# Monkeypox:
# Perspectives from the US

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# Outline

- Background
- Clinical manifestations
- Case studies from Massachusetts General Hospital
- Monkeypox case trends from the US
- JYNNEOS vaccination
- Treatment (including new randomized trials)

# Microbiology

- Disease caused by infection with the *Monkeypox virus*
  - Closely related to *Variola* (cause of smallpox) and *Vaccinia* (smallpox vaccine)
- Probable small rodent reservoir in Central/West Africa
- Named due to initial identification in a research monkey colony
- Prior to the current outbreak, low number of cases outside of Africa

# Microbiology

- Outbreak first detected in May 2022
- Hypothesized to be the result of “superspreader” events
- Likely human-to-human transmission in Nigeria at least as early as 2017.
- Perhaps due to loss of *Vaccinia* population immunity, urbanization
- 80% of these cases were adults 21-40 years of age (3:1 M:F).
- More deposited genomic data suggests at least low-level cryptic transmission outside of Africa since at least as early as 2021
- Mutations have been noted in an immunogenic surface glycoprotein
- Unclear if any mutations have increased inherent transmissibility

Nguyen et al., 2021; Jolly and Scaria, 2022; Isidro et al., 2022

# Clinical presentation

- Prior to the eruption of the rash, many (but not all) have a prodrome of systemic symptoms
- The prodrome may be coincident with the eruption of rash
- Feverishness, chills, cervical and inguinal lymphadenopathy, pharyngitis, and malaise are all common
- Proctitis (anorectal lesions), urethritis (urethral lesions), and odynophagia (oropharyngeal lesions) have been seen as well

Thornhill et al., 2022; Martinez et al, 2022

# Monkeypox evaluation

- **History**:
  - Timeline of illness: date of rash onset and prodromal symptoms, if present.
  - Rash characteristics (body site(s), presence of pain/itching, previous similar rash?)
  - Prodrome characteristics (feverishness, malaise, LAD, myalgias, sore throat, proctitis)
  - History of presumptive STI or cellulitis diagnosis that did not improve on empiric antibiotics
  - Epidemiologic factors: number and gender of sexual partners in past month, date of last sexual contact, type of sex (i.e. insertive or receptive oral, anal, vaginal), higher risk sex (anonymous or semi-anonymous partner, group sex, sex while using substances)
  - Close or intimate contact with someone with a previous rash, or with confirmed monkeypox infection

- **Past medical history:** HIV infection or other immunosuppression, history of sexually transmitted infections, eczema/atopic dermatitis

