

# Human Monkeypox Virus 101: What Clinicians Need to Know

**John T. Brooks, MD**

Chief Medical Officer, Multinational Monkeypox Outbreak Response  
Center for Disease Control and Prevention  
Atlanta, Georgia



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## MONKEYPOX

### Monkeypox 101: What Clinicians Need to Know

Tuesday, October 18, 2022  
RWHAP Clinical Conference, San Diego CA

**John T. Brooks, M.D.**  
Chief Medical Officer  
Multinational Monkeypox Outbreak Response



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### Learning Objectives

After attending this presentation, learners will be able to:

- Define key epidemiologic features of the current U.S. monkeypox outbreak.
- Characterize how the clinical presentation of monkeypox during the current U.S. outbreak differs from its classic presentation previously in west and central Africa.
- Understand the importance of screening patients undergoing evaluation for monkeypox for sexually transmitted infections including HIV.
- Describe current criteria for the use of tecovirimat as treatment for monkeypox.

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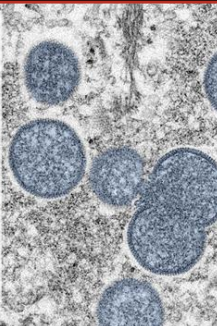
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### Monkeypox virus

- **Monkeypox virus** belongs to the *Orthopoxvirus* genus
  - *Variola virus* (which causes smallpox)
  - *Vaccinia virus* (used in the current smallpox vaccine)
  - *Cowpox virus* (first virus used for smallpox vaccination)
- First discovered in 1958 following two outbreaks of a pox-like disease in colonies of monkeys kept for research (hence the name 'monkeypox')
- Specific animal reservoir unknown, but likely small African mammals




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### Monkeypox virus

- Formerly rare, mostly in west and central Africa
- Spreading widely in 2022 global outbreak
- WHO declared Public Health Emergency of International Concern (PHEIC) in July 2022
- U.S. HHS declared Public Health Emergency in August 2022




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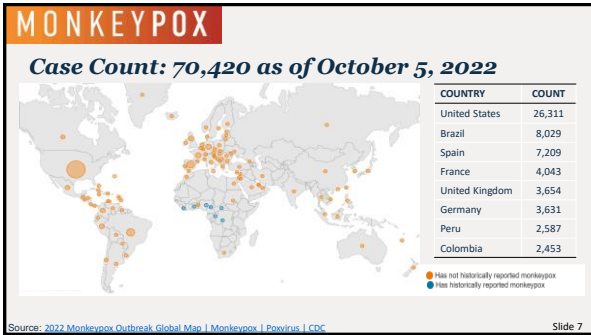
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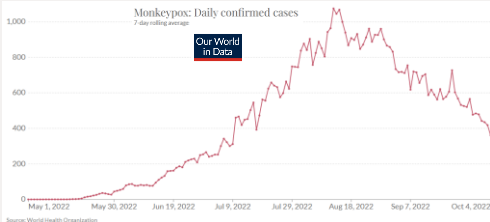
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# MONKEYPOX

## Worldwide Trend in Cases



Source: Monkeypox - Our World in Data

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# MONKEYPOX

## Select Demographic and Clinical Characteristics

Characteristic	All Persons (N = 528)
Median age (range) — yr	38 (18–68)
Sex or gender — no. (%)	
Male	527 (>99)
Female	0
Trans or nonbinary	1 (<1)
Sexual orientation — no. (%) †	
Heterosexual	9 (2)
Homosexual	509 (96)
Bisexual	10 (2)

Source: Thornhill 2022, *N Engl J Med*

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# MONKEYPOX

## Select Demographic and Clinical Characteristics

Characteristic	All Persons (N = 528)
Median age (range) — yr	38 (18–68)
Sex or gender — no. (%)	
Male	527 (>99)
Female	0
Trans or nonbinary	1 (<1)
Sexual orientation — no. (%) †	
Heterosexual	9 (2)
Homosexual	509 (96)
Bisexual	10 (2)
HIV positive — no. (%)	
Median no. of sex partners in previous 3 months (IQR)	?
Microbiologically confirmed concomitant STI present — no./total no. screened (%)	

