Pandemic Update: Monkeypox and COVID-19

Michael G. Ison, MD MS FIDSA FAST
Professor, Divisions of Infectious Diseases and Organ Transplantation
Director, Transplant and Immunocompromised Host Infectious Diseases Service
Director, NUCATS Center for Clinical Research
Northwestern University Feinberg School of Medicine
Disclosures

• Research Support°
  o GlaxoSmithKline, Pulmocide

• Paid Consultation
  o Adagio, ADMA Biologics, AlloVir, Cidara, Genentech/Roche, Janssen, Shionogi, Takeda, Viracor Eurofins

• Royalties
  o UpToDate

• Data & Safety Monitoring Board Participation
  o Adamis, AlloVir, CSL Behring, Janssen, Merck, Sequiris, Takeda, Talaris

As of 8/26/21; ° Paid to Northwestern University.
Monkeypox: Current State of Cases

https://extranet.who.int/publicemergency/#
Monkeypox: Current State of Cases

https://www.cdc.gov/poxvirus/monkeypox/response/2022/mpx-trends.html
Monkeypox: Clinical Presentation

• Incubation Period
  - Monkeypox symptoms usually start within 3 weeks of exposure to the virus
  - If someone has flu-like symptoms, they will usually develop a rash 1-4 days later
  - Monkeypox can be spread from the time symptoms start until the rash has healed, all scabs have fallen off, and a fresh layer of skin has formed
  - The illness typically lasts 2-4 weeks

• Clinical Presentation
  - Often a flu-like prodrome before rash
  - Some presents with rash at onset
  - Other symptoms: Fever, chills, swollen lymph nodes, fatigue, muscle aches, headache, respiratory symptoms
Monkeypox: *Rash*

![Monkeypox rash images](image)

**Progression of Monkeypox Rash**

1. Flat red bumps
2. Firm, fluid-filled raised bumps
3. Scabs that heal over many weeks

Individuals diagnosed with monkeypox should isolate at home and avoid contact with others until all skin lesions have healed.
## Monkeypox: Rash

<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).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Finally, lesions typically develop a depression in the center (umbilication).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Scabs will remain for about a week before beginning to fall off.</td>
</tr>
</tbody>
</table>

[https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html](https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html)
Monkeypox: Current State of Cases

Monkeypox cases reported to CDC: Symptoms

- Rash: 98.6%
- Malaise (tiredness or not feeling well): 72.7%
- Fever: 72.1%
- Chills: 68.9%
- Headache: 65.2%
- Enlarged lymph nodes (swollen glands): 64.3%
- Myalgia (muscle aches): 61.8%
- Pruritis (itching): 43.9%
- Rectal pain: 26%
- Pus or blood on stools: 25%
- Rectal bleeding: 23.1%
- Tenesmus (pain when wanting to pass stool): 19%
- Abdominal pain (stomach ache): 18%
- Vomiting or nausea: 18%
- Proctitis (swelling, soreness in the rectal area): 16.3%
- Conjunctivitis (redness or pain in the eye): 6%

https://www.cdc.gov/poxvirus/monkeypox/response/2022/mpx-trends.html
Monkeypox: Transmission

• Close or Intimate Contact
  o Monkeypox can spread to anyone through close, personal, often skin-to-skin contact, including:
  o Direct contact with monkeypox rash, scabs, or body fluids from a person with monkeypox.
  o Touching objects, fabrics (clothing, bedding, or towels), and surfaces that have been used by someone with monkeypox.
  o Contact with respiratory secretions.

• This direct contact can happen during intimate contact, including:
  o Oral, anal, and vaginal sex or touching the genitals (penis, testicles, labia, and vagina) or anus (butthole) of a person with monkeypox.
  o Hugging, massage, and kissing.
  o Prolonged face-to-face contact.
  o Touching fabrics and objects during sex that were used by a person with monkeypox and that have not been disinfected, such as bedding, towels, fetish gear, and sex toys.