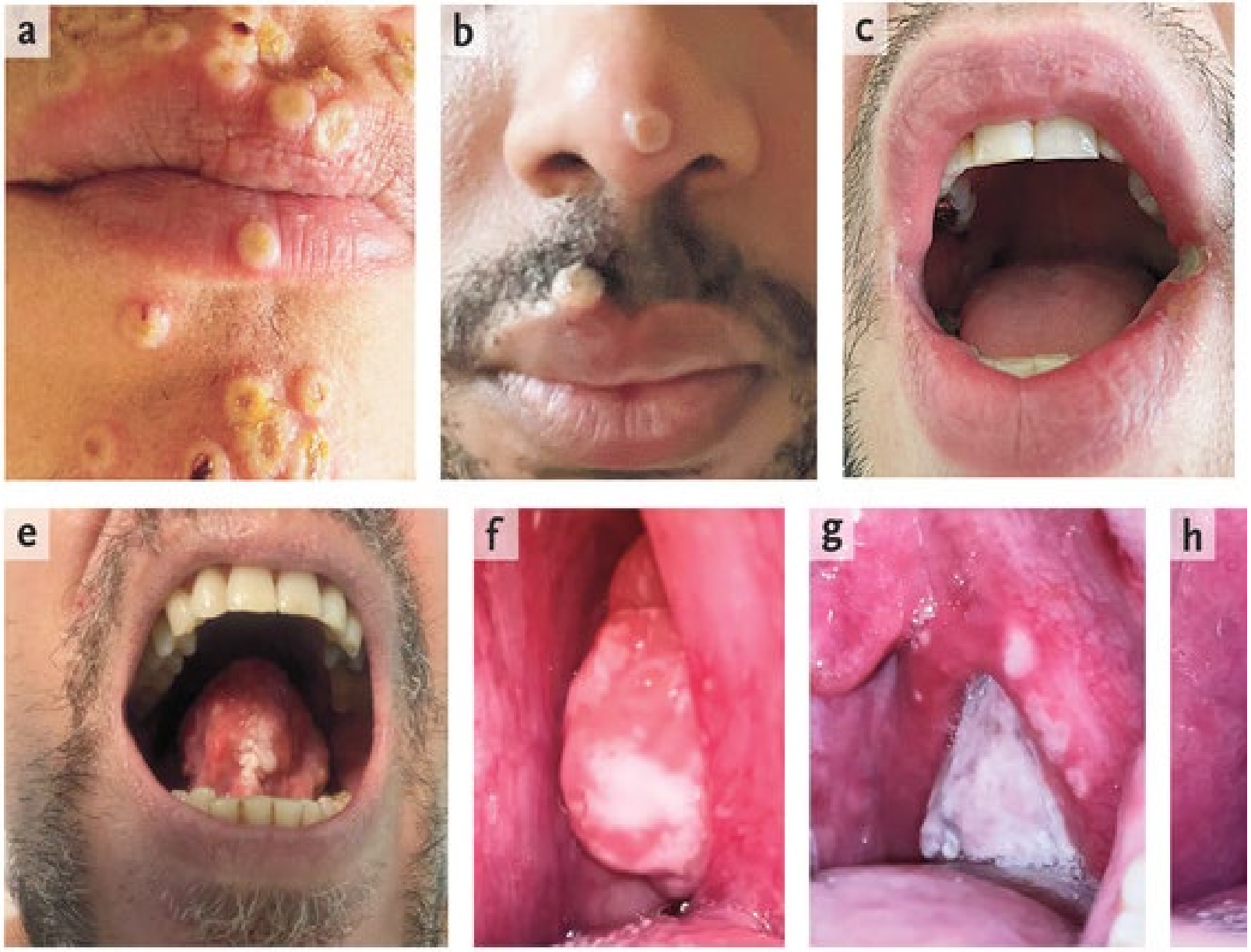
# Monkeypox evaluation

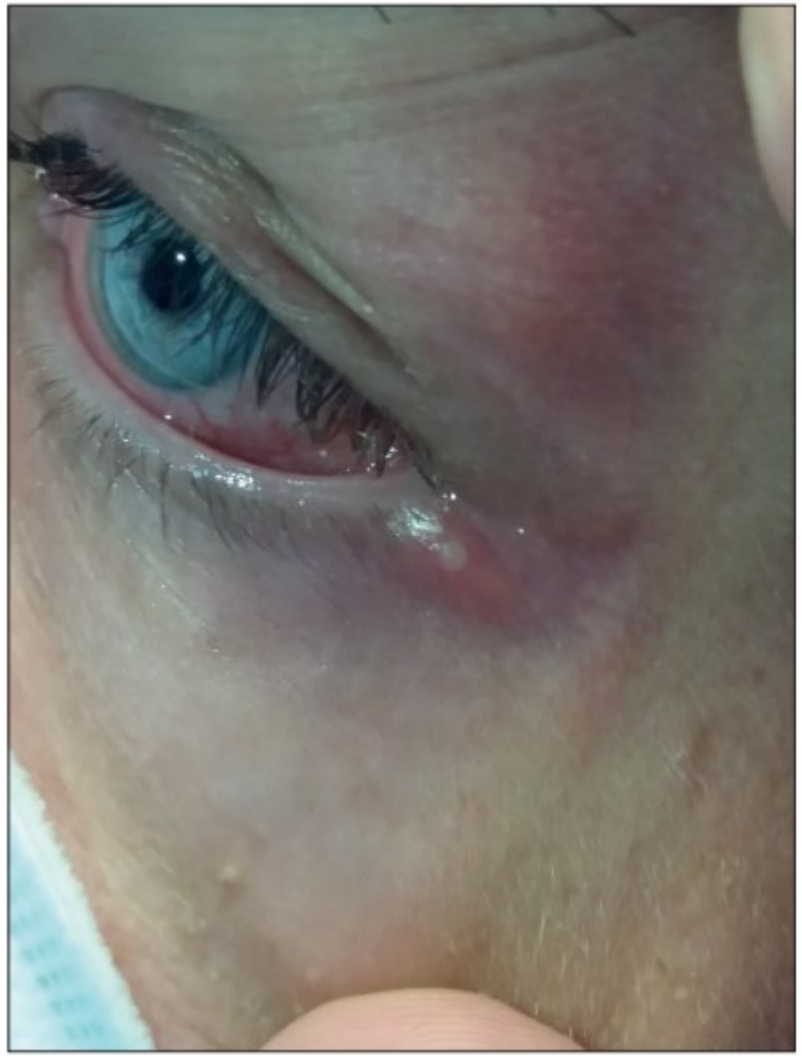
- **Physical exam:**
  - Vital signs, general examination for systemic toxicity (rare)
  - HEENT: Examination of the conjunctiva, complete oropharyngeal exam
  - Lymph: Cervical and inguinal
  - Skin: Complete skin exam
  - GU: Complete examination including penis, scrotum, perineum, and anal/perianal region. Rectal examination if complaints of proctitis.

# Monkeypox evaluation

- **Non-monkeypox testing:**
  - Gonorrhea and chlamydia (throat, anorectal, urine).
  - Syphilis
  - HIV antibody/antigen
  - HIV viral load if sex in the past 2 weeks (and concern for acute HIV)

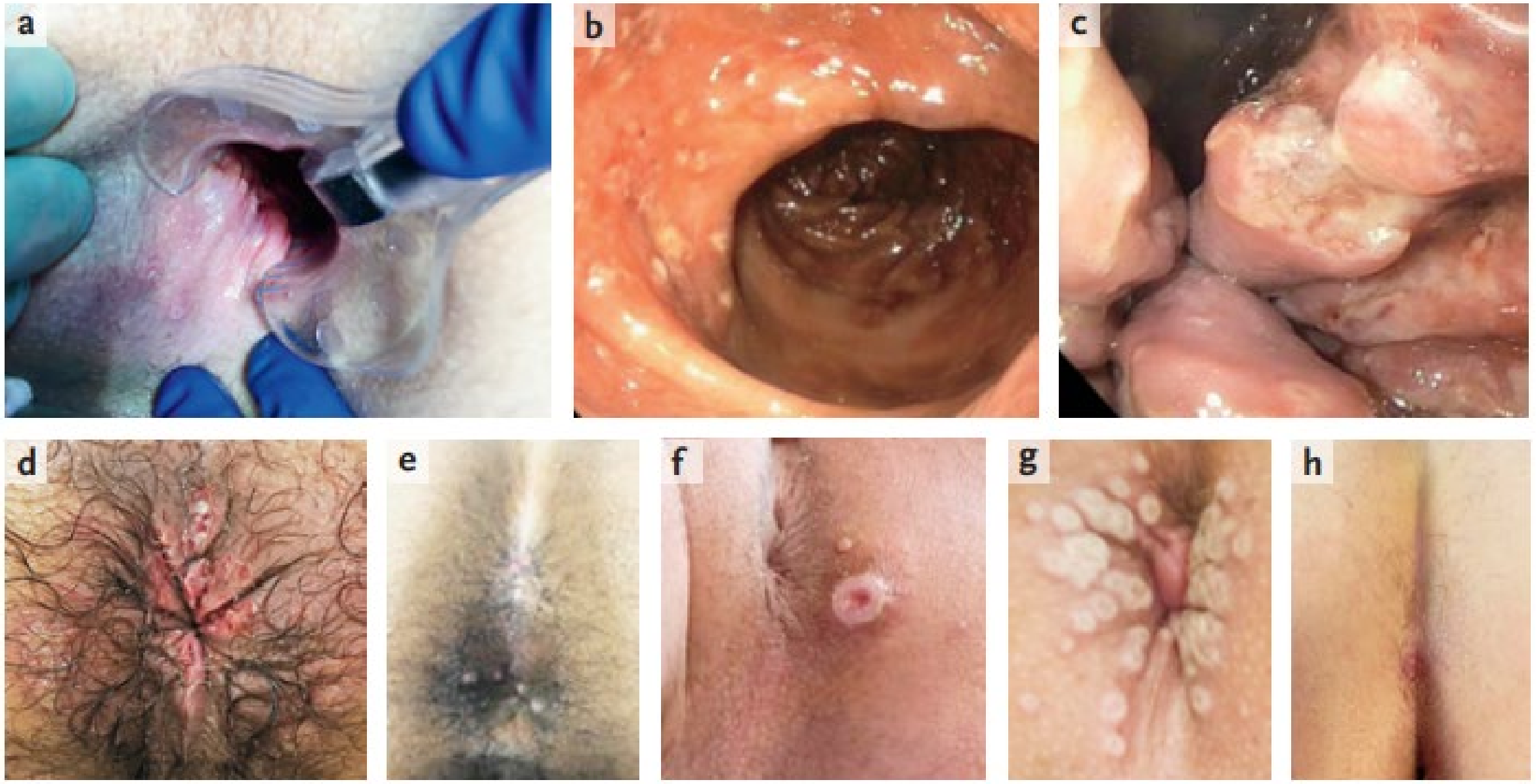
Bacterial STI's have been detected in up to 1/3 of patients with monkeypox. New HIV diagnoses are being made as well.