Source: Thornhill 2022, *N Engl J Med*

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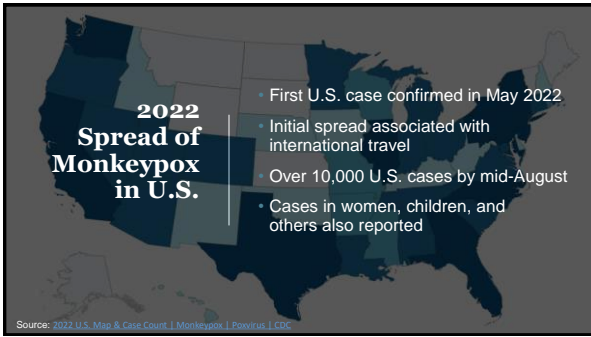
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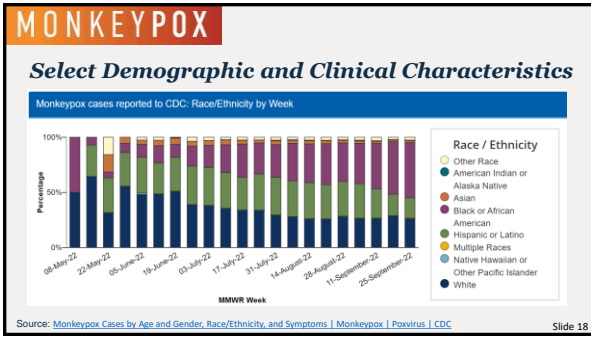
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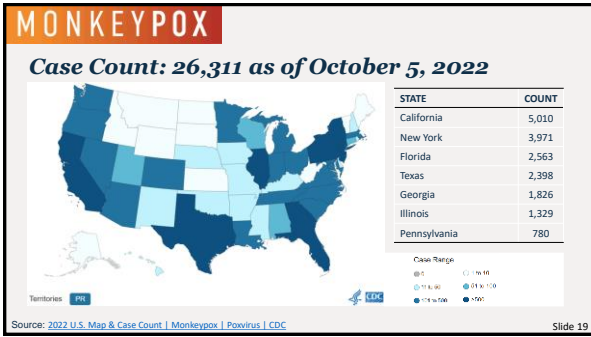
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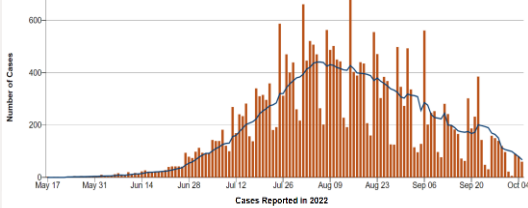
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# MONKEYPOX

## U.S. Monkeypox Case Trends Reported to CDC



Source: U.S. Monkeypox Case Trends Reported to CDC | Monkeypox | Poecivirus | CDC

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# MONKEYPOX

## Clinical Illness: 'Classic'

- **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**

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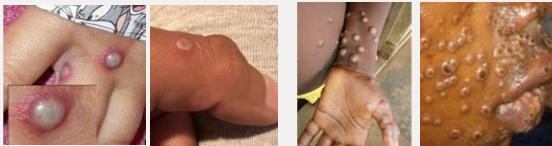
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# MONKEYPOX

## Clinical Illness: 'Classic'



Lesions observed during 2003 U.S. monkeypox outbreak

Lesions observed in endemic countries

Source: <https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html>

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# MONKEYPOX

## Transmission

- Spread person-to-person through:
  - Direct contact with the infectious rash, scabs, or body fluids
  - Respiratory secretions during prolonged, face-to-face contact, or during intimate physical contact, such as kissing, cuddling, or sex
  - Touching items (such as clothing or linens) that previously touched the infectious rash or body fluids
  - Through placenta in an infected pregnant person to their fetus
- Patients are infectious once symptoms begin (whether prodromal or rash symptoms) and remain infectious until lesions form scabs, scabs fall off, and a fresh layer of skin forms

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# MONKEYPOX

## Clinical Illness: '2022 Lesions'

- 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
  - Urethritis: complicated by balanitis/phimosis
  - Proctitis: anorectal pain (lancinating), 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

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# MONKEYPOX

## Clinical Illness: '2022 Lesions'

Site of skin lesions — no. (%)	
Anogenital area	383 (73)
Face	134 (25)
Trunk or limbs	292 (55)
Palms or soles	51 (10)
More than one site per person may have been reported.	
Mucosal lesions present — no. (%)	217 (41)
Site of mucosal lesions — no./total no. (%)	
Anogenital only	148/217 (68)
Oropharyngeal only	50/217 (23)
Anogenital and oral	16/217 (7)
Nasal and eye	3/217 (1)



Source: Thornhill 2022, N. Engl. J. Med., Ogoina 2022, Ceiog (pre-print)

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# MONKEYPOX

## Clinical Illness: '2022 Lesions'

PRODROME



ANOGENITAL LESIONS



Thanks to Collen Kelley (Emory).