• Not transmitted through routine day-to-day exposures (riding CTA, going to the bathroom)
Monkeypox: Approach

Monkeypox: Vaccines

- Two vaccines are available
  - ACAM2000: Live Smallpox Vaccine, skin prick (85% effective against MPV)
  - Jynneos: Non-replicating virus, SubQ injection 4 weeks apart

Monkeypox: Vaccines

• Jynneos Use
  o The sooner it is given the better
  o Use within 4 days of exposure is associated with prevention of onset of disease
  o Use between 4 and 14 days may be associated with reduced severity of infection
  o Protection 2 weeks after 2nd dose
  o If prior smallpox vaccine >3 years ago, would get revaccinated
### Table 3. Pooled Solicited and Unsolicited Adverse Events during the Active Trial Phase in Each Vaccination Period (Full-Analysis Population). *

<table>
<thead>
<tr>
<th>Event</th>
<th>Period 1 MVA (N=220)</th>
<th>P Value†</th>
<th>Period 2 MVA (N=208)</th>
<th>P Value†</th>
<th>Periods 1 and 2 MVA (N=220)</th>
<th>P Value†</th>
<th>Period 3 ACAM2000 (N=196)</th>
<th>P Value†</th>
<th>ACAM2000-Only Group (N=213)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Documented adverse event</td>
<td>169 (76.8)</td>
<td>&lt;0.001</td>
<td>135 (64.9)</td>
<td>&lt;0.001</td>
<td>184 (83.6)</td>
<td>181 (92.3)</td>
<td>0.008</td>
<td>209 (98.1)</td>
<td></td>
</tr>
<tr>
<td>Nonserious adverse event within 29 days after vaccination</td>
<td>168 (76.4)</td>
<td>&lt;0.001</td>
<td>135 (64.9)</td>
<td>&lt;0.001</td>
<td>183 (83.2)</td>
<td>181 (92.3)</td>
<td>0.008</td>
<td>209 (98.1)</td>
<td></td>
</tr>
<tr>
<td>Serious adverse event;‡</td>
<td>2 (0.9)</td>
<td>1.0</td>
<td>0</td>
<td>1.0</td>
<td>2 (0.9)</td>
<td>0</td>
<td>1.0</td>
<td>1 (0.5)</td>
<td></td>
</tr>
<tr>
<td>Adverse event of special interest</td>
<td>2 (0.9)</td>
<td>0.44</td>
<td>2 (1.0)</td>
<td>0.68</td>
<td>4 (1.8)</td>
<td>2 (1.0)</td>
<td>0.69</td>
<td>4 (1.9)</td>
<td></td>
</tr>
<tr>
<td>Related adverse event within 29 days after vaccination§</td>
<td>112 (50.9)</td>
<td>&lt;0.001</td>
<td>76 (36.5)</td>
<td>&lt;0.001</td>
<td>130 (59.1)</td>
<td>61 (31.1)</td>
<td>&lt;0.001</td>
<td>158 (74.2)</td>
<td></td>
</tr>
<tr>
<td>Adverse event grade ≥3 within 29 days after vaccination</td>
<td>13 (5.9)</td>
<td>&lt;0.001</td>
<td>4 (1.9)</td>
<td>&lt;0.001</td>
<td>17 (7.7)</td>
<td>10 (5.1)</td>
<td>&lt;0.001</td>
<td>64 (30.0)</td>
<td></td>
</tr>
<tr>
<td>Related adverse event grade ≥3§</td>
<td>3 (1.4)</td>
<td>&lt;0.001</td>
<td>2 (1.0)</td>
<td>&lt;0.001</td>
<td>5 (2.3)</td>
<td>3 (1.5)</td>
<td>&lt;0.001</td>
<td>22 (10.3)</td>
<td></td>
</tr>
<tr>
<td>Related adverse event grade ≥3 within 29 days§</td>
<td>3 (1.4)</td>
<td>&lt;0.001</td>
<td>2 (1.0)</td>
<td>&lt;0.001</td>
<td>5 (2.3)</td>
<td>3 (1.5)</td>
<td>&lt;0.001</td>
<td>22 (10.3)</td>
<td></td>
</tr>
<tr>
<td>Adverse event leading to withdrawal from trial</td>
<td>2 (0.9)</td>
<td>0.5</td>
<td>0</td>
<td>NA</td>
<td>2 (0.9)</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Adverse event leading to withdrawal from vaccination</td>
<td>2 (0.9)</td>
<td>0.5</td>
<td>0</td>
<td>NA</td>
<td>2 (0.9)</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Monkeypox: Vaccine Update