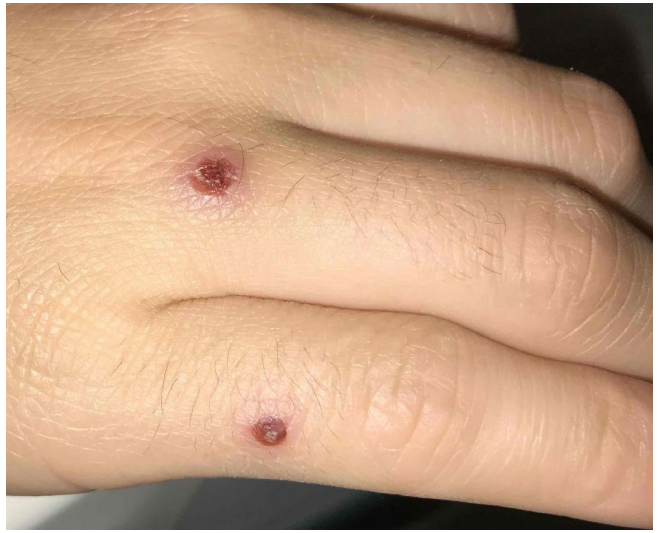



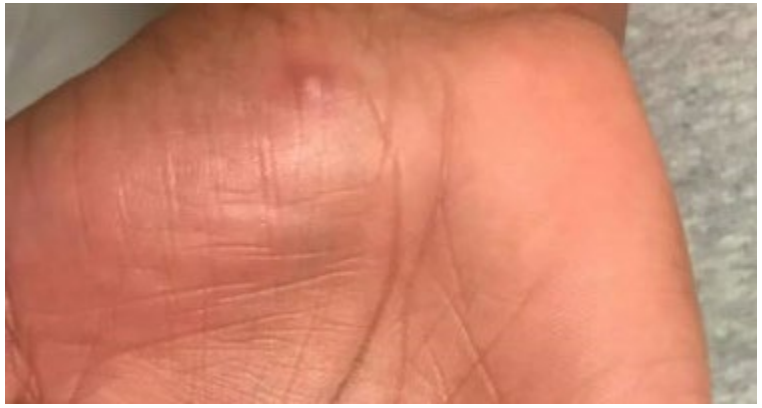
Thornhill *et al.*

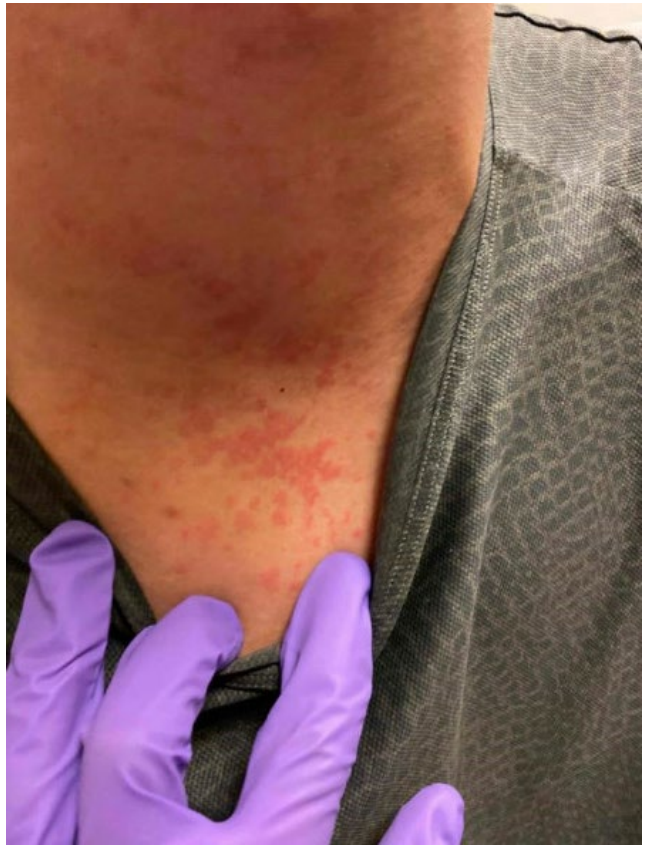
Benatti *et al.*

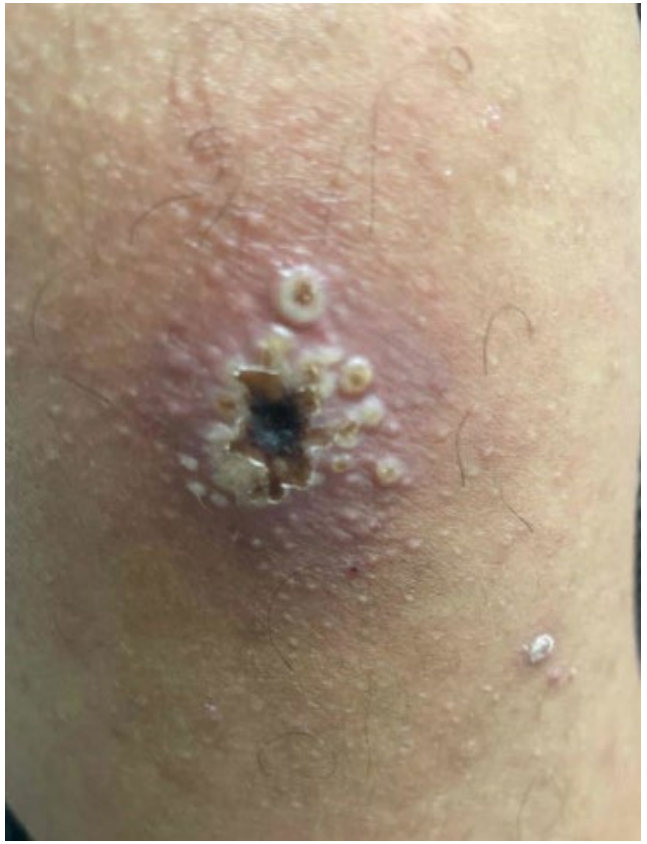



Thornhill *et al.*





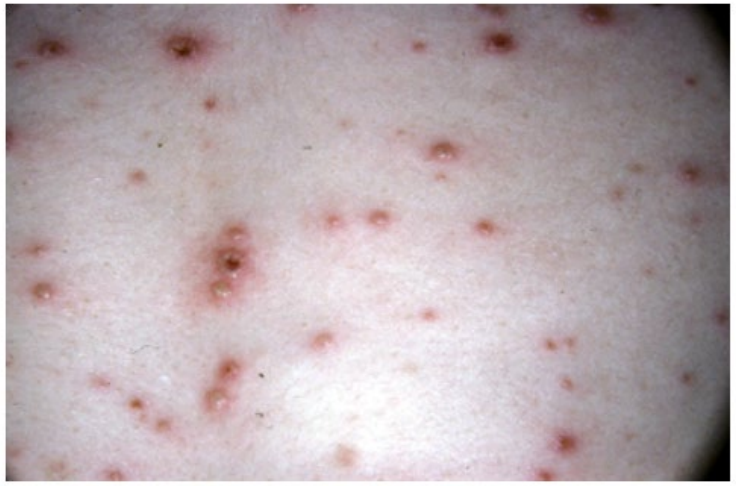




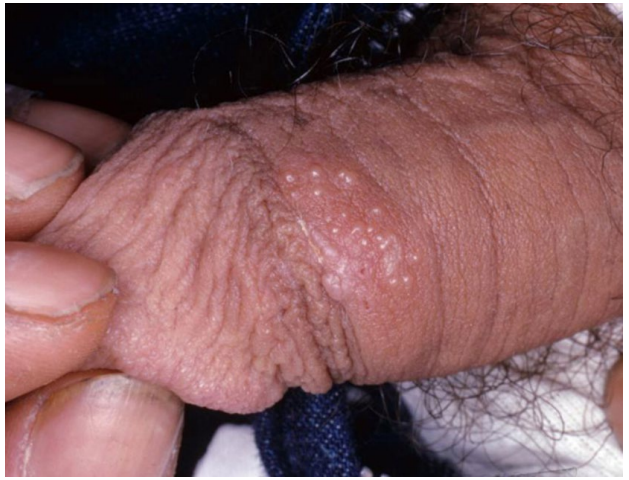
De-identified MGH patients

# Differential diagnosis

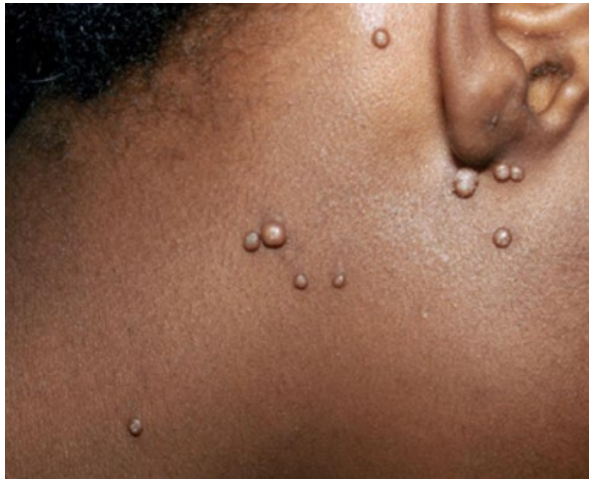
Varicella



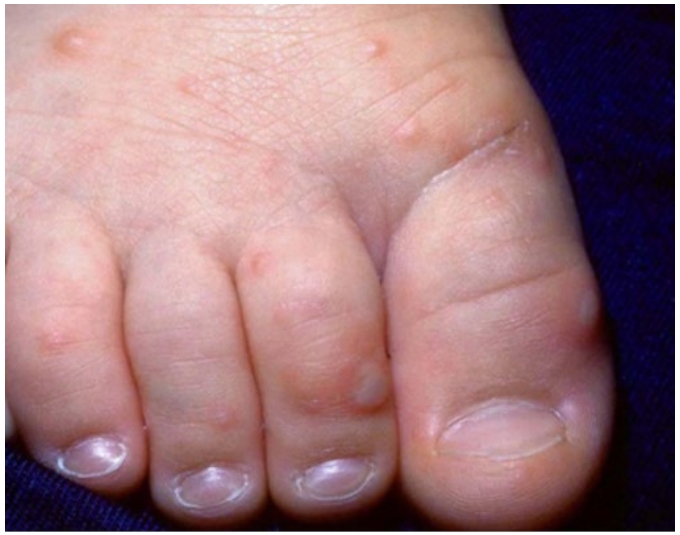
Herpes



