Monkeypox: The State of the Science

August 18, 2022
5:00 – 6:30pm ET
Victor Dzau
President
National Academy of Medicine
Georges Benjamin
Executive Director
American Public Health Association
This webinar will be recorded. The recording, a transcript, and speaker slides will be available early next week on the Monkeypox page on the APHA website. (link in chat)
Demetre Daskalakis
White House National Monkeypox Response Deputy Coordinator
Monkeypox Update

Demetre C. Daskalakis, MD, MPH
Deputy Coordinator
National Monkeypox Response
Agenda

- Monkeypox Situation Update
- Current Epidemiology
- Clinical Presentation
- Multidomain Prevention Strategies
Monkeypox Situation Update
Situation Update - 8/15/22

11,890 Total confirmed monkeypox/orthopoxvirus cases

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

For recent monkeypox case numbers see CDC Situation Summary: https://www.cdc.gov/poxvirus/monkeypox/response/2022/index.html
Current Epidemiology
Race/Ethnicity - Through August 4, 2022

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic</td>
<td>35.2%</td>
</tr>
<tr>
<td>White</td>
<td>33.3%</td>
</tr>
<tr>
<td>Black</td>
<td>27.7%</td>
</tr>
<tr>
<td>Asian</td>
<td>3.3%</td>
</tr>
<tr>
<td>Multiple races</td>
<td>0.2%</td>
</tr>
<tr>
<td>American Indian or Alaskan Native</td>
<td>0.1%</td>
</tr>
<tr>
<td>Native Hawaiian/other Pacific Islander</td>
<td>0.1%</td>
</tr>
</tbody>
</table>
Gender Identity, May 17-July 22, 2022

<table>
<thead>
<tr>
<th>Characteristic (no. with available information)</th>
<th>No. (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>1,195 (100)</td>
</tr>
<tr>
<td>Gender identity (1,195)</td>
<td></td>
</tr>
<tr>
<td>Man</td>
<td>1,178 (98.7)</td>
</tr>
<tr>
<td>Transgender man</td>
<td>3 (0.3)</td>
</tr>
<tr>
<td>Woman</td>
<td>5 (0.4)</td>
</tr>
<tr>
<td>Transgender woman</td>
<td>5 (0.4)</td>
</tr>
<tr>
<td>Prefer not to answer</td>
<td>4 (0.3)</td>
</tr>
<tr>
<td>Missing</td>
<td>0 (—)</td>
</tr>
</tbody>
</table>

Exposure History, May 17-July 22, 2022

358/1178 (30%) of men (cis and trans) provided information on recent sexual behaviors and gender of sex partners in the 3 weeks prior to presentation

– 337 (94%) reported sex or close intimate contact with a man
– Among 291 men who reported information about their male sexual partners:
  • 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 more detailed sexual histories:
  • 33 (38%) reported group sex
Other Features, May 17-July 22, 2022

- HIV status reported in 334 persons
  - 41% reported living with HIV
- Hospitalization status reported in 954 persons
  - 77 (8%) hospitalized
- Vaccination status reported in 339 persons
  - 48 (14%) reported previous smallpox vaccine
    - 11 (23%) with JYNNEOS 1 of 2 doses
    - 11 (23%) with Pre-Exposure Prophylaxis before outbreak
    - 26 (54%) did not specify
- No deaths reported
Clinical Presentation
“Classic” Monkeypox

- **Incubation period**: 5–13 days on average (range 4–17 days)
- **Prodrome**: fever, malaise, headache, weakness, and lymphadenopathy that may be generalized or localized to several areas (e.g., neck and armpit)
- **Rash**: appears shortly after prodrome starts
  - Typically lesions develop simultaneously and evolve together on any given part of the body
  - Four stages – macular, papular, vesicular, to pustular – before scabbing over and resolving
  - Well-circumscribed, deep seated with umbilication, painful
  - When disseminated tend to be centrifugal: more on arms, legs, hands, feet
  - Can involve palms and soles
- **Illness duration is typically 2–4 weeks**
“Classic” Rash Presentation