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# MONKEYPOX

## Examination and Diagnosis

- Collect a **complete sexual and travel history for past 21 days**
  - Consider possibility of foreign or domestic animal or animal product contact
- Perform a **thorough skin and mucosal examination** (e.g., genital, anal, oral) in a room with *good lighting*
- If rash present, consider a **broad differential** (e.g., syphilis, varicella zoster, herpes simplex, molluscum contagiosum), especially if the person has epidemiologic risk factors for monkeypox infection in the current outbreak
- Evaluate for STIs per the [2021 CDC STI Treatment Guidelines](#)
  - Persons with monkeypox have had STIs including acute HIV

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# MONKEYPOX

## Uncommon Manifestations of Illness (<2%)

- **Ophthalmologic:** conjunctivitis, corneal ulceration and scarring
- **Neurologic:** confusion, seizure, encephalomyelitis
- **Cardiovascular:** myocarditis, pericarditis
- **Rheumatologic:** acute arthritis/synovitis

Conjunctival lesion with corneal ulceration



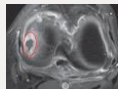
Abnormal T2/fluid attenuated inversion recovery signal



Inferior and anterolateral T-wave inversions



Synovitis with subchondral demarcation zone (red circle)



Source: Pastula 2022, [MMWR](#), Badenoch 2022, [Eclin Med](#), Rodriguez-Nava 2022, [Emerg Infect Dis](#), Fonti 2022, [Lancet](#) Slide 28

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# MONKEYPOX

## Severe Disease

This is an official  
**CDC HEALTH ADVISORY**

Distributed via the CDC Health Alert Network  
September 29, 2022 02:15 PM ET  
CDCHAN-00475

### Severe Manifestations of Monkeypox among People who are Immunocompromised Due to HIV or Other Conditions

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# MONKEYPOX

## Severe Disease (<1%)

- Atypical or persistent rash, coalescing or necrotic lesions (>100), new crops of lesions despite treatment with tecovirimat and other antivirals
- Multiple organ systems and associated comorbidities:
  - Ocular, oropharyngeal, pulmonary, neurologic, cardiac, urologic
- Obstructive lesions:
  - Exudative bowel lesions causing significant tissue edema and bowel obstruction
  - Severe sometimes necrotizing lymphadenopathy that can obstruct airways
- Lesions leading to stricture and scar formation resulting in significant morbidity such as urethral and bowel strictures, phimosis, and facial scarring.
- Secondary bacterial or fungal infections, sepsis and hemodynamic compromise

Source: HAN Archive - 00475 | Health Alert Network (HAN) | cdc.gov

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# MONKEYPOX

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**TEST FOR HIV  
AND OTHER STIS**

Source: HAN Archive - 00475 | Health Alert Network (HAN) | cdc.gov

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# MONKEYPOX

## Managing Monkeypox in People with HIV

Morbidity and Mortality Weekly Report

### Interim Guidance for Prevention and Treatment of Monkeypox in Persons with HIV Infection — United States, August 2022

Jesse O'Shea, MD<sup>1,2</sup>; Thomas D. Filardo, MD<sup>1,2,3</sup>; Sapna Ramrah Marth, MD<sup>1</sup>; John Weiner, MD<sup>1</sup>; Brett Petersen, MD<sup>1</sup>; John T. Brooks, MD<sup>1</sup>

US Department of Health and Human Services/Centers for Disease Control and Prevention MMRW / August 12, 2022 / Vol. 71 / No. 32 1023

Follow here for updates:

<https://www.cdc.gov/poxvirus/monkeypox/clinicians/people-with-HIV.html>

Source: <https://www.cdc.gov/mmwr/volumes/71/ser/mm7132e4.htm> and <https://www.cdc.gov/poxvirus/monkeypox/clinicians/people-with-HIV.html> Slide 32

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# MONKEYPOX

## Managing Monkeypox in People with HIV

- **People with advanced HIV or who are not virologically suppressed**
  - Increased risk of severe disease related to monkeypox virus infection
- **Post-exposure prophylaxis with vaccine**
  - Available for MSM with known or presumed exposure to monkeypox
  - Vaccination with JYNNEOS is considered safe for people with HIV
- **Antiviral treatments are available for people with a monkeypox infection**
  - No major interactions with antiretroviral medications if already taking ART
  - Delay starting long-acting cabotegravir/rilpivirine for two weeks after completing tecovirimat treatment

