MONKEYPOX: UPDATE ON CURRENT OUTBREAK; FOCUS ON INFECTION PREVENTION

David J. Weber, MD, MPH, FIDSA, FSHEA, FRSM (London)
Sanders Distinguished Professor of Medicine, Pediatrics and Epidemiology
Associate Chief Medical Officer
Medical Director, Hospital Epidemiology

Disclosures: Consultancy; Pfizer, Merck, Sanofi, PDI, Germitec, Wellair
Thanks to Dr. David Henderson for some slides
All drugs/vaccines issues discussed consistent with FDA approvals or authorizations
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
INTERACTIONS AMONG HUMANS, DISEASE VECTORS AND THE ENVIRONMENT THAT CONTRIBUTE TO DISEASE EMERGENCE

**Emergence factors**
- Adaptation
- Mutation
- Variation
- Selective pressure
- Zoonotic pool

**Zoonotic hosts**

**Disease manifestation**

**Spread of infection**

**Emergence factors**
- Economic development and land use

**Microbial population**

**Vectors**

**Human**

**Emergence factors**
- Demographics
- Travel
- Behavior
- Infrastructure breakdown
- Technology
- Commerce
- Industry

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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
- 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): ~10% (unvaccinated)
MONKEYPOX IN THE US, HISTORY

• 2003 outbreak from imported mammals: In 2003, forty-seven confirmed and probable cases of monkeypox were reported from six states—Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin. All people infected with monkeypox in this outbreak became ill after having contact with pet prairie dogs. The pets were infected after being housed near imported small mammals from Ghana. This was the first time that human monkeypox was reported outside of Africa.
  • Case-control study to evaluate risk factors for acquisition revealed (after adjustment for smallpox vaccination): case-patients were more likely than controls to have had daily exposure to a sick animal (odds ratio [OR] 4.0, 95% confidence interval [CI] 1.2–13.4), cleaned cages and bedding of a sick animal (OR 5.3, 95% CI 1.4–20.7), or touched a sick animal (OR 4.0, 95% CI 1.2–13.4).

• July 2021 travel-associated case: CDC and the Texas Department of State Health Services confirmed on July 15, 2021 a case of human monkeypox in a U.S. citizen who traveled from Nigeria to the United States on two commercial flights. CDC supported state and local health officials to identify more than 200 people who had possible contact with the patient. Contacts were asked to monitor their health for 21 days. In early September, 21 days had passed without additional cases identified, and the monitoring period for the remaining contacts ended.

• November 2021 travel-associated case: CDC and the Maryland Department of Health confirmed on November 16, 2021 a case of monkeypox in a U.S. resident who recently returned from Nigeria to the United States.

https://www.cdc.gov/poxvirus/monkeypox/outbreak/us-outbreaks.html; Reynolds MG, et al. EID 2007;13:1332
CURRENT OUTBREAK

- Monkeypox is endemic in multiple African countries; during 2022, cases in Africa have been reported in Cameroon, Central African Republic, the Democratic Republic of the Congo, Nigeria and the Republic of the Congo.
  - Cases have been increasing since smallpox was declared eradicated in 1980 and that increase has accelerated over the past decade, likely due to a decline in smallpox vaccine induced immunity (80% coverage 40 years ago, 30% at present)
  - In the past 5 years, scientists have confirmed only 8 cases where travelers carried monkeypox to countries outside Africa, including 2 cases last year in the US. Each was linked to a person who had recently spent time in Nigeria, a country that experienced a resurgence in monkeypox starting in 2017.

- Since May 18, multiple cases have been confirmed in the world, most among patients with no travel history. The majority of cases have been in young men who have sex with men (MSM), who have presented to either primary care or sexual health clinics.

- Genome sequencing results from virus recovered from the patient in Massachusetts display similarities to other published genomes in this outbreak from Europe (Nextstrain/monkeypox) and are related to the 2017–2018 monkeypox outbreak in Nigeria.