Lesions observed during 2003 U.S. monkeypox outbreak

Lesions observed in endemic countries

https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html
Monkeypox 2022

- Pattern: scattered or localized to a body site rather than diffuse
- Rash often starts in mucosal areas (e.g., genital, perianal, oral mucosa) and may not develop simultaneously in all body areas
  - **Proctitis**: anorectal pain, tenesmus, and rectal bleeding; associated with visible perianal vesicular, pustular, or ulcerative skin lesions and proctitis
  - **Oropharyngitis**: complicated by tonsillar swelling, abscess, dysphagia
- “Prodromal” symptoms can be absent or follow rash onset
Rash Presentations – 2022
Monkeypox Outbreak


Shared with permission from patients, CDC 2022
Multidomain Prevention Strategies
Harm Reduction Guidance

**Safer Sex, Social Gatherings, and Monkeypox**

Updated August 5, 2022

While CDC works to contain the current monkeypox outbreak and learn more about the virus, this information can help you make informed choices when you are in situations or places where monkeypox could be spread. Monkeypox is not considered a sexually transmitted disease, but it is often transmitted through close, sustained physical contact, which can include sexual contact.

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**How can a person lower their risk during sex?**

**Vaccination** is an important tool in preventing the spread of monkeypox. But given the current limited supply of vaccine, consider temporarily changing some behaviors that may increase your risk of being exposed. These temporary changes will help slow the spread of monkeypox until vaccine supply is adequate.

Reducing or avoiding behaviors that increase risk of monkeypox exposure is also important when you are between your first and second shots of vaccine. Your protection will be highest two weeks after your second dose of vaccine.

Make a habit of exchanging contact information with any new partner to allow for sexual health follow-up, if needed.

Talk with your partner about any **monkeypox symptoms** and be aware of any new or

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**How can a person lower the chance of getting monkeypox at places like raves, parties, clubs, and festivals?**

When thinking about what to do, seek out information from trusted sources like the local health department. Second, consider how much close, personal, skin-to-skin contact is likely to occur at the event you plan to attend. If you feel sick or have a rash, do not attend any gathering, and see a healthcare provider.

- Festivals, events, and concerts where attendees are fully clothed and unlikely to share skin-to-skin contact are safer. However, attendees should be mindful of activities (like kissing) that might spread monkeypox.
- A rave, party, or club where there is minimal clothing and where there is direct, personal, often skin-to-skin contact has some risk. Avoid any rash you see on others and consider minimizing skin-to-skin contact.
- Enclosed spaces, such as back rooms, saunas, sex clubs, or private and public sex parties where intimate, often anonymous sexual contact with multiple partners occurs, may have a higher likelihood of spreading monkeypox.
• **August 9, 2022**, FDA issued an Emergency Use Authorization after review of data supporting the use of the intradermal dose of JYNNEOS vaccine in the setting of the National Monkeypox Public Health Emergency in people ≥18.

• The intradermal dose allows a single vial of vaccine to be **used for up to 5 intradermal doses**, expanding supply of current vaccine by up to **5-fold**.
  - 200,000 vials=200,000 doses (Subcutaneous)
  - 200,000 vials= UP to 1,000,000 doses (Intradermal)

• Speed of EUA was necessary to spare doses of vaccine in the field to achieve an urgent match between supply and need for people who could benefit from vaccine.

The JYNNEOS vaccine given at the subcutaneous dose generates immune responses measured in the lab, including in those with immunocompromising conditions, that are thought to prevent monkeypox.

Reviewed data show that the JYNNEOS vaccine given at the intradermal dose generates immune responses on lab tests nearly identical to subcutaneous dosing and has a similar side effect profile to the subcutaneous route. Other intradermal vaccines have similar immune responses when compared to other dosing routes, including in immunocompromised.

Based on these data, that support equivalence of effect and similar safety profiles, intradermal dosing means that up to 5-fold more doses are available to safely vaccinate people who could benefit from the immune protection provided by the vaccine without sacrificing effectiveness as measured using similar methods.

Regardless of dose or route, vaccine surveillance and studies will measure the “real world” effectiveness and safety of the vaccine in the setting of an unprecedented monkeypox outbreak.

