
<td>PO (tablets, oral suspension)</td>
<td>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</td>
<td>Phosphorylated to active metabolite, cidofivir diprophosphate, which selectively inhibits orthopoxvirus DNA polymerase-mediated viral DNA synthesis</td>
<td>Diarrhea, nausea, vomiting, and abdominal pain</td>
<td>None</td>
<td>OATP1B1 and 1B3 inhibitors increase Brincidofovir exposure which may increase Brincidofovir-associated adverse reactions.</td>
<td></td>
</tr>
<tr>
<td>Cidofovir</td>
<td>IV</td>
<td>5 mg/kg once weekly for 2 weeks, followed by 5 mg/kg IV once every other week</td>
<td>Undergoes cellular phosphorylation, then selectively inhibits orthopoxvirus DNA polymerase-mediated viral DNA synthesis</td>
<td>Decreased serum bicarbonate, proteinuria, infection, hypotony of eye, iritis, uveitis, neptotoxicity, fever</td>
<td>Hypersensitivity to cidofovir or any component of the formulation; history of clinically-severe hypersensitivity to probenecid or other sulfa-containing medications; serum creatinine &gt; 1.5 mg/dL or CrCl ≤ 55 mL/minute; urine protein &gt; 100 mg/dL (≥ 2+ proteinuria); use with or within 7 days of nephrotoxic agents; direct intracellular injection</td>
<td>Probencid, agents of nephrotoxic potential</td>
<td></td>
</tr>
</tbody>
</table>
• 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, impétigo, 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 than 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 (drug 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
KEY LINKS

- UNC-MC Monkeypox policies and guidelines: https://uncmedicalcenter.intranet.unchcare.org/dept/Epidemiology/Pages/Monkeypox.aspx
- UNC-Health Monkeypox guidelines: https://unchcs.intranet.unchcare.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. 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
THANK YOU