Use of JYNNEOS During Mpox Outbreaks: Clinical Guidance

Agam Rao, MD

CAPT, US Public Health Service
Medical Officer
Poxvirus and Rabies Branch

Advisory Committee on Immunization Practices

June 23, 2023

Vote passed during February 2023 ACIP meeting

ACIP recommends the 2-dose* JYNNEOS vaccine series for persons aged 18 years and older at risk of mpox during an mpox outbreak§

*Dose 2 administered one month after dose 1

§ Public health authorities determine whether there is an mpox outbreak; a single case may be considered an mpox outbreak at the discretion of public health authorities. Other circumstances in which a public health response may be indicated include ongoing risk of introduction of mpox into a community due to disease activity in another geographic area.

Vaccination with JYNNEOS is a 2-dose series

- Post-exposure: Concerning exposure should trigger consideration for vaccination regardless of where the exposure occurs (e.g., healthcare setting vs. community)
- Pre-exposure: Whether specific populations (e.g., children, pregnant persons) should receive vaccinations is dependent on the risk during a specific outbreak

- Goal of clinical guidance: Provide general information that can inform decision-making for specific mpox outbreaks

Clinical guidance

- Vaccinating at-risk populations during an outbreak
  - Persons <18 years of age
  - Pregnant persons
  - Breastfeeding persons
- Vaccinating HCP and certain laboratorians during an outbreak
  - Healthcare personnel (HCP)
  - Certain laboratorians
- Administration guidance
  - Coadministration with COVID-19 vaccines
  - Immunoglobulin products
  - Other guidance

Vaccinating at-risk populations during an mpox outbreak

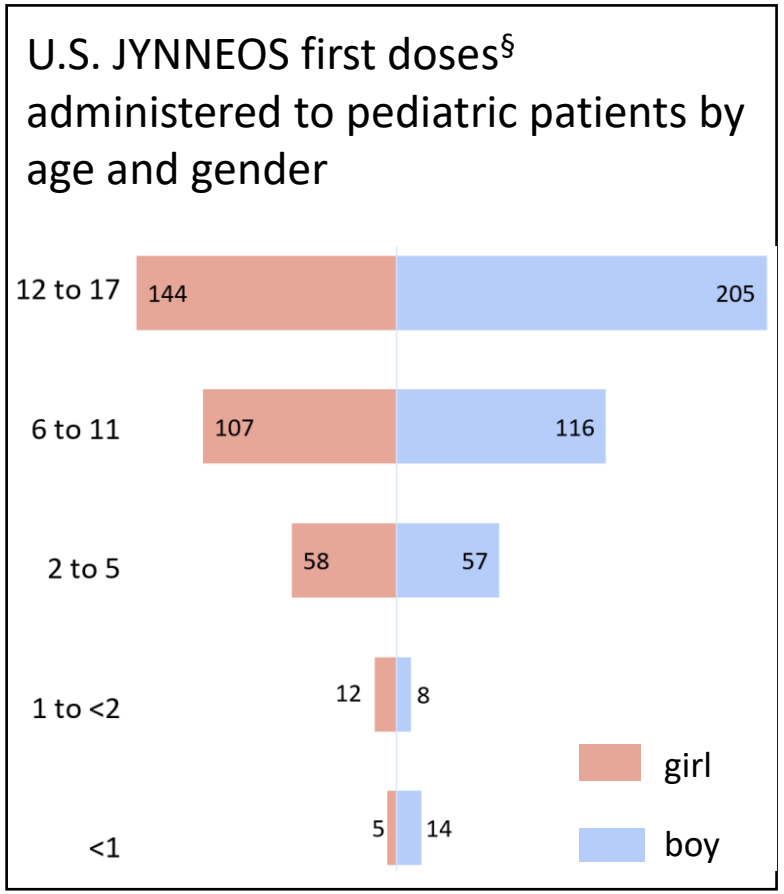
Mpox in persons <18 years of age, 1970-2022

- Central and West Africa, Clades I (n= <1638*) and IIa (n= 6)
  - 1970-1985: Increased incidence and severity in children ≤ 8 years of age compared to adolescents and adults, likely because younger children had not been routinely vaccinated to prevent smallpox
  - 2006-2015: No difference in incidence or severity in children compared to adults, likely reflecting cessation of childhood smallpox vaccinations among persons who were adults at the time of evaluations
- United States and United Kingdom, Clades IIa (n= 12) and IIb (n= 125)
  - 2 children hospitalized during 2003 U.S. outbreak and 1 child hospitalized during 2021 in United Kingdom; all recovered
  - No severe manifestations among U.S. children during current outbreak
  - Severe manifestation reported among a neonate in UK (adenovirus co-infection)