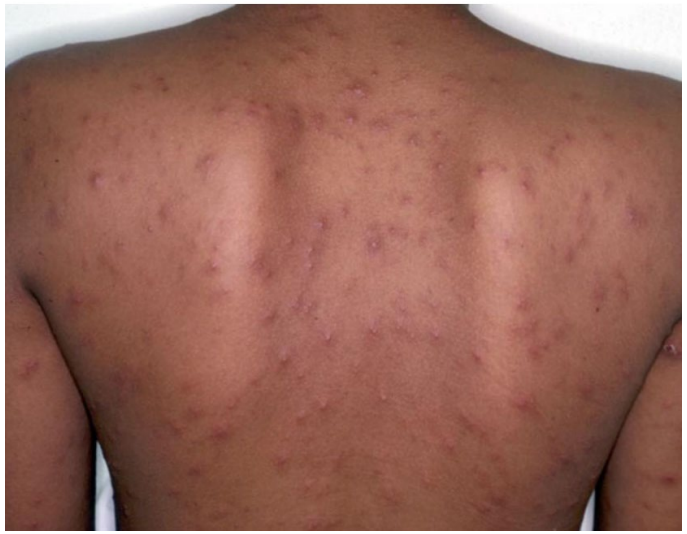
Molloscum



Hand-foot-and-mouth



Secondary syphilis



UpToDate

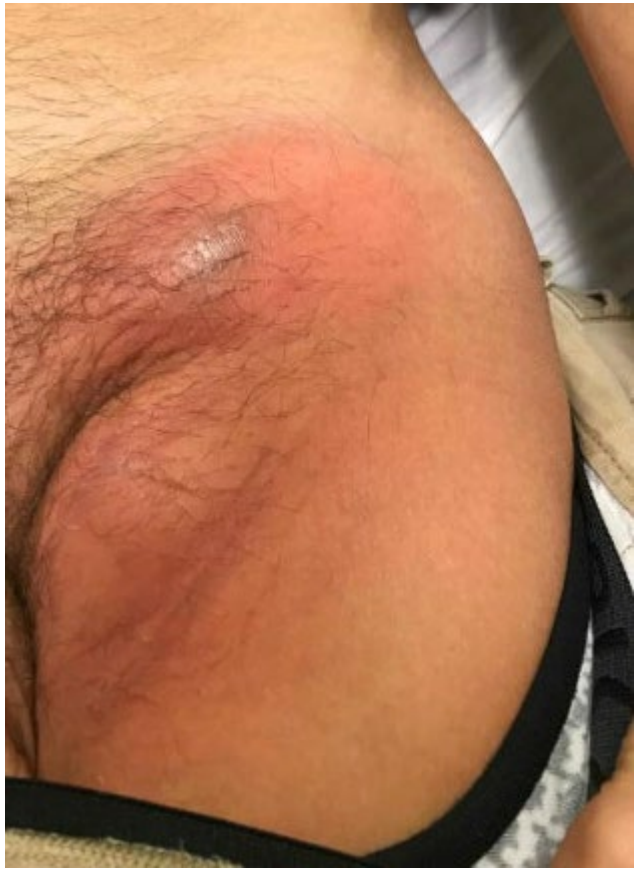
# Cases from Massachusetts General Hospital

# Case study 1

An otherwise healthy man in his thirties on HIV PrEP presented with painful left inguinal lymphadenopathy

One month prior, following multiple sexual encounters with men, he experienced fevers, chills, painless inguinal lymphadenopathy, and multiple umbilicated pustules which resolved.