Source: <https://www.cdc.gov/mmwr/volumes/71/ser/mm7132e4.htm> and <https://www.cdc.gov/poxvirus/monkeypox/clinicians/people-with-HIV.html> Slide 33

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# MONKEYPOX

## Treatments for Monkeypox



- **Tecovirimat (TPOXX)**, FDA-approved for smallpox and available through an investigational new drug (IND) protocol from CDC for monkeypox
- Other drugs possibly useful but no human data about their effectiveness against monkeypox:
  - Vaccinia Immune Globulin Intravenous (VIGIV)
  - Cidofovir antiviral medication
  - Brincidofovir

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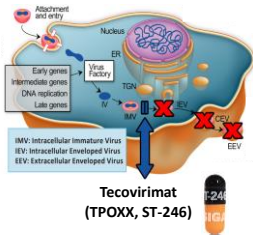
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## Antipox therapeutic: Tecovirimat



- Tecovirimat inhibits the viral envelope formation (“wrapping complex”) during intracellular maturation
- Target: vaccinia protein 37 (VP37)
- Blocking VP37 thus stops further spread of virus
- Approved under “Animal Rule” for smallpox (not monkeypox)
- No human data on effectiveness

Source: [https://www.siga.com/wp-content/uploads/2022/06/TPOXXFactSheet\\_2022.pdf](https://www.siga.com/wp-content/uploads/2022/06/TPOXXFactSheet_2022.pdf), Hruby 2006, Microbe. Slide 35

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## FDA Monkeypox Response

### Risk of Viral Resistance to TPOXX

(Updated September 15, 2022)

- **In cell culture:** monkeypox virus VP37 drug target very susceptible to single amino acid substitution that was associated with high-level phenotypic resistance
- **In non-human primates:** monkeypox-infected animals treated with tecovirimat developed VP37 amino acid substitutions and succumbed to disease
- **In an individual with progressive vaccinia infection:** VP37 amino acid substitutions were detected after tecovirimat-treated



Source: <https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/fda-monkeypox-response#therapeutics> Slide 36

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## Guidance for Tecovirimat Use Under Expanded Access Investigational New Drug Protocol during 2022 U.S. Monkeypox Outbreak (Updated September 15, 2022)

### Tecovirimat should be considered for use in people who have:

- **Severe disease:** hemorrhagic disease, large number of lesions, encephalitis, sepsis, ocular/periorbital infections, other conditions requiring hospitalization
- **Sensitive anatomic areas** with lesions that could lead to severe sequelae (e.g., pharynx, penile foreskin, vulva, vagina, urethra, anus)
- **High risk for severe disease**
  - Immunocompromise
  - Pediatric populations
  - Pregnant or breastfeeding
  - Condition affecting skin integrity (e.g., atopic dermatitis, eczema)

Source: <https://www.cdc.gov/poxvirus/monkeypox/clinicians/Tecovirimat.html> Slide 37

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### CDC Clinical Consultation Service

Available 24/7 through health departments

Can facilitate

- Treatment with stockpiled VIGIV, IV TPOXX, and in the future, brincidofovir
- Determination of antibody response (i.e., serology)
- Evaluation of certain biopsy and autopsy specimens for orthopoxviruses
- Genome sequencing, including to evaluate for tecovirimat resistance
- Case specific advice based on accumulated clinical knowledge

Learn together about clinical manifestations so that national guidance about use of stockpiled therapeutics and other countermeasures can be made accordingly

Consider consultation with CDC Monkeypox Response Clinical Escalations Team (email [eocevent482@cdc.gov](mailto:eocevent482@cdc.gov) or healthcare providers may contact the CDC Emergency Operations Center at (770) 488-7100)

Source:

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Tecovirimat should be considered for use in people who have

- **Severe disease:** hemorrhagic conjunctivitis, meningitis, encephalitis, sepsis, oculogingivitis, or severe skin disease
- **Severe disease progression:** severe skin disease (e.g., necrotic skin lesions)
- **High risk for severe disease:**
  - Immunocompromised
  - Pediatric populations
  - Pregnant or breastfeeding
  - Condition affecting skin integrity (e.g., atopic dermatitis, eczema)