Total JYNNEOS Vaccine Doses Administered and Reported to CDC

https://www.cdc.gov/poxvirus/monkeypox/response/2022/mpx-trends.html
Monkeypox: Vaccine Update

JYNNEOS Vaccine Doses Administered, by Age

Number of Doses Administered

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Doses Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 years</td>
<td>34</td>
</tr>
<tr>
<td>5-11 years</td>
<td>26</td>
</tr>
<tr>
<td>12-17 years</td>
<td>32</td>
</tr>
<tr>
<td>18-24 years</td>
<td>15,011</td>
</tr>
<tr>
<td>25-39 years</td>
<td>107,305</td>
</tr>
<tr>
<td>40-49 years</td>
<td>36,046</td>
</tr>
<tr>
<td>50-64 years</td>
<td>35,117</td>
</tr>
<tr>
<td>65+ years</td>
<td>7,693</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
</tr>
</tbody>
</table>

First doses administered

https://www.cdc.gov/poxvirus/monkeypox/response/2022/mpx-trends.html
Monkeypox: Tecovirimat for Treatment
## Monkeypox: Tecovirimat for Treatment

Table 6: Survival Rates in Tecovirimat Treatment Studies in Cynomolgus Macaques and NZW Rabbits Exhibiting Clinical Signs of Orthopoxvirus Disease

<table>
<thead>
<tr>
<th>Treatment Initiation&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Survival Percentage (# survived/n)</th>
<th>p-value&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Survival Rate Difference&lt;sup&gt;c&lt;/sup&gt; (95% CI)&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Tecovirimat</td>
<td></td>
</tr>
<tr>
<td><strong>Cynomolgus Macaques</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 1</td>
<td>Day 4</td>
<td>0% (0/7)</td>
<td>80% (4/5)</td>
</tr>
<tr>
<td></td>
<td>Day 4</td>
<td>0% (0/6)</td>
<td>100% (6/6)</td>
</tr>
<tr>
<td>Study 3</td>
<td>Day 4</td>
<td>0% (0/3)</td>
<td>83% (5/6)</td>
</tr>
<tr>
<td></td>
<td>Day 5</td>
<td></td>
<td>83% (5/6)</td>
</tr>
<tr>
<td></td>
<td>Day 6</td>
<td></td>
<td>50% (3/6)</td>
</tr>
<tr>
<td><strong>NZW Rabbits</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 4</td>
<td>Day 4</td>
<td>0% (0/10)</td>
<td>90% (9/10)</td>
</tr>
<tr>
<td>Study 5</td>
<td>Day 4</td>
<td>NA&lt;sup&gt;e&lt;/sup&gt;</td>
<td>88% (7/8)</td>
</tr>
</tbody>
</table>
### Table 2: Adverse Reactions Reported in ≥ 2% of Healthy Adult Subjects Receiving at Least One Dose of TPOXX 600 mg

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>TPOXX 600 mg N = 359 (%)</th>
<th>Placebo N = 90 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Nausea</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Abdominal pain&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

<sup>a</sup> Includes abdominal pain, abdominal pain upper, abdominal distension, abdominal discomfort, abdominal pain lower, epigastric pain
Tecovirimat may be considered for treatment in people infected with *Monkeypox virus*:

- With severe disease (e.g., hemorrhagic disease, confluent lesions, sepsis, encephalitis, or other conditions requiring hospitalization)

- Who are at high risk of severe disease:
  - People with immunocompromising conditions
  - Pediatric populations, particularly patients younger than 8 years of age
  - Pregnant or breastfeeding women
  - People with a history or presence of atopic dermatitis, people with other active exfoliative skin conditions (e.g., eczema, burns, impetigo, varicella zoster virus infection, herpes simplex virus infection, severe acne, severe diaper dermatitis with extensive areas of denuded skin, psoriasis, or Darier disease)
  - People with one or more complication (e.g., secondary bacterial skin infection; gastroenteritis with severe nausea/vomiting, diarrhea, or dehydration; bronchopneumonia; concurrent disease or other comorbidities)

- With aberrant infections involving accidental implantation in eyes, mouth, or other anatomic areas where *Monkeypox virus* infection might constitute a special hazard (e.g., the genitals or anus)
COVID-19: Global Trends

Cases: 599,176,353
Daily Average: 740,842
Deaths: 6,460,533
Daily Deaths: 2,292

Accessed 26 August 2022
COVID-19: Global Trends

COVID-19: US Trends

New reported cases by day

Test positivity rate

Covid patients in hospitals and I.C.U.s
Early data may be incomplete.