One week later, he had recrudescence of fevers as well as pain and rapid growth of two distinct left inguinal lesions.

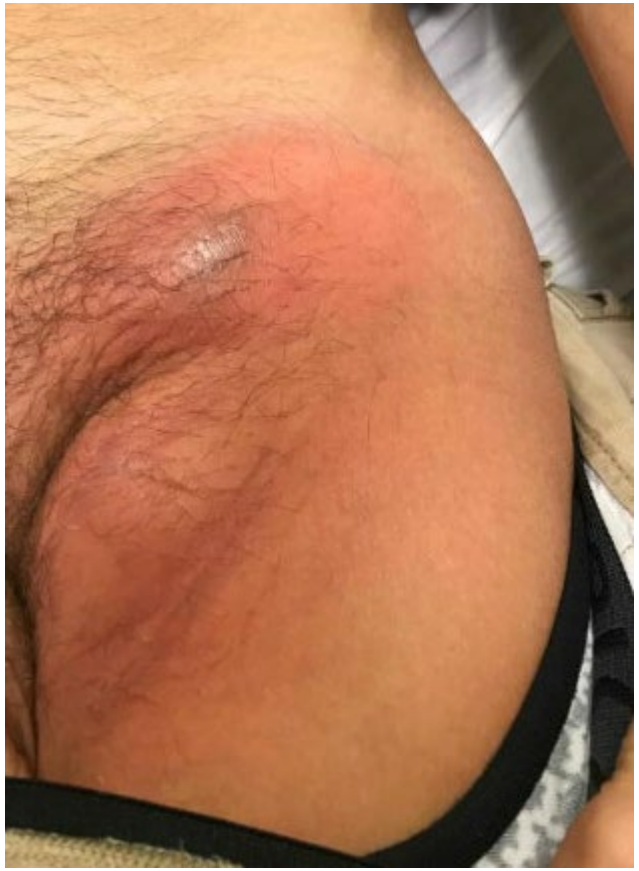


Phillips et al., submitted.

# Case study 1

- Cultures from surgical aspiration grew *Streptococcus pyogenes.*
- *Orthopoxvirus* PCR was positive as well.
- Anorectal *Chlamydia* NAAT was also positive.

**Diagnosis:** *Streptococcus pyogenes* lymphadenitis complicating human monkeypox infection, with presumptive concomitant lymphogranuloma venereum (LGV).



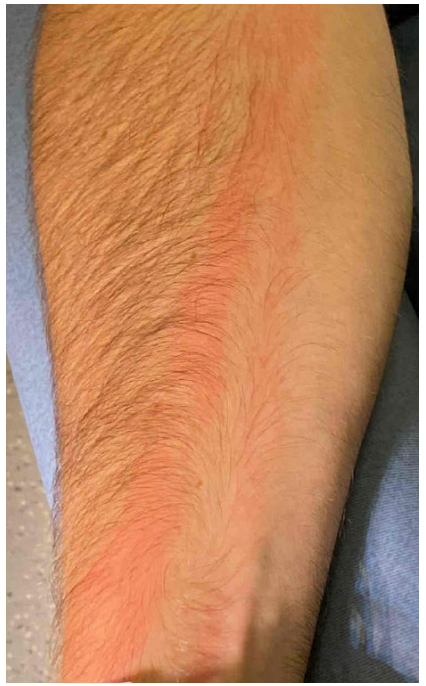
Phillips et al., submitted.

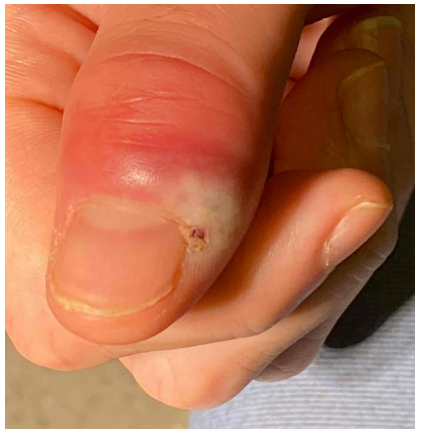
# Case study 2

An otherwise healthy man in his twenties presented to our emergency department with R thumb paronychia with lymphangitic streaking.

Labs on admission were remarkable for a moderate transaminitis.

He underwent I&D in the ER and was admitted to our orthopedic service. He was started on broad spectrum antibacterials.





De-identified MGH patient

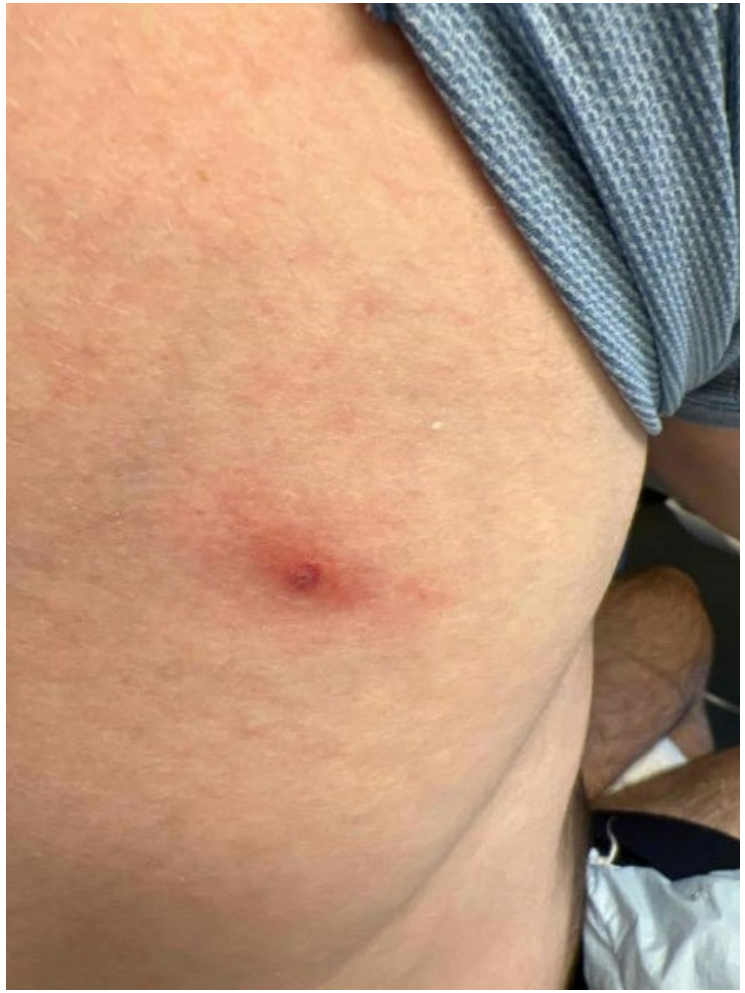
# Case study 2

Subsequently, two pustular lesions were noted on his thigh, and he had evolution of more pustules on his torso.