**What about people with mild disease that might progress to severe illness with pain?**

Source: <https://www.cdc.gov/poxvirus/monkeypox/clinicians/tecovirimat.html>

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- AIDS Clinical Trials Group study A5418
- Opportunity for persons with minimal or mild disease to access treatment and participate in research
  - >65 clinical centers enrolling (1<sup>st</sup> enrollee September 12, 2022)
  - Fully remote option under development
- Randomized 2:1 to receive drug-vs-placebo for 14 days
  - If evidence of disease progression after 5 days, can receive tecovirimat
- People who are at higher risk for severe disease because of their age or their medical history will be assigned to receive open-label tecovirimat for 14 days

Source: <https://actgnetwork.org/studies/a5418-study-of-tecovirimat-for-human-monkeypox-virus-stomp/>

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Call Center: 1-855-876-9997 (U.S. only)

STOMPTPOXX.org

Source: <https://actnetwork.org/studies/45418-study-of-treatments-for-human-monkeypox-virus-stomp/>

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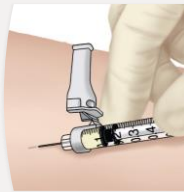
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## MONKEYPOX

### JYNNEOS Vaccine

- JYNNEOS vaccine considered safe for people with HIV
  - Live but non-replicating virus vaccine (modified vaccinia Ankara, or MVA)
- Licensed for prevention of smallpox and monkeypox
- Mild side effects compared with ACAM2000 (a live replicating vaccine)
- Distributed from the Strategic National Stockpile



Source: [JYNNEOS Vaccine | Monkeypox | Poxvirus | CDC](#)

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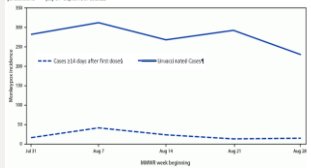
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## MONKEYPOX

### Vaccine Effectiveness

IRR = 14.3 (95% CI = 5.0–41.0)

FIGURE. Weekly monkeypox incidence\* by first dose vaccination status† among males aged 18–49 years eligible for vaccination†—2022, jurisdictions\*\* July 31–September 3, 2022



“Among persons eligible for MPX vaccination, unvaccinated persons had 14-fold greater risk of MPX compared with vaccinated persons who received one dose of JYNNEOS vaccine”

\* Incidence is defined as confirmed cases of MPX. \*\* Jurisdictional incidence of MPX was reported by 10 jurisdictions: Arizona, California, Colorado, Connecticut, Florida, Georgia, Illinois, Michigan, Minnesota, and New York. † Eligible for vaccination if aged 18–49 years and unvaccinated or aged 18–49 years and vaccinated. ‡ Incidence is defined as confirmed cases of MPX. § Incidence is defined as confirmed cases of MPX. ¶ Incidence is defined as confirmed cases of MPX. \*\* Jurisdictional incidence of MPX was reported by 10 jurisdictions: Arizona, California, Colorado, Connecticut, Florida, Georgia, Illinois, Michigan, Minnesota, and New York. † Eligible for vaccination if aged 18–49 years and unvaccinated or aged 18–49 years and vaccinated. ‡ Incidence is defined as confirmed cases of MPX. § Incidence is defined as confirmed cases of MPX. ¶ Incidence is defined as confirmed cases of MPX.

Source: <https://www.cdc.gov/mmwr/volumes/71/wr/mm7140a3.htm>

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## Communication Challenges

- Communication efforts calling out gay and bisexual men have left the community feeling alienated and stigmatized
- Media has at times been homophobic and racist
- Community is reminded of HIV epidemic, being blamed for another disease outbreak
- Criticism for addressing gay and bisexual men but also for not calling out that this population is disproportionately affected
- How do you disseminate messages to a specific audience without stigmatizing them?

Source: [Monkeypox isn't like HIV, but gay and bisexual men are at risk of unfair stigma \(theconversation.com\)](https://www.theconversation.com/monkeypox-isn-t-like-hiv-but-gay-and-bisexual-men-are-at-risk-of-unfair-stigma)

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## Community Outreach & Partnership Engagement (COPE) Team

- Using lessons learned from STI/HIV communication
  - Gay, bisexual, and other men who have sex with men leading much of the response efforts
- Engaging gay and bisexual men where they are
- Using non-stigmatizing, gender neutral, and sex positive language for general population messaging



Image Source: [Meet Dr. Demetre Daskalakis, Biden's New Weapon Against HIV \(hivplusmag.com\)](https://www.hivplusmag.com)

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## MONKEYPOX

**Gay, bisexual, and other men who have sex with men are taking steps to protect themselves and their partners from monkeypox.**

? %

reduced number of sex partners

? %

reduced one-time sexual encounters

? %

reported reducing sex with partners met on dating apps or at sex venues

Source: [Impact of Monkeypox Outbreak on Select Behaviors | Monkeypox | Pwvirus | CDC](https://www.cdc.gov/mmwr/mmwr-reports/monkeypox-outbreak-on-select-behaviors)

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# MONKEYPOX

Gay, bisexual, and other men who have sex with men are taking steps to protect themselves and their partners from monkeypox.