*Includes 18–19-year-olds from the Democratic Republic of the Congo

Use of JYNNEOS in persons aged <18 years

- 12-17 years of age, n=349
  - No safety signals identified via CDC surveillance systems
  - No efficacy data from pre-licensure trials
  - Unable to evaluate real-world VE during current outbreak
  - NIH clinical trial underway to evaluate safety and efficacy
- 0-11 years of age, n=377
  - No safety signals identified via CDC surveillance systems
  - No efficacy data from pre-licensure trials
  - Unable to evaluate real-world VE during current outbreak
  - Concerns that dose may be different for those in the younger ages
  - No clinical trials or other studies planned at this time
- Data from recent publication* is encouraging



§ Fewer children received 2 doses (compared to 1 dose); CDC unpublished data (does not include data from one state)

* Ladhani et al. Lancet Infect Dis. 2023

Clinical guidance for children and adolescents

- For persons 6 months-17 years, JYNNEOS should be administered as PrEP or PEP (as indicated by public health authorities for a specific outbreak) if a high-risk exposure has occurred
  - For younger children (e.g., <6 years of age), clinicians should be aware that no studies involving JYNNEOS have been performed to determine appropriate dose
  - Decisions about vaccination with JYNNEOS should involve risk/benefit assessment for every pediatric age group during a specific outbreak
  - After completion of ongoing clinical trial, ACIP may consider a vote re: use of JYNNEOS in children 12-17 years of age during mpox outbreaks
- For children < 6 months of age, VIGIV should be administered in lieu of JYNNEOS if PEP is indicated

Detection and transmission of MPXV during the current outbreak

MPXV in Human Samples and Implications for Transmission			
Exposure source	**MPXV DNA detected by PCR**	**Replication-competent virus detected/isolated**	**Epidemiologically supported source of infection**
Skin	Yes	Yes	Yes
Oropharynx and saliva	Yes*	Yes	Yes
Anorectum	Yes	Yes	Yes†
Semen	Yes*	Yes	Insufficient data
Urine/urethra	Yes	Yes	Insufficient data
Conjunctivae or ocular fluid	Yes	Yes	Insufficient data
Blood/plasma/serum	Yes	Insufficient data	Insufficient data
Feces	Yes	Insufficient data	Insufficient data
Vagina	Yes	Insufficient data	Insufficient data†
Breastmilk	Insufficient data	Insufficient data	Insufficient data
Contaminated sharp‡	Insufficient data	Insufficient data	Yes

* DNA has been detected at Ct values <35 in recovered patients more than 30 days after illness onset in an upper respiratory tract swab, saliva, and semen.
† The preponderance of existing data support exposure to anorectal and vulvovaginal tissues and fluids as capable of transmitting infection; however, it is difficult with current evidence to definitively isolate these exposures from other concomitant exposures (see text).
‡ Includes body modification with piercings and tattooing.
https://www.cdc.gov/poxvirus/monkeypox/about/science-behind-transmission.html

Mpox in pregnant persons

- Historically*
  - Mpox known to have been transmitted pre and perinatally to at least 2 neonates
  - Neonatal outcomes among neonates born to mothers who had mpox (n=5) included a stillbirth, self-limited rash, and healthy neonates
- During 2022/2023 U.S. outbreak
  - Outcomes among pregnant women are being evaluated
  - Transmission to neonate known to have occurred

*This information is limited to published reports from countries where MPXV is endemic

Use of JYNNEOS in pregnant persons

- Unknown if JYNNEOS administered to pregnant persons during 2022/2023 outbreak
- No adverse events (passively reported via VAERS) have been received
- 2022 ACIP recommendations for persons at risk for occupational exposure explicitly states JYNNEOS not contraindicated in pregnant persons

Mpox spread during breastfeeding and use of JYNNEOS among breastfeeding persons*

- Mpox known to be transmitted when child exposed to mpox skin lesions (e.g., under breast)
- Mpox not known to be transmitted via breast milk; for one patient during 2022 outbreak, breast milk samples negative for MPXV DNA by PCR