August 9th EUA Logic
Thank you
Prevention and Treatment of Monkeypox

Boghuma K. Titanji, MD MSc DTM&H PhD
Assistant Professor of Medicine
Emory University
Pre-exposure prevention – Vaccines

- Infection with an orthopoxvirus or immunization with an orthopoxvirus vaccine lends immunologic cross-protection against other viruses in the genus.
Vaccines – Live inactivated virus

- Replication deficient vaccinia virus strain.
- JYNNEOS licensed in the US for prevention of smallpox and monkeypox since 2019.
- Effectiveness inferred from animal challenge studies and immunogenicity studies in humans.
- 2-doses administered subcutaneously 28 days apart.
Vaccines – Live inactivated virus

• Correlates of protection against monkeypox are not known.

• Intradermal administration of 1/5 dose yields comparable antibody responses to SC dosing.

• Limited doses globally. Vaccination currently mainly in high risk groups in Europe and N. America.
Vaccines – Replication competent virus

• Replication competent vaccinia virus.
• ACAM2000 licensed in the US for prevention of smallpox.
• Higher risk for severe adverse reactions – progressive vaccinia, myocarditis, eczema vaccinatum.
Vaccines – Special considerations

• Post-exposure prophylaxis – ideally within 4 days of a high risk exposure for monkeypox.

• Inactivated vaccines safe for use in immunocompromised persons.

• Insufficient data for safety of inactivated vaccines in pregnant persons.

• Currently vaccines are licensed in individuals >18 years old. JYNNEOS can be used in pediatric populations under EA-IND protocols.

• Replication competent vaccines contra-indicated for ALL immunocompromised persons.
Vaccines - Outstanding Questions

• How effective are these vaccines against monkeypox?
• How durable is the immunity they confer?
• Will boosters be needed? If yes how soon?
• What are the correlates of protection?
• What is the impact of different dosing strategies and routes of administration on efficacy?
• What is the impact of vaccination as post-exposure prophylaxis?
• What about vaccine responses in special groups – pregnancy, pediatric, immunocompromised individuals?
Antiviral treatments - Tecovirimat

- Targets a gene which encodes for virus membrane protein p37 and impacts formation of extra-cellular enveloped virus.
- Efficacy against monkeypox demonstrated in animal models.
- Good safety profile in human studies (Phase I and II).
- Paucity of randomized trials for efficacy in humans.
Antivirals - Brincidofovir and Cidofovovir

- Inhibit virus DNA synthesis.
- Both have *in-vitro* antiviral activity against orthopox viruses.
- Animal models support efficacy against orthopox virus infection.
- Data in humans limited to case reports, true efficacy remain uncertain.
- Unfavorable adverse effects profile.
Antiviral therapy – Outstanding Questions

• How effective are these antiviral medications against monkeypox in humans?
• Is there a role for combination therapy in severe disease?
• Is development of antiviral drug resistance a concern?
• What about antivirals as pre-exposure and post exposure prophylaxis?
Warning: Graphic Images on next slide!!!
Adjunctive therapies

- Skin protectants e.g. Petroleum jelly, Sarna for itching, Calamine lotion.
- Proctitis – lidocaine based preparations, topical anti-inflammatory agents e.g. mesalamine suppositories.
- Perineal lesions – Sitz baths
- Systemic analgesics – Opioids
- Engage the assistance of dermatologists early.

Monkeypox lesions are painful. Managing this pain is an important part of treatment.
David Heymann
Professor of Infectious Disease Epidemiology
London School of Hygiene & Tropical Medicine
## Orthopox viruses and susceptible hosts