He reported sex with women, last 3 weeks prior as well as significant travel to different hotels the three prior weekends.

*Orthopoxvirus* PCR testing was positive.

**Diagnosis:** Monkeypox paronychia ("monkeypox whitlow") with bacterial superinfection and lymphangitic spread. Additional lesions either from auto-inoculation or secondary viremia. Possible monkeypox hepatitis.



De-identified MGH patient

# Case study 3

A man in his thirties with well-controlled HIV presented to our ED with 3-4 days of pubic lesions and 1-2 days of fever.

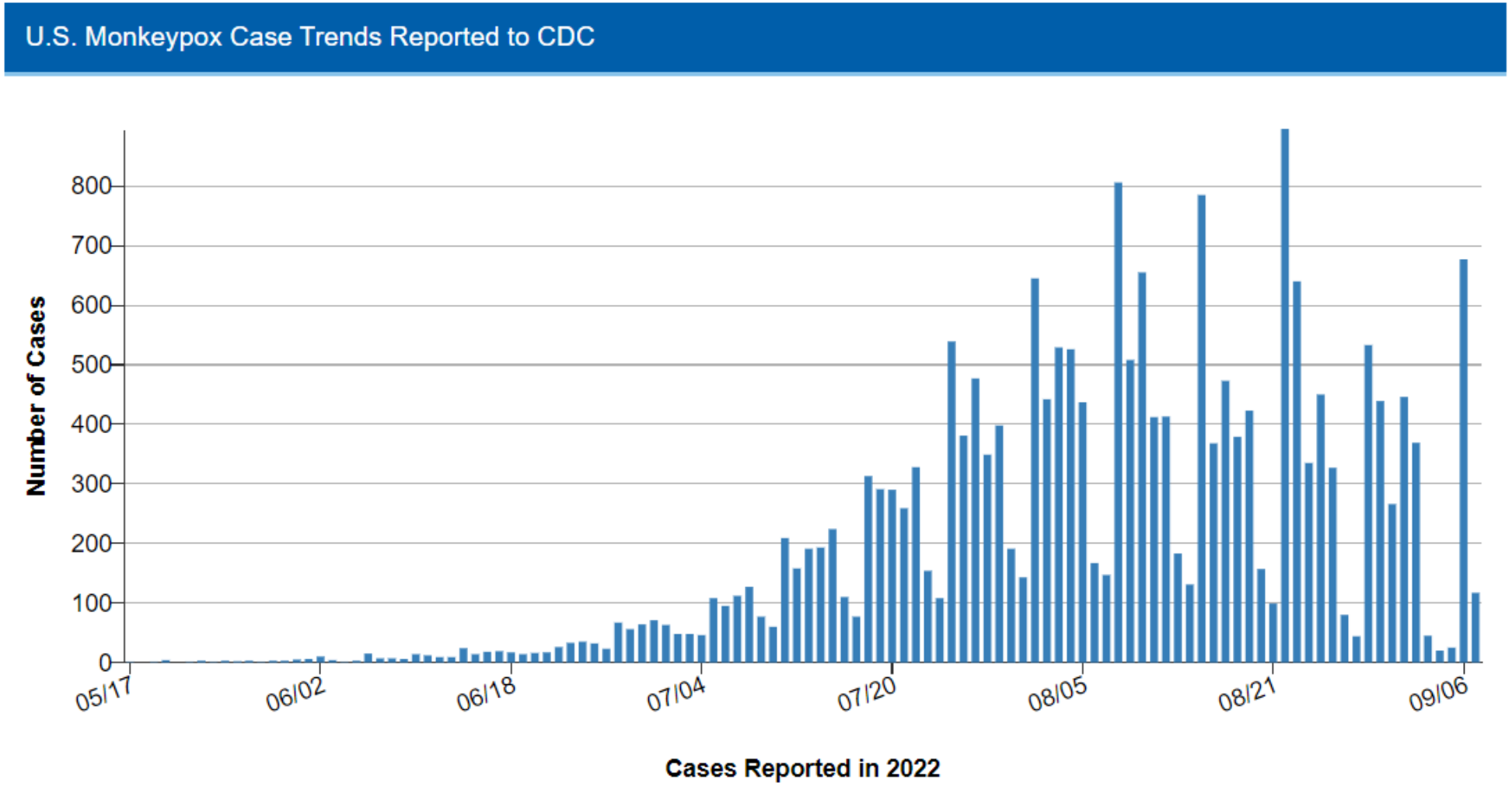
He was sexually active with male partners, last 6 days prior to his presentation.

He shaved his pubic area immediately prior to the onset of the rash and initially thought the rash was folliculitis.