New reported deaths by day

COVID-19: US Trends October 2021

Cases: 46,683,764
Deaths: 701,178

COVID-19:  US Trends Mid-December 2021

Cases: 46,683,764
Daily New Cases: 119,301
Hospitalizations: 65,962
Deaths: 800,922
Daily Deaths: 1,298


Cases: 52,244,696  
Daily New Cases: 214,499  
Hospitalizations: 71,034  
Deaths: 814,970  
Daily Deaths: 1,328

Current Situation:  *United States – Mid-January*

- **Cases:**
  - Total: 67,705,330
  - Daily: 756,752
- **Hospitalizations**
  - Daily: 156,894
- **Deaths**
  - Total: 853,740
  - Daily: 1,889

Current Situation:  United States – April 2022

- Cases:
  - Total: 81,237,905
  - Daily: 56,869

- Hospitalizations
  - Daily: 16,897
  - ICU: 1,973

- Deaths
  - Total: 991,921
  - Daily: 316

Current Situation: United States – Current Status

Cases:
- Total: 86,899,773
- Daily: 102,818

Hospitalizations:
- Daily: 31,650
- ICU: 3,498

Deaths:
- Total: 1,012,486
- Daily: 348

Current Situation: United States – Current Status

- Cases:
  - Total: 88,800,868
  - Daily: 129,858

- Hospitalizations
  - Daily: 38,517
  - ICU: 4,330

- Deaths
  - Total: 1,018,360
  - Daily: 396

Current Situation: United States – Current Status

- **Cases:**
  - Total: 93,838,712
  - Daily: 91,400

- **Hospitalizations**
  - Daily: 39,071
  - ICU: 4,653

- **Deaths**
  - Total: 1,039,018
  - Daily: 460

COVID-19: US Risk by Age

10 daily admissions per 100,000

5 daily admissions

COVID-19: Booster Uptake is Slow

COVID-19: Illinois Trends and Vaccination

Current Situation: Chicago

SARS-CoV-2 Key Variant

- **Omicron Variant:**
  - 30 mutations and deletions in the spike protein
  - Associated with increase rates of infection, reduced protection from 2 doses of vaccine
Omicron BA.5: What Do We Know?

A Mutational Lineage of SARS-CoV-2 Subvariants

B Vaccinated Participants before and after Booster Dose

C Infected Participants with BA.1 or BA.2 Subvariant

COVID-19 Vaccine: Schedules

**AT-A-GLANCE**

**COVID-19 Vaccination Schedules**

Use the schedules below to determine how many total COVID-19 vaccine doses are recommended based on primary series product, age, and immune status. This schedule does not include clinical details necessary for administering COVID-19 vaccines. For clinical details, see the resources at the end of this document.

**COVID-19 Vaccination Schedule for Most People**

**Number and intervals of COVID-19 vaccine doses**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Dose 1 (primary)</th>
<th>Dose 2 (primary)</th>
<th>Dose 3 (primary)</th>
<th>Dose 4 (2nd mRNA booster)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer-BioNTech (ages 6 months–4 years)</td>
<td>In 3 weeks</td>
<td>In at least 4 weeks</td>
<td>In at least 4 months</td>
<td><strong>2nd</strong> booster for some groups</td>
</tr>
<tr>
<td>Pfizer-BioNTech (ages 5 years and older)</td>
<td>In 3 weeks</td>
<td>In at least 5 months</td>
<td>In at least 4 months</td>
<td><strong>2nd</strong> mRNA booster*</td>
</tr>
<tr>
<td>Moderna (ages 6 months–5 years)</td>
<td>In 4 weeks</td>
<td>In at least 3 months</td>
<td>In at least 4 months</td>
<td><strong>2nd</strong> mRNA booster*</td>
</tr>
<tr>
<td>Moderna (ages 18 years and older)</td>
<td>In 4 weeks</td>
<td>In at least 3 months</td>
<td>In at least 4 months</td>
<td><strong>2nd</strong> mRNA booster*</td>
</tr>
<tr>
<td>Janssen (J&amp;J) (ages 18 years and older)*</td>
<td>In at least 2 months</td>
<td>In at least 4 months</td>
<td>Dose 3 (2nd mRNA booster)*</td>
<td>People ages 50 years and older get a 2nd booster.</td>
</tr>
</tbody>
</table>