<table>
<thead>
<tr>
<th>Virus</th>
<th>Infections in</th>
<th>Spectrum of hosts</th>
<th>Natural host</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variola (VARV)</td>
<td>human</td>
<td>narrow</td>
<td>human</td>
</tr>
<tr>
<td>Vaccinia (VACV)</td>
<td>human, buffalo, cattle, elephant, pig, rabbit, etc.</td>
<td>broad</td>
<td>unknown</td>
</tr>
<tr>
<td>VACV-like Brazilian isolates (BRZ-VACV)</td>
<td>human, cattle, rodent</td>
<td>broad</td>
<td>rodent</td>
</tr>
<tr>
<td>Buffalopox (BPXV-VACV)</td>
<td>buffalo, cattle, human</td>
<td>broad</td>
<td></td>
</tr>
<tr>
<td>Rabbitpox (RPV-VACV)</td>
<td>rabbits in breeding establishments</td>
<td>broad</td>
<td></td>
</tr>
<tr>
<td>Monkeypox (MPXV)</td>
<td>human, ape, monkey, rodent, prairie dog, etc.</td>
<td>broad</td>
<td>rodent, sciuridae</td>
</tr>
<tr>
<td>Cowpox (CPXV)</td>
<td>human, cat, cattle, elephant, rodent, rhinoceros, etc.</td>
<td>broad</td>
<td>rodent</td>
</tr>
<tr>
<td>Camelpox* (GMLV)</td>
<td>camel</td>
<td>narrow</td>
<td>unknown</td>
</tr>
<tr>
<td>Ectromelia (ECTV)</td>
<td>mouse, laboratory mouse</td>
<td>narrow</td>
<td>vole?</td>
</tr>
<tr>
<td>Raccoonpox</td>
<td>racoon</td>
<td>broad</td>
<td>unknown</td>
</tr>
<tr>
<td>Volepox</td>
<td>vole, pinon mouse</td>
<td>narrow</td>
<td>vole</td>
</tr>
<tr>
<td>Uasin-Gisha pox</td>
<td>horse</td>
<td>medium (?)</td>
<td>unknown</td>
</tr>
<tr>
<td>Taterapox</td>
<td>tatera kempi (gerbil)</td>
<td>narrow</td>
<td>gerbil?</td>
</tr>
</tbody>
</table>

*Camelpox viruses show a very close relationship to VARV. Infections with camelpox virus in humans, however, have not been observed [133].

[Orthopox Viruses: Infections in Humans - PMC (nih.gov)]
Variola major: smallpox

- Droplet transmission face to face, direct contact
- Every infection clinically expressed in same manner
- 20% - 40% case fatality rate
- 100% permanent facial scarring
- 2.7 million deaths 1967

Fenne F, et al.. Smallpox and its Eradication. World Health Organization
Smallpox: factors that favoured eradication

- Every infection symptomatic and clinically expressed in the same manner
- Permanent protective immunity against future infection after recovery
- Thermostable vaccine that produced lifelong protection against infection, and modified the course of illness if given within 4 days of infection
- No animal reservoir

Fenner F et al. Smallpox and its Eradication. World Health Organization
Human monkeypox 1970: identification of a new infection in humans

World Health Organization photo library
Human monkeypox 1958 – 1979: Congo basin clade

First identified: captive (laboratory) monkeys, 1958, Copenhagen
Case investigations 1970 – 1979:
- sporadic West and Central Africa (n=48)
- 72% of cases animal contact
- 3 generations transmission maximum, occurred in 8% of outbreaks
- case fatality 10%, some facial scarring
- primary cases rare over 15 years of age
- most secondary/tertiary infections in unvaccinated parent or sibling

1980: is human monkeypox a threat to smallpox eradication?

- Smallpox vaccination discontinued with certification
- Presumed reservoir of virus in nature: rodents/monkeys in tropical rainforests, West and Central Africa
- Sporadic breaches in species barrier between rodents and humans
- Secondary and tertiary cases appeared to occur in unvaccinated contacts

Concern: as residual herd immunity from smallpox vaccination decreases, will human monkeypox fill the epidemiological niche left by smallpox and become endemic?
Is human monkeypox epidemiology changing as smallpox herd immunity continues to wane?