Source: Impact of Monkeypox Outbreak on Select Behaviors | Monkeypox | Poxvirus | CDC Slide 49

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# MONKEYPOX

Gay, bisexual, and other men who have sex with men are taking steps to protect themselves and their partners from monkeypox.



Source: Impact of Monkeypox Outbreak on Select Behaviors | Monkeypox | Poxvirus | CDC Slide 50

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# MONKEYPOX

## Summary

- Monkeypox is disproportionately affecting sexually active MSM, a population known to be at increased risk of STIs, including HIV
  - All persons undergoing evaluation for monkeypox should be tested for STDs and HIV
- In the current outbreak, clinical disease is characterized by predominance of anogenital lesions and less prodrome
  - Consider a broad differential in suspect patients
- Persons with advanced HIV are experiencing severe disease
  - Test all persons of unknown HIV status for HIV
- Tecovirimat may be used under an EA-IND protocol
  - Consider reserving use of drug for severely ill or high-risk patients
  - Refer persons with mild or minimal disease to STOMP Study

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1-800-CDC-INFO (232-4636)  
 TTY: 1-888-232-6348 www.cdc.gov

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### Tecovirimat and the Treatment of Monkeypox — Past, Present, and Future Considerations

Adam Sherwat, M.D., John T. Brooks, M.D., Debra Birnkrant, M.D., and Peter Kim, M.D. (NEJM August 18, 2022)

**Need to balance competing ethical principles; reminiscent of HIV treatment era**

- “*Judicious use*” – ensure treatments are safe (‘do not harm’) and effective
- “*Compassionate use*” – ensure access to potentially effective medicine for persons with severe or life-threatening illness



ACT UP protesters outside the FDA headquarters in Bethesda, Maryland on October 11, 1986. They denounced the release of zalcitabine (ddC) for those living with HIV/AIDS with ongoing protests; ‘never had a chance’ to get the medicine and a trial for the sake of the FDA. (AP/Wide World)

Source: Sherwat 2022. *N Engl J Med* Slide 53

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### Tecovirimat and the Treatment of Monkeypox — Past, Present, and Future Considerations

Adam Sherwat, M.D., John T. Brooks, M.D., Debra Birnkrant, M.D., and Peter Kim, M.D. (NEJM August 18, 2022)

**Need to balance competing ethical principles; reminiscent of HIV treatment era**

- NIH: conduct definitive efficacy trial in parallel
- CDC & FDA: make drug available investigational new drug protocol
  - Streamlined the substantial paperwork requirement
- ASPR took drug from strategic national stockpile
  - Prepositioned it at the state level
  - Developed electronic ordering system



Source: Sherwat 2022. *N Engl J Med* Slide 54

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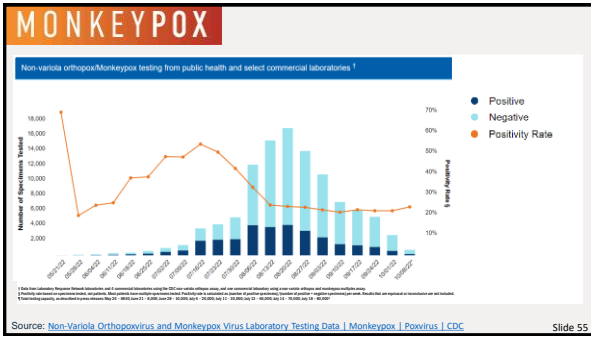
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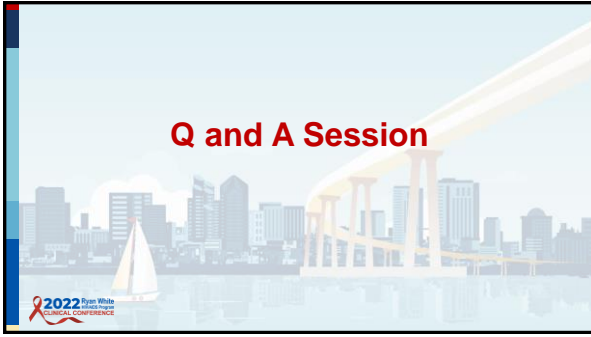
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