Table 2. Cases of monkeypox in endemic countries between 16 December 2021 to 1 May 2022

<table>
<thead>
<tr>
<th>Country</th>
<th>Time period</th>
<th>Cumulative cases</th>
<th>Cumulative deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cameroon</td>
<td>15 December 2021 to 22 February 2022</td>
<td>25</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Central African Republic</td>
<td>4 March to 10 April 2022</td>
<td>6</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Democratic Republic of the Congo</td>
<td>1 January to 1 May 2022</td>
<td>1238</td>
<td>57</td>
</tr>
<tr>
<td>Nigeria</td>
<td>1 January 2022 to 30 April 2022</td>
<td>46</td>
<td>0</td>
</tr>
</tbody>
</table>

Covey E. IDSA Infect Dis Special Edition, 2 June 2022; Harris E. JAMA 2022;27 May; WHO: https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON385
https://www.cdc.gov/mmwr/volumes/71/wr/pdfs/mm7123e1-H.pdf
Clinical features and management of human monkeypox: A retrospective observational study in the UK

• Background: To describe the longitudinal clinical course of monkeypox in a high-income setting, coupled with viral dynamics, and any adverse events related to novel antiviral therapies

• Methods: Retrospective observational study, we report the clinical features, longitudinal virological findings, and response to off-label antivirals in seven patients with monkeypox who were diagnosed in the UK between 2018 and 2021

• Results: Three acquired monkeypox in the UK: one patient was a healthcare worker who acquired the virus nosocomially, and one patient who acquired the virus abroad transmitted it to an adult and child within their household cluster. Notable disease features included viraemia, prolonged monkeypox virus DNA detection in upper respiratory tract swabs, reactive low mood, and one patient had a monkeypox virus PCR-positive deep tissue abscess. Five patients spent more than 3 weeks (range 22–39 days) in isolation due to prolonged PCR positivity. Three patients were treated with brincidofovir (200 mg once a week orally), all of whom developed elevated liver enzymes resulting in cessation of therapy. One patient was treated with tecovirimat (200mg twice daily for 2 weeks orally), experienced no adverse effects, and had a shorter duration of viral shedding and illness (10 days hospitalisation) compared with the other six patients. One patient experienced a mild relapse 6 weeks after hospital discharge.

Skin and Soft Tissue Manifestations of Monkeypox

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)

2022 Monkeypox and Orthopoxvirus Outbreak Global Map

Data as of 10 Jun 2022 5:00 PM EDT

<table>
<thead>
<tr>
<th>Country</th>
<th>Total Confirmed Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td>396</td>
</tr>
<tr>
<td>Spain</td>
<td>275</td>
</tr>
<tr>
<td>Portugal</td>
<td>200</td>
</tr>
<tr>
<td>Germany</td>
<td>165</td>
</tr>
<tr>
<td>Canada</td>
<td>116</td>
</tr>
<tr>
<td>France</td>
<td>91</td>
</tr>
<tr>
<td>Netherlands</td>
<td>60</td>
</tr>
<tr>
<td>United States</td>
<td>48</td>
</tr>
<tr>
<td>Italy</td>
<td>29</td>
</tr>
<tr>
<td>Belgium</td>
<td>24</td>
</tr>
<tr>
<td>Switzerland</td>
<td>14</td>
</tr>
<tr>
<td>United Arab Emirates</td>
<td>13</td>
</tr>
<tr>
<td>Ireland</td>
<td>9</td>
</tr>
<tr>
<td>Australia</td>
<td>0</td>
</tr>
<tr>
<td>Czechia</td>
<td>6</td>
</tr>
<tr>
<td>Slovenia</td>
<td>5</td>
</tr>
<tr>
<td>Sweden</td>
<td>4</td>
</tr>
<tr>
<td>Denmark</td>
<td>4</td>
</tr>
<tr>
<td>Israel</td>
<td>4</td>
</tr>
<tr>
<td>Finland</td>
<td>3</td>
</tr>
<tr>
<td>Argentina</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>1472</td>
</tr>
</tbody>
</table>

Notes: Numbers shown are sourced from publicly available official sources, such as the WHO, European CDC, US CDC, and Ministries of Health. Data are provided for situational awareness only and are subject to change.

https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html
2022 Monkeypox and Orthopoxvirus Outbreak US Map

https://www.cdc.gov/poxvirus/monkeypox/response/2022/index.html
### MONKEYPOX SYMPTOMS, US, 2003 and 2022 OUTBREAKS