**COVID-19 Vaccination Schedule for People Who Are Moderately or Severely Immunocompromised**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Dose 1 (primary)</th>
<th>Dose 2 (primary)</th>
<th>Dose 3 (primary)</th>
<th>Dose 4 (booster)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer-BioNTech (ages 5–11 years)</td>
<td>In 3 weeks</td>
<td>In at least 4 weeks</td>
<td>In at least 3 months</td>
<td>In at least 4 months</td>
</tr>
<tr>
<td>Pfizer-BioNTech (ages 12 years and older)</td>
<td>In 3 weeks</td>
<td>In at least 4 weeks</td>
<td>In at least 3 months</td>
<td>In at least 4 months</td>
</tr>
<tr>
<td>Moderna (ages 6 months–5 years)</td>
<td>In 4 weeks</td>
<td>In at least 4 weeks</td>
<td>In at least 3 months</td>
<td>In at least 4 months</td>
</tr>
<tr>
<td>Moderna (ages 18 years and older)</td>
<td>In 4 weeks</td>
<td>In at least 4 weeks</td>
<td>In at least 3 months</td>
<td>In at least 4 months</td>
</tr>
<tr>
<td>Janssen (J&amp;J) (ages 18 years and older)*</td>
<td>In 4 weeks</td>
<td>In at least 2 months</td>
<td>In at least 4 months</td>
<td>In at least 4 months</td>
</tr>
</tbody>
</table>

*Age-appropriate mRNA COVID-19 vaccines are preferred over Janssen COVID-19 Vaccine for primary and booster vaccination. Janssen COVID-19 Vaccine should only be used in limited situations. See: https://www.cdc.gov/vaccines/pubs/ovd-19-clinical-considerations/interim-considerations-usa.htm#considerations-janssen.

For more specific clinical guidance, see:
- Interim COVID-19 Immunization Schedule
- Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Approved or Authorized in the United States

[cdc.gov/coronavirus]
SARS-CoV-2 Boosters: Bivalent Vaccine

• Same Moderna and Pfizer vaccine technology

• Contains mRNA for 2 different spike proteins
  o Original Wuhan-like virus
  o Omicron virus
  o Studies of the BA.1 virus showed improvement in protection but less protection vs. BA.5
  o New vaccine to include BA.4/BA.5 spike protein
    ▪ Using studies to suggest what the antibody levels against BA.5 will be with this approach
    ▪ Clinical studies will follow authorization
Numbers are Going Back Up: *Have a Plan to Stay Safe*

- Generally anything outdoors is safe
- Masking in any public indoor space is the safest
- Many with symptoms are mild (even allergy like) – test if unsure
- Get Evusheld if you are eligible
- Get your booster and stay Up To Date on vaccine
- Call your doctor if sick, especially if you have COVID-19
- More than COVID-19 is circulating!
What to Expect for the Fall

• There will be more variants that emerge
• There will be a bivalent COVID-19 booster available SOON
• There will be a heavy and early flu season this year (along with lots and lots of other viruses in addition to COVID-19)
• I suspect that most people will get COVID-19 before the end of the year

• What can you do?
  o Keep your guard up
  o Get your boosters, wear your mask and keep others that are sick away
  o Get your flu shot (and there is likely to be an RSV shot in the near future)
  o Call your doctor if you are sick and have plans to access medications if you will be traveling
What Else to Expect for the Fall: Dr. Ison to Move to NIH!
Are you a registered organ donor? I am!

Questions?

Michael G. Ison, MD MS
+1-312-695-4186
mgison@northwestern.edu