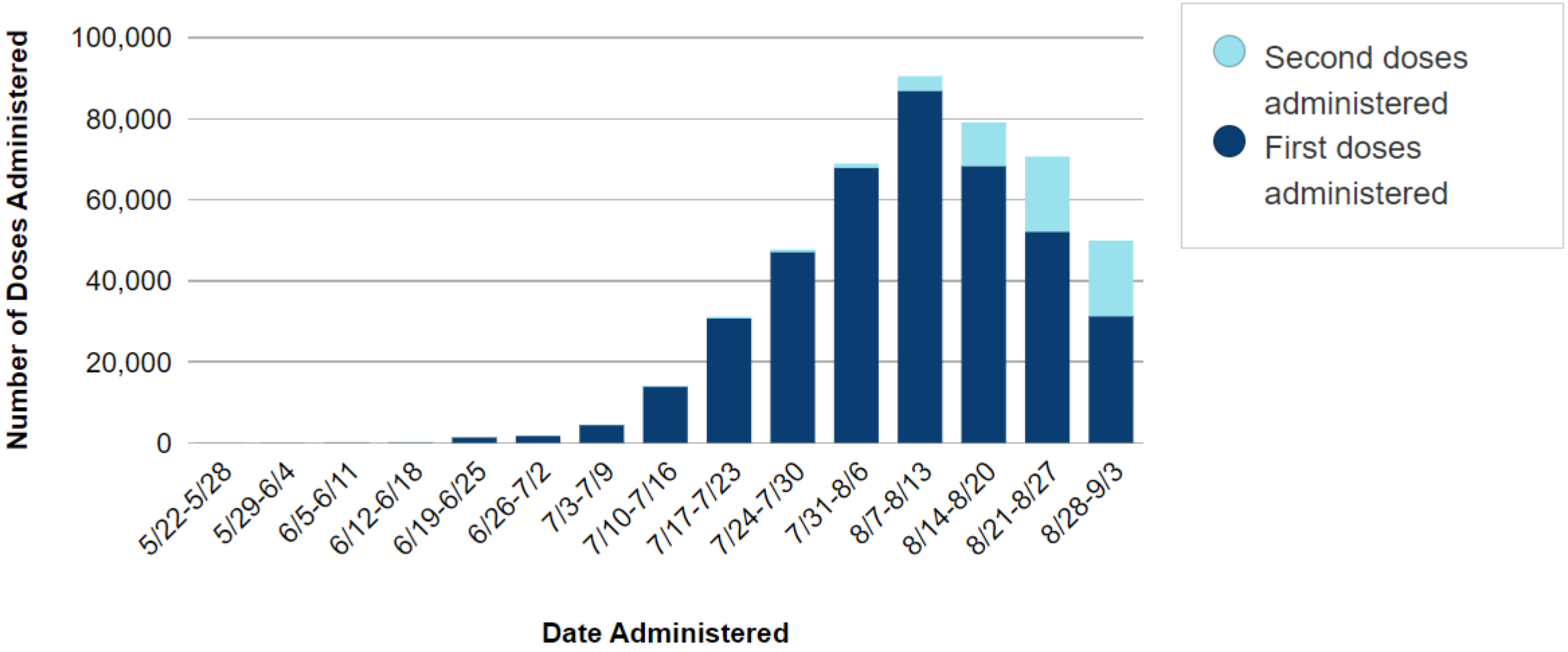
**Diagnosis:** Monkeypox infection with likely autoinoculation from shaving

De-identified MGH patient

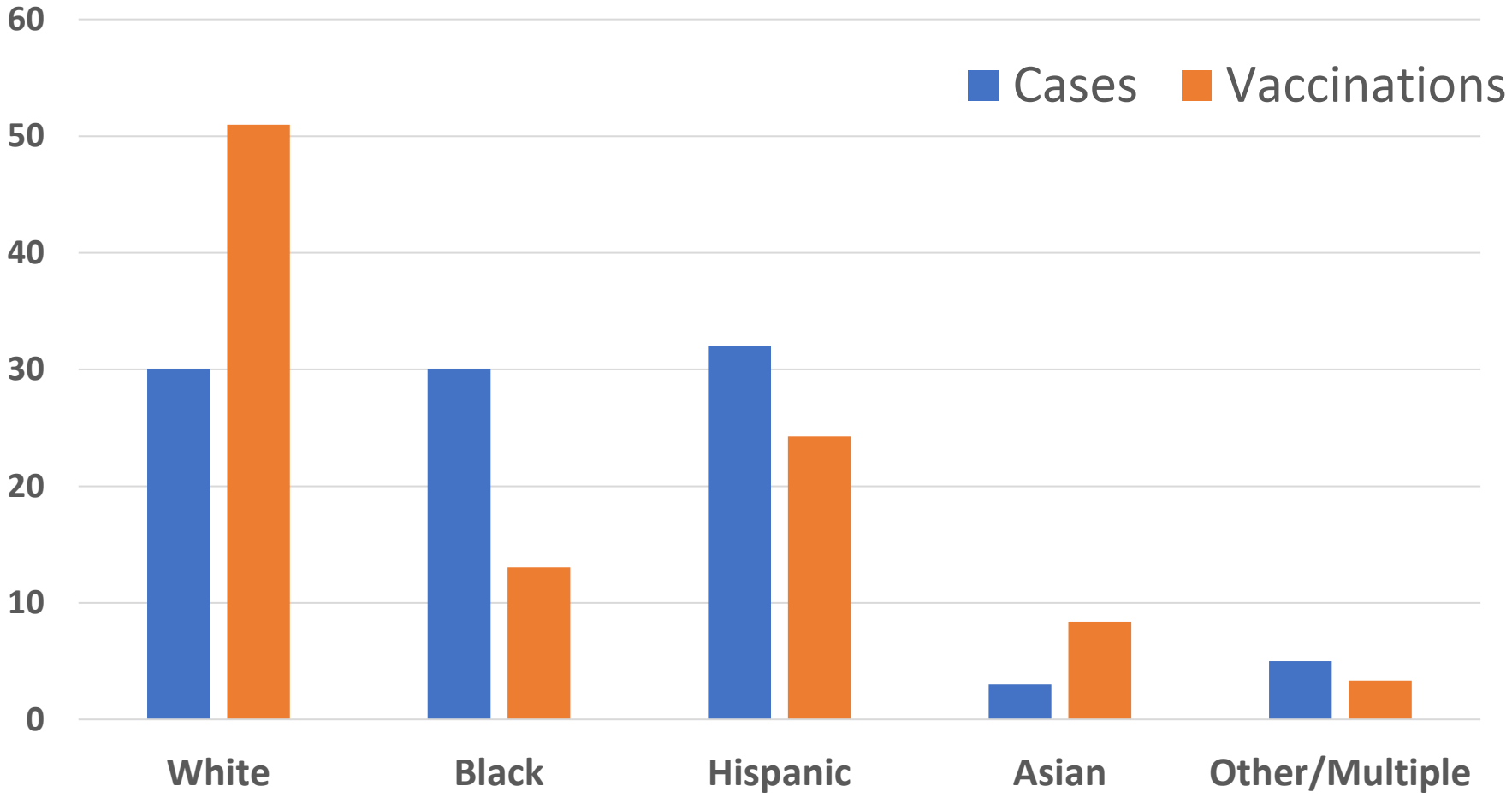
# Trends in Cases, United States, through 96



# Trends in Vaccination, United States, through 9/6



# Trends in Vaccination, by race, United States



# Behavioral trends, United States

48%

reduced number of sex partners

50%

reduced one-time sexual encounters

50%

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

# Massachusetts vaccination

- JYNNEOS vaccine (also known as Imvamune or Imvanex) is available to individuals who live and work in Massachusetts, prioritizing those who are most at risk of exposure to an individual with monkeypox.
  - Known contact identified by the public health department
  - The patient knows that a sexual partner in the past 14 days was diagnosed with monkeypox
  - The patient has had multiple sexual partners in the past 14 days
- Fourteen vaccination sites across the commonwealth. The MGH Sexual Health Clinic has administered almost 3,000 doses of vaccine.

# JYNNEOS

- Third-generation non-replicating derivative of the ACAM2000 *Vaccinia* vaccine. ACAM2000 itself is a second-generation derivative of the Dryvax vaccine that facilitate smallpox eradication.
- ACAM2000 is expected to cause similar side effects to Dryvax including high fevers and because it is replication-competent, can cause severe disease especially in immunocompromised patients.
- Because of the very low mortality in this epidemic of monkeypox, the safer JYNNEOS vaccination is being prioritized. JYNNEOS is safe for use in immunocompromised patients. However, initial JYNNEOS availability was limited.

Volz and Sutter, 2017

# JYNNEOS

- Grown in primary Chicken Embryo Fibroblast cells in sterile culture. Each 0.5 mL dose may contain:
  - ≤ 500 microgram chicken/egg protein
  - ≤ 0.4 microgram gentamicin
  - ≤ 0.005 microgram ciprofloxacin.

- Contraindications:
  - Severe allergic reaction (e.g., anaphylaxis) after a previous JYNNEOS dose
- Precautions:
  - History of severe allergic reaction (e.g., anaphylaxis) to gent or cipro
  - History of severe allergic reaction (e.g., anaphylaxis) to chicken/egg protein AND currently avoiding all chicken and egg products
  - Persons with precaution to vaccination may be vaccinated with a 30-minute observation period or referred for allergist-immunologist consultation prior to vaccination

- Two dose regimen: Day 0 and Day 28

Package insert, CDC JYNNEOS Standing Orders

# JYNNEOS

- Because of limited availability, an alternative regimen to the 0.5 mL subcutaneous standard regimen is endorsed
- In this alternative regimen, 0.1 mL is administered intradermally
- Intradermal vaccination has been found to yield robust immune responses to a number of antigens. It is limited by ease of vaccination as well as reactogenicity
- A study of around 150 healthy subjects who received subcutaneous to 150 who received intradermal revealed equivalent immune response (and hints at superiority) for intradermal administration
- Intradermal vaccination is endorsed for immunocompromised patients. A third dose is not currently recommended.
- Patients who received their first dose subcutaneous should receive their second intradermal.

Frey et al., 2015

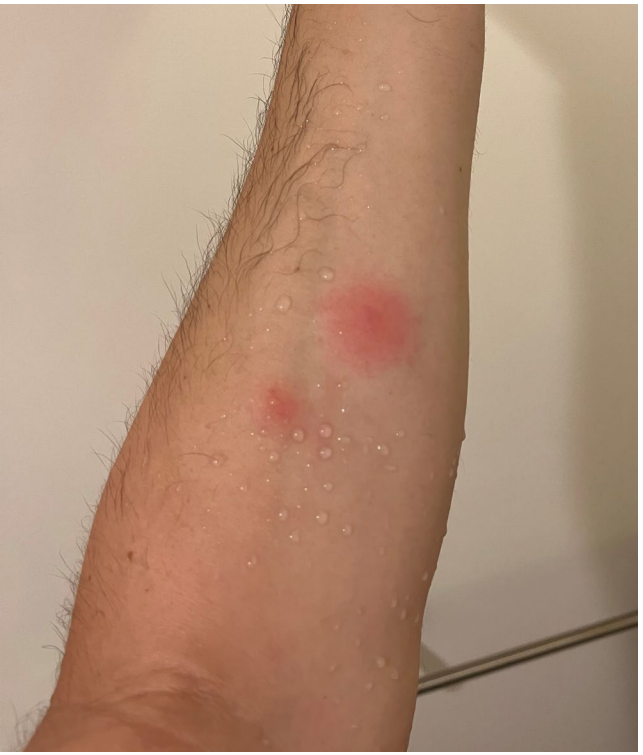
# JYNNEOS

- Less systemic reactogenicity with intradermal, but pronounced local reactogenicity
- After dose 2, nearly 80% of intradermal (compared to 40% of subcutaneous) had >30 mm of erythema or induration
- In mild cases, this looks like a “positive PPD.”
- Because of this, a unique contraindication for intradermal administration if history of keloid scarring

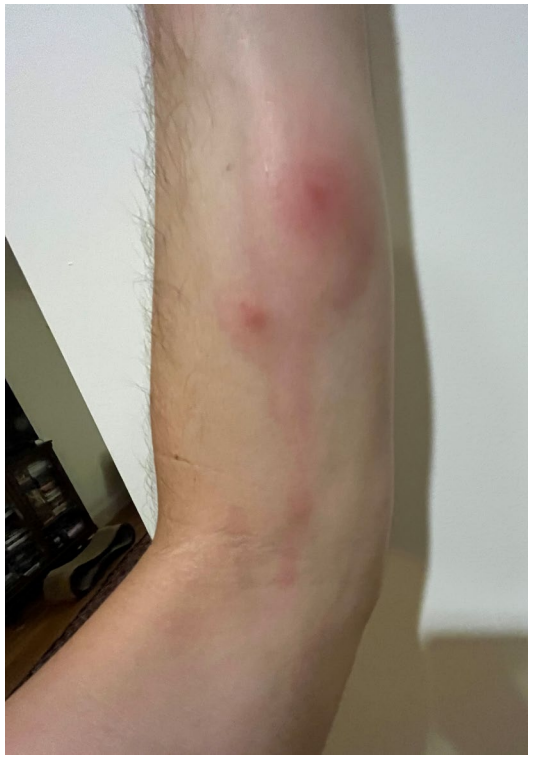
Frey et al., 2015

# JYNNEOS

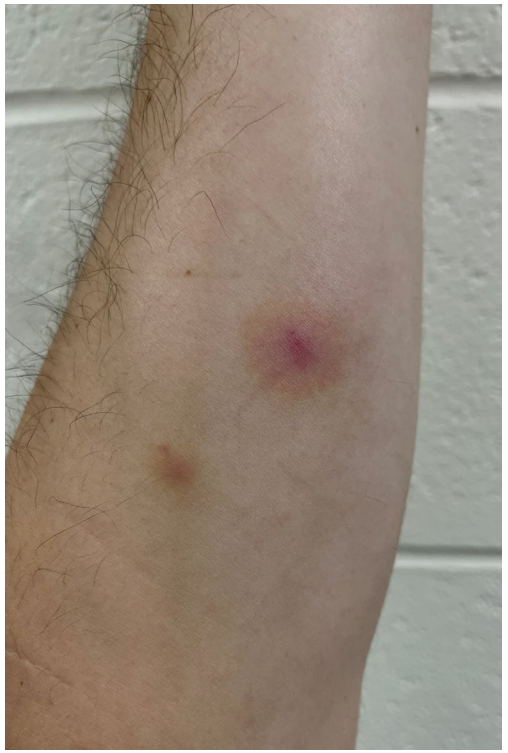
- In severe cases, induration, erythema, and pain can be marked and resemble bacterial infection