<table>
<thead>
<tr>
<th>Symptoms postexposure</th>
<th>No. (%)</th>
<th>2003</th>
<th>2022</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>205 (93.3)</td>
<td>2 (66.7)</td>
<td>4 (14.3)</td>
<td>270</td>
</tr>
<tr>
<td>Rash</td>
<td>30 (100)</td>
<td>1 (33.3)</td>
<td>7 (25.0)</td>
<td>38</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>20 (66.7)</td>
<td>1 (33.3)</td>
<td>4 (14.3)</td>
<td>25</td>
</tr>
<tr>
<td>Mouth sores</td>
<td>8 (26.7)</td>
<td>0</td>
<td>1 (3.6)</td>
<td>9</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>4 (13.3)</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Cough</td>
<td>17 (56.7)</td>
<td>0</td>
<td>2 (7.1)</td>
<td>19</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>50</td>
<td>3</td>
<td>28</td>
<td></td>
</tr>
</tbody>
</table>

### TABLE 2. Clinical characteristics of patients with confirmed orthopoxvirus and monkeypox (N = 17) — United States, May 2022

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
<th>At illness onset</th>
<th>Prodromal period†</th>
<th>At any point in illness</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Signs and symptoms§ during illness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>5 (29)</td>
<td>NA</td>
<td>17 (100)</td>
<td></td>
</tr>
<tr>
<td>Fatigue or malaise</td>
<td>3 (18)</td>
<td>13 (76)</td>
<td>12 (71)</td>
<td></td>
</tr>
<tr>
<td>Chills</td>
<td>0 (—)</td>
<td>4 (24)</td>
<td>12 (71)</td>
<td></td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>0 (—)</td>
<td>1 (6)</td>
<td>9 (53)</td>
<td></td>
</tr>
<tr>
<td>Inguinal</td>
<td>0 (—)</td>
<td>0 (—)</td>
<td>6 (35)</td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>0 (—)</td>
<td>1 (6)</td>
<td>3 (18)</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>2 (12)</td>
<td>5 (29)</td>
<td>8 (47)</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>6 (35)</td>
<td>5 (29)</td>
<td>7 (41)</td>
<td></td>
</tr>
<tr>
<td>Body ache</td>
<td>1 (6)</td>
<td>2 (12)</td>
<td>6 (35)</td>
<td></td>
</tr>
<tr>
<td>Sore throat or cough</td>
<td>2 (12)</td>
<td>3 (18)</td>
<td>5 (29)</td>
<td></td>
</tr>
<tr>
<td>Sweat</td>
<td>1 (6)</td>
<td>2 (12)</td>
<td>4 (24)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3 (18)</td>
<td>4 (24)</td>
<td>13 (76)</td>
<td></td>
</tr>
<tr>
<td><strong>Rash locations§</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm</td>
<td>4 (24)</td>
<td>NA</td>
<td>9 (53)</td>
<td></td>
</tr>
<tr>
<td>Trunk</td>
<td>1 (6)</td>
<td>NA</td>
<td>9 (53)</td>
<td></td>
</tr>
<tr>
<td>Leg</td>
<td>0 (—)</td>
<td>NA</td>
<td>8 (47)</td>
<td></td>
</tr>
<tr>
<td>Face</td>
<td>2 (12)</td>
<td>NA</td>
<td>7 (41)</td>
<td></td>
</tr>
<tr>
<td>Hand</td>
<td>1 (6)</td>
<td>NA</td>
<td>6 (35)</td>
<td></td>
</tr>
<tr>
<td>Perianal</td>
<td>5 (29)</td>
<td>NA</td>
<td>6 (35)</td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td>0 (—)</td>
<td>NA</td>
<td>9 (53)</td>
<td></td>
</tr>
<tr>
<td>Neck</td>
<td>1 (6)</td>
<td>NA</td>
<td>5 (29)</td>
<td></td>
</tr>
<tr>
<td>Genital (penis or vagina)</td>
<td>4 (24)</td>
<td>NA</td>
<td>4 (24)</td>
<td></td>
</tr>
<tr>
<td>Feet</td>
<td>1 (6)</td>
<td>NA</td>
<td>4 (24)</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations**: NA = not applicable.

* Data final through May 31, 2022; 11:59 p.m. EDT.
† Any symptoms before rash onset. The development of initial symptoms (eg, fever, malaise, headache, and weakness) marks the beginning of the prodromal period.
§ Multiple response options possible per patient.

<table>
<thead>
<tr>
<th>Clinical and laboratory classification</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Suspected</strong></td>
<td>New characteristic rash* OR Meets one of the epidemiologic criteria and has high clinical suspicion† for monkeypox</td>
</tr>
<tr>
<td><strong>Probable</strong></td>
<td>No suspicion of other recent orthopoxvirus exposure (e.g., <em>Vaccinia virus</em> in ACAM2000 vaccination) AND demonstration of the presence of: Orthopoxvirus DNA by polymerase chain reaction testing of a clinical specimen OR Orthopoxvirus using immunohistochemical or electron microscopy testing methods Demonstration of detectable levels of antiotheropoxvirus IgM antibody during the period of 4–56 days after rash onset</td>
</tr>
<tr>
<td><strong>Confirmed</strong></td>
<td>Demonstration of the presence of <em>Monkeypox virus</em> DNA by polymerase chain reaction testing or next-generation sequencing of a clinical specimen OR Isolation of <em>Monkeypox virus</em> in culture from a clinical specimen</td>
</tr>
</tbody>
</table>

**Epidemiologic classification**

Within 21 days of illness onset

Reports having contact with a person or persons with a similar appearing rash or received a diagnosis of confirmed or probable monkeypox OR
Had close or intimate in-person contact with persons in a social network experiencing monkeypox activity, including MSM who meet partners through an online website, digital app, or social event (e.g., a bar or party) OR
Traveled outside the United States to a country with confirmed cases of monkeypox or where *Monkeypox virus* is endemic OR
Had contact with a dead or live wild animal or exotic pet that is an African endemic species, or used a product derived from such animals (e.g., game meat, creams, lotions, or powders)

**Exclusions**

A case might be excluded as a suspect, probable or confirmed case if:

An alternative diagnosis* can fully explain the illness OR
A person with symptoms consistent with monkeypox does not develop a rash within 5 days of illness onset OR
A case where high-quality specimens do not demonstrate the presence of *Orthopoxvirus* OR *Monkeypox virus* or antibodies to *Orthopoxvirus*

**Abbreviations:** IgM = Immunoglobulin M; MSM = men who have sex with men.

* The characteristic rash associated with monkeypox lesions involve the following: deep-seated and well-circumscribed lesions, often with central umbilication; and lesion progression through specific sequential stages: macules, papules, vesicles, pustules, and scabs. The rash can sometimes be confused with other diseases that are more commonly encountered in clinical practice (e.g., secondary syphilis, herpes, and *Varicella zoster*). Historically, sporadic accounts of patients co-infected with *Monkeypox virus* and other infectious agents (e.g., *Varicella zoster* or syphilis) have been reported, therefore patients with a characteristic rash should be considered to receive testing, even if other test results are positive.

† Clinical suspicion can exist if initial signs and symptoms are consistent with illnesses confused with monkeypox (e.g., secondary syphilis, herpes, and *Varicella zoster*).

https://www.cdc.gov/mmwr/volumes/71/wr/pdfs/mm7123e1-H.pdf
CLASSIC MONKEYPOX COMPARED WITH CURRENT OUTBREAK

Clinical presentation: Classical

- Usually, prodromal, or early, symptoms develop 1 to 2 weeks after a person is infected with the monkeypox virus and can include fever, chills, and swollen lymph nodes, according to the CDC. A few days later, a rash develops. Monkeypox lesions then progress through several stages from blister-like lesions to scabs, each lasting 1 to 2 days. After their lesion scabs fall off to reveal healthy tissue underneath, which usually takes 2 to 4 weeks after symptom onset, the individual is no longer infectious.

Clinical presentation: Current outbreak (altered presentation)

- In these new cases, what we’re hearing is that those prodromal symptoms might be really mild or absent. In the current cases including the one confirmed in Massachusetts on May 18—the rash has started instead in the genital or perianal region before spreading to the person’s extremities. Some patients have presented with proctitis, or inflammation of the rectum.

Epidemiology: Classical

- Almost cases have occurred in endemic African countries. Occasional non-African cases in travelers from Africa with occasional secondary transmission

- 2003 US outbreak (71 cases) in 6 Midwestern states – outbreak traced to Gambian pouched rats imported into the US - the rats were shipped from TX to an IL distributor, who housed them with prairie dogs. No deaths were reported. No human-to-human transmission was found. All cases involved direct contact with infected prairie dogs

Epidemiology: Current outbreak

- Multiple countries and continents involved; substantial number of cases

- Many cases acquired outside of Africa – many cases without known source

- Likely sexual transmission in a number of cases
MONKEYPOX: ROUTES OF TRANSMISSION

- Animal-to-human via bite/scratch, direct contact, and direct contact (cleaning cages, animal products)
- Human-to-human
  - Respiratory (droplet transmission) – prolonged face-to-face contact (no data regarding risk from patients with pneumonia)
  - Direct contact (mucosal) 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 (transpacental)
- Mortality: The case fatality rate for the Central African clade is 10.6% versus 3.6% for the West African clade
  - Likely an overestimate (biased by severity)
  - Currently outbreak expected mortality <1%; highest risk immunocompromised, pregnant women, young children

Bunge EM, et al. PLOS Neglected Tropical Diseases 2022:11 February;
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
  - Eating utensils
- Nosocomial transmission to HCP has been reported
- 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; survival in cotton may be as long as 18 months
- Smallpox, disinfectant susceptibility: Ethanol, isopropanol, 60-95% ≤1min; 1% benzalkonium Chloride ≤1min
- Vaccinia: Sodium hypochlorite, QAUT plus CHG inactivating virus at all concentrations tested

# Key Orthopox Viruses: Clinical Characteristics

McCollum AM, Damon IK. CID 2014;58:260

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Smallpox</th>
<th>Monkeypox</th>
<th>Varicella</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incubation period</td>
<td>7–17 d</td>
<td>7–17 d</td>
<td>10–21 d</td>
</tr>
<tr>
<td>Prodromal period</td>
<td>1–4 d</td>
<td>1–4 d</td>
<td>0–2 d</td>
</tr>
<tr>
<td>Rash period (from appearance of lesions to desquamation)</td>
<td>14–28 d</td>
<td>14–28 d</td>
<td>10–21 d</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prodromal fever</td>
<td>Yes</td>
<td>Yes</td>
<td>Uncommon, mild fever if present</td>
</tr>
<tr>
<td>Fever</td>
<td>Yes, often &gt;40°C</td>
<td>Yes, often between 38.5°C and 40.5°C</td>
<td>Yes, up to 38.8°C</td>
</tr>
<tr>
<td>Malaise</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Headache</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Lesions on palms or soles</td>
<td>Yes</td>
<td>Yes</td>
<td>Rare</td>
</tr>
<tr>
<td>Lesion distribution</td>
<td>Centrifugal</td>
<td>Centrifugal</td>
<td>Centrifugal</td>
</tr>
<tr>
<td>Lesion appearance</td>
<td>Hard and deep, well-circumscribed, umbilicated</td>
<td>Hard and deep, well-circumscribed, umbilicated</td>
<td>Superficial, irregular borders, “dew drop on a rose petal”</td>
</tr>
<tr>
<td>Lesion progression</td>
<td>Lesions are often in one stage of development on the body; slow progression with each stage lasting 1–2 d</td>
<td>Lesions are often in one stage of development on the body; slow progression with each stage lasting 1–2 d</td>
<td>Lesions are often in multiple stages of development on the body; fast progression</td>
</tr>
</tbody>
</table>

* Differences in the appearance of rash have been noted in vaccinated (vaccination <20 years prior to illness) vs unvaccinated individuals. Vaccinated individuals were noted to have fewer lesions, smaller lesions, and better presentation of regional monomorphism and centrifugal distribution of rash.
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
UNC MEDICAL CENTER MONKEYPOX MANAGEMENT PLANS

• Inpatient management
• ED management
• Personal protective equipment; donning and doffing
• Waste management
OCCUPATIONAL HEALTH / TESTING

- Risk assessment for exposed persons – work closely with public health, occupational health
  https://www.cdc.gov/poxvirus/monkeypox/clinicians/monitoring.html
  - High – unprotected contact with skin/mucous membranes, lesion, or body fluids
  - Intermediate - ≤6 ft of unmasked patient for ≥3 hours without at least a surgical mask
  - Low/unknown – HCP masked but no eye protection
  - Consider activities that may cause direct contact, aerosolization of viral particles

- PEP with vaccinia virus vaccines may be offered through CDC to high and intermediate risk contacts
  - Within 4 days of exposure, can prevent infection; after 4 days, can modify infection
  - JYNNEOS: 3rd gen, replication-deficient modified vaccinia Ankara (MVA), safer and studied in HIV-infected persons CD4 ≥200.
  - ACAM2000: 2nd gen version of older, replicating, reactogenic vaccinia virus (only would be used if JYNNEOS not available)

- PEP issue to discuss with HCP: Verification of exposure classification, Review of data, Risk of transmission in healthcare settings, Review literature of MPX in healthcare settings, Vaccine Safety, Vaccine Efficacy, Clinical course of Monkeypox, Support regardless of decision made, Specialty counseling from maternal-fetal medicine specialist

- Testing – Lesion fluid from ≥2 sites (in duplicate) for orthopoxvirus PCR to state lab, then confirmatory MPX sequencing at CDC
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  - Jynneos: 3rd gen, replication-deficient modified vaccinia Ankara (MVA), safer and studied in HIV-infected persons CD4 ≥ 200.

• Treatment is largely supportive care although specific therapy is available

• Antiviral (tecovirimat), available through CDC under eIND, can be used for severe cases/vulnerable hosts

• Awareness and sensitivity, avoidance of stigmatizing, collaboration with public health
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
FACTORS MITIGATING AGAINST PANDEMIC

- Monkeypox is less infectious than current SARS-CoV-2 variants
- Easier identification than COVID-19 (i.e., distinctive rash)
- Diagnostic tests available
- 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
- FDA approved therapies available for smallpox (IND required for Monkeypox)
  - Tecovirimat likely 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 (government stockpile)
Monkeypox: What You Need to Know

Monkeys are a rare disease that can infect animals and people. It is usually found in parts of Africa, but cases have recently been detected in other parts of the world, including the United States.

How is Monkeypox spread?

- Direct contact with the skin of an infected person, especially a Monkeypox lesion.
- Breathing in the droplets produced when an infected person sneezes or coughs nearby.
- Touching objects that are contaminated with the virus, including bedding, clothing, or shared eating utensils.
- Rarely, from an infected pregnant woman to her fetus.

Infection with Monkeypox usually takes close contact with an infected person. For example, some people who have been diagnosed with Monkeypox in the United States may have been infected during sex. Unlike COVID-19, Monkeypox is not typically spread through small particles in the air, making it harder to become infected. So, if someone infected with Monkeypox coughs or sneezes, only those within a few feet of the person might catch it.

What does Monkeypox look like?

People who have been diagnosed with Monkeypox outside of Africa have all had skin blisters. Some have only a few—often even a single lesion—on the penis, anus, hands, feet, arm, legs, or face. Sometimes blisters form on the palms or soles of the feet, which are unusual places to have a rash.

The blister usually starts with a bump that has fluid inside. The bump then becomes dry and crusts. Some, but not all, of those diagnosed with Monkeypox have fever, headache, tiredness, or swollen glands. These symptoms may occur before any skin lesions appear.

How serious is Monkeypox?

While Monkeypox can be a serious infection, most people recover completely. In parts of Africa where Monkeypox is more common, 99% of infected people survive.

Are there tests for Monkeypox?

There are PCR tests for Monkeypox, which is the same technology used to diagnose COVID. For Monkeypox, a swab of a blister is sent to be tested.

Is there treatment for Monkeypox?

There are medicines that can be used to treat Monkeypox, and these are available in the United States. Vaccines that have been made to prevent Smallpox can also be used to prevent Monkeypox. These vaccines can be given before or after an exposure to someone with Monkeypox.

What should I do if I think I might have Monkeypox?

If you think you have Monkeypox, you should immediately contact your provider or local health department before you travel to a clinic or hospital. If you have a skin lesion, it can be tested for the Monkeypox virus.

Where can I learn more about Monkeypox?

You can find more information about Monkeypox by visiting these sites:

- CDC: [www.cdc.gov/monkeypox/index.html](http://www.cdc.gov/monkeypox/index.html)
- NC Department of Health and Human Services: [https://egov.dhhs.nc.gov/Clinical/disease/monkeypox](https://egov.dhhs.nc.gov/Clinical/disease/monkeypox)
<table>
<thead>
<tr>
<th><strong>Therapeutics</strong></th>
<th><strong>Dosing-and-Administration</strong></th>
<th><strong>Availability</strong></th>
<th><strong>Notes</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>JYNNEOS</strong> (Smallpox and Monkeypox vaccine)</td>
<td>0.5 mL SC x 1 and repeat at 4 weeks • if given between days 4-14 after exposure, vaccination may reduce symptoms of monkeypox but not prevent disease.</td>
<td>US-Government-supply; National Strategic Stockpile</td>
<td>Live: Non-replicating-modified Vaccinia Ankara-Bavarian-Nordic (MVA-BN), an attenuated non-replicating orthopoxvirus. Storage &amp; Handling: 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 12 hours.</td>
</tr>
</tbody>
</table>
| **Tecovirimat** (TPOXX) | PO, IV formulations • Total Duration: 14 days • Oral: Take within 30 minutes after a full meal. • Refer to package insert if patient cannot take capsules intact. • \( 
\begin{align*} 
& \rightarrow 13 \text{ to } \leq 25 \text{ kg: } 200 \text{ mg PO-BID} \\
& \rightarrow 25 \text{ to } \leq 40 \text{ kg: } 400 \text{ mg PO-BID} \\
& \rightarrow 40 \text{ kg to } \leq 120 \text{ kg: } 600 \text{ mg PO-BID} \\
& \rightarrow \geq 120 \text{ kg: } 600 \text{ mg PO-TID} \\
\end{align*} 
\)  | Available by IND only; National Strategic Stockpile | For patients with symptomatic disease (prodrome or rash). In animal studies, efficacy was higher when started within 5 days of infection. Tecovirimat orally administered for 14 days was found to be safe in a trial of 452 healthy volunteers (361 assigned to active drug, 91 to placebo). If IV treatment is necessary, switch to capsules as soon as possible. Give first oral dose at the time of next scheduled IV dose. |

Approved by UNC Health Anti-Infectives Committee, 9 June 2022
## 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>&quot;Take&quot; 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>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Risk for cardiac adverse events</td>
<td>Myopericarditis in 5.7 per 1,000 primary vaccines</td>
<td>Clinical trial data limited in evaluating this outcome; however, no significant events in data abstracted from single study arms⁵</td>
</tr>
<tr>
<td>Assessment of effectiveness</td>
<td>FDA assessed by comparing immunologic response and take rates to Dryvax⁶</td>
<td>FDA assessed by comparing immunologic response to ACAM2000 and animal studies</td>
</tr>
<tr>
<td>Administration</td>
<td>Percutaneously using a bifurcated needle by multiple puncture (scarification) technique; single dose</td>
<td>Subcutaneously; 2 doses 28 days apart</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.

⁵ 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.

⁶ https://www.fda.gov/media/75792/download

Contraindication to JYNNEOS = serious vaccine component allergy

MMWR 2022;71:3 June
Some recommended references

- CDC MPX Website: [https://www.cdc.gov/poxvirus/monkeypox/clinicians/index.html](https://www.cdc.gov/poxvirus/monkeypox/clinicians/index.html)
- Duque et al, Portugal: [https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.22.2200424](https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.22.2200424)
- Vivancos et al, UK: [https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.22.2200422](https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.22.2200422)
- Antoniri et al, Italy: [https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.22.2200421](https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.22.2200421)
- Hammerschlag et al, Australia: [https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.22.2200411](https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.22.2200411)
- Minhaj et al, US MMWR June 3, 2022: [http://dx.doi.org/10.15585/mmwr.mm7123e1](http://dx.doi.org/10.15585/mmwr.mm7123e1)
- Ogoina et al, Nigerian MPX case series preceding this outbreak: [https://academic.oup.com/cid/article/71/8/e210/5734993](https://academic.oup.com/cid/article/71/8/e210/5734993)
- Adler et al, UK MPX case series preceding this outbreak: [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00228-6/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00228-6/fulltext)
- CDC COCA Call: [https://emergency.cdc.gov/coca/calls/2022/callinfo_052422.asp](https://emergency.cdc.gov/coca/calls/2022/callinfo_052422.asp)
THANK YOU