- No information about whether breast-feeding persons received JYNNEOS during ongoing outbreak; however, no VAERS reports were received that mentioned breast-feeding persons

*https://www.cdc.gov/mmwr/volumes/72/wr/mm7201a2.htm?s_cid=mm7201a2_w

Proposed clinical guidance for pregnant and breastfeeding persons

- JYNNEOS not contraindicated in persons who are pregnant or breastfeeding
- Available human data insufficient to determine vaccine-associated risks in pregnancy. However, animal models including rats and rabbits have shown no evidence of harm to developing fetus
- Safety and efficacy of JYNNEOS not been evaluated in breastfeeding women. It is not definitively known whether JYNNEOS is excreted in human milk. Data are not available to assess the impact of JYNNEOS on milk production or the safety of JYNNEOS in breastfed infants. However, because JYNNEOS vaccine is replication-deficient, it likely does not present a risk of transmission to breastfed infants and can be administered to women who are breastfeeding after weighing the benefits and harms
- If high-risk exposures cannot be avoided or have already occurred, persons who are pregnant or breastfeeding may receive JYNNEOS

Vaccinating HCP and certain laboratorians during an mpox outbreak

Mpox acquired via laboratory or healthcare exposures

- 2022/2023 U.S. mpox outbreak
  - Laboratory personnel: No reports
  - HCP: 23 potential exposures
    - Most associated with sharps injuries while attempting to unroof, open, or aspirate mpox lesions*
    - Some associated with suboptimal PPE use
- Historical data from endemic countries
  - Laboratory personnel: No data
  - HCP: Acquired providing care to family members/friends in homes or with little PPE

*Unroofing or aspirating lesions is discouraged https://www.cdc.gov/poxvirus/mpox/clinicians/prep-collection-specimens.html

Detection and transmission of MPXV during the current outbreak

MPXV in Human Samples and Implications for Transmission			
Exposure source	**MPXV DNA detected by PCR**	**Replication-competent virus detected/isolated**	**Epidemiologically supported source of infection**
Skin	Yes	Yes	Yes
Oropharynx and saliva	Yes*	Yes	Yes
Anorectum	Yes	Yes	Yes†
Semen	Yes*	Yes	Insufficient data
Urine/urethra	Yes	Yes	Insufficient data
Conjunctivae or ocular fluid	Yes	Yes	Insufficient data
Blood/plasma/serum	Yes	Insufficient data	Insufficient data
Feces	Yes	Insufficient data	Insufficient data
Vagina	Yes	Insufficient data	Insufficient data†
Breastmilk	Insufficient data	Insufficient data	Insufficient data
Contaminated sharp‡	Insufficient data	Insufficient data	Yes

* DNA has been detected at Ct values <35 in recovered patients more than 30 days after illness onset in an upper respiratory tract swab, saliva, and semen.
† The preponderance of existing data support exposure to anorectal and vulvovaginal tissues and fluids as capable of transmitting infection; however, it is difficult with current evidence to definitively isolate these exposures from other concomitant exposures (see text).
‡ Includes body modification with piercings and tattooing.
https://www.cdc.gov/poxvirus/monkeypox/about/science-behind-transmission.html

Use of JYNNEOS for preexposure vaccination of persons at risk for occupational exposure to orthopoxviruses: Recommendations of the ACIP—United States, 2022

- For research laboratory personnel* and clinical laboratory personnel performing diagnostic testing for orthopoxviruses§, ACIP recommends use of JYNNEOS for primary vaccination as an alternative to ACAM2000
- For healthcare personnel who administer ACAM2000 or care for patients infected with orthopoxviruses, ACIP recommends use of JYNNEOS (as an alternative to ACAM2000) based on shared clinical decision-making

*Research laboratory personnel are those who directly handle cultures or animals contaminated or infected with replication-competent vaccinia virus, recombinant vaccinia viruses derived from replication-competent vaccinia strains (i.e., those that are capable of causing clinical infection and producing infectious virus in humans), or other orthopoxviruses that infect humans (e.g., Monkeypox virus, Cowpox virus, and Variola virus)

§Clinical laboratory personnel who perform routine chemistry, hematology, and urinalysis testing, including for patients with suspected or confirmed orthopoxvirus infections, are not included in this recommendation because their risk for exposure is low