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>% infections &gt; 15 years</td>
<td>Rare</td>
<td>85%</td>
</tr>
<tr>
<td>Index case with animal contact</td>
<td>72%</td>
<td>23%</td>
</tr>
<tr>
<td>Transmission chains (generations)</td>
<td>3 generations from 8% of index cases</td>
<td>9 generations from 16% of index cases</td>
</tr>
<tr>
<td>Case fatality rate</td>
<td>10%</td>
<td>10%</td>
</tr>
</tbody>
</table>

**Conclusion:** intensified surveillance must continue
Confirmed, probable and/or possible human monkeypox cases 2000-2009

The changing epidemiology of human monkeypox—A potential threat? A systematic review - PMC (nih.gov)
Changing epidemiology of human monkeypox, 2009

**Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo**

Anne W. Rimoin,ab1 Prime M. Mulembakani,c Sara C. Johnston,d James O. Lloyd Smith,be Neville K. Kisalu,f Timothee L. Kinkela,c Seth Blumberg,be Henri A. Thomassen,g Brian L. Pike,h Joseph N. Fair,h Nathan D. Wolfe,h Robert L. Shongo,i Barney S. Graham,j Pierre Formenty,k Emile Okitolonda,c Lisa E. Hensley,d Hermann Meyer,l Linda L. Wright,m and Jean-Jacques Muyemben

- Comparison of active surveillance data in the same health zone from the 1980s (0.72 per 10,000) and 2006–07 (14.42 per 10,000) suggests a 20-fold increase in human monkeypox incidence.
- Vaccinated persons had a 5.21-fold lower risk of monkeypox as compared with unvaccinated persons (0.78 vs. 4.05 per 10,000)
- Improved surveillance and epidemiological analysis is needed to better assess the public health burden and develop strategies for reducing the risk of wider spread of infection.

Confirmed, probable and/or possible human monkeypox cases 2010-2019
## Cases per clade, human monkeypox, 1970 - 2019

<table>
<thead>
<tr>
<th>Decade</th>
<th>Central African Clade (N)</th>
<th>West African Clade (N)</th>
<th>Total Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1970–1979</td>
<td>38</td>
<td>9</td>
<td>47</td>
</tr>
<tr>
<td>1980–1989</td>
<td>355</td>
<td>1</td>
<td>356</td>
</tr>
<tr>
<td>1990–1999</td>
<td>520</td>
<td>0</td>
<td>520</td>
</tr>
<tr>
<td>2000–2009</td>
<td>92 confirmed</td>
<td>47</td>
<td>139</td>
</tr>
<tr>
<td></td>
<td>10,027 suspected²</td>
<td></td>
<td>10,027</td>
</tr>
<tr>
<td>2009–2019</td>
<td>85 confirmed</td>
<td>195</td>
<td>280</td>
</tr>
<tr>
<td></td>
<td>18,788 suspected²</td>
<td></td>
<td>18,788</td>
</tr>
</tbody>
</table>

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1. The changing epidemiology of human monkeypox—A potential threat? A systematic review - PMC (nih.gov)
Case fatality rate, human monkeypox by clade

Pooled case fatality rate in confirmed, probable, and/or possible monkeypox cases.

<table>
<thead>
<tr>
<th>Countries/Clade</th>
<th>Case Fatality Rate</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All countries</td>
<td>78/892 = 8.7%</td>
<td>7.0%–10.8%</td>
</tr>
<tr>
<td>Central African clade</td>
<td>68/640 = 10.6%</td>
<td>8.4%–13.3%</td>
</tr>
<tr>
<td>West African clade</td>
<td>9/247 = 3.6%</td>
<td>1.7%–6.8%</td>
</tr>
<tr>
<td>West African clade, African countries only</td>
<td>9/195 = 4.6%</td>
<td>2.1%–8.6%</td>
</tr>
</tbody>
</table>

The changing epidemiology of human monkeypox—A potential threat? A systematic review - PMC (nih.gov)
Suspect and confirmed human monkeypox infections, 1970-2019

Will human monkeypox replace the epidemiological niche left by smallpox?
Human monkeypox: questions remain

- Is every infection symptomatic and clinically expressed in the same manner?
- Is there permanent protective immunity against future infection after recovery?
- Does infection cause more severe illness in those who are immunocompromised?
- Does vaccine modify disease if provided within four days of infection?
- Does the current smallpox vaccine produce lifelong protection against infection?
- What is the animal reservoir?

Source: WHO
Emily Erbelding
Director
Division of Microbiology and Infectious Diseases
National Institute of Allergy and Infectious Diseases
Thank you for attending!