Pre-exposure prophylaxis: Use of JYNNEOS during mpox outbreaks

- For research laboratory personnel* and clinical laboratory personnel performing diagnostic testing for mpox[§], ACIP recommends use of JYNNEOS for pre-exposure vaccination as an alternative to ACAM2000
- For clinical laboratory personnel who handle specimens that may have a higher possibility of containing replication competent MPXV (e.g., lesion material, throat swabs, oral swabs, rectal swabs), and certain healthcare personnel who care for patients infected with mpox or administer ACAM2000 [§], ACIP recommends use of JYNNEOS (as an alternative to ACAM2000) based on shared clinical decision-making

*Research laboratory personnel are those who directly handle cultures or animals contaminated or infected with monkeypox virus (MPXV)

[§]Vaccination is not routinely recommended for clinical laboratory personnel who perform routine chemistry, hematology, and urinalysis testing, including for patients with suspected or confirmed MPXV infection, healthcare personnel who care for patients with mpox or administer ACAM2000. Recommended infection prevention and control practices are effective in minimizing transmission. Vaccination can be offered based on site- and activity- specific biosafety risk assessments (e.g., identification of laboratory procedures with a high likelihood of generating aerosols or inadequate PPE availability)

Administration guidance

Coadministration of JYNNEOS with COVID-19 vaccines

- There is no required minimum interval between receiving any COVID-19 vaccine and JYNNEOS vaccine (e.g., for mpox prevention), regardless of which vaccine is administered first
- People, particularly adolescent and young adult males, who are recommended to receive both vaccines might consider waiting 4 weeks between vaccines. This is because of the observed risk for myocarditis and pericarditis after receipt of ACAM2000 orthopoxvirus vaccine and COVID-19 vaccines and the hypothetical risk for myocarditis and pericarditis after JYNNEOS vaccine. However, if a patient's risk for mpox or severe disease due to COVID-19 is increased, administration of JYNNEOS and COVID-19 vaccines should not be delayed

Implications of JYNNEOS administration in close temporal proximity to immunoglobulin products

- Antibodies to measles and varicella high in immune globulin products; administration of these in close temporal proximity can prevent the vaccine from entering cells and being effective
- Antibodies to orthopoxviruses are believed to be low in most immune globulin products (e.g., IVIG) and will likely remain low in the future
- Antibodies to orthopoxviruses are present in VIGIV (purified immunoglobulin from persons vaccinated against smallpox); however, whether these could prevent the vaccine from being effective is unknown

Clinical guidance when JYNNEOS and immunoglobulin products are temporally administered

- Most immunoglobulin products: No precautions are necessary if JYNNEOS is administered in close temporal proximity to IVIG
- VIGIV
  - VIGIV could interfere with immune response to JYNNEOS
    - Ideally, administration of JYNNEOS should be delayed if VIGIV was recently administered
    - The duration for which it should be delayed is unknown; during outbreaks, it is acceptable to administer a dose of JYNNEOS; however, public health consultation should be obtained for case specific guidance about an additional dose at a later time
  - Unlikely that VIGIV would be administered in close proximity to JYNNEOS

Other administration guidance

- Unintentional delays do not require restarting the series; the second dose should be administered as soon as possible even if >1 year has elapsed
- In settings where subcutaneous administration is not preferred (e.g., vaccine is in short supply), the vaccine can be administered intradermally
- In settings where intradermal administration is not possible (e.g., because staff are not trained or uncomfortable)
  - Jurisdictions may administer subcutaneous vaccinations and prioritize first doses of the 2-dose JYNNEOS series
  - Second doses should be administered as soon as vaccine availability allows
- Decisions about vaccine administration should ensure equitable distribution of vaccine doses

Acknowledgements

- Faisal Minhaj
- Jim Campbell
- Jafar Razeq
- Mark Russi
- Howard Minkoff
- Sathesh Panayampalli
- Christina Hutson
- David Kuhar
- Marie de Perio
- John Brooks
- Amanda Cohn
- Melinda Wharton
- Manisha (Mo) Patel
- Paul Rota
- Rosalind Carter
- Catherine McLean
- Jonathan Duffy
- Ian Kracalik
- Leora Feldstein
- Andrea McCollum
- ACIP Mpox WG
- Sara Oliver
- Tara Anderson
- Evelyn Twentyman
- Allie Tuttle
- AAP's COID and Redbook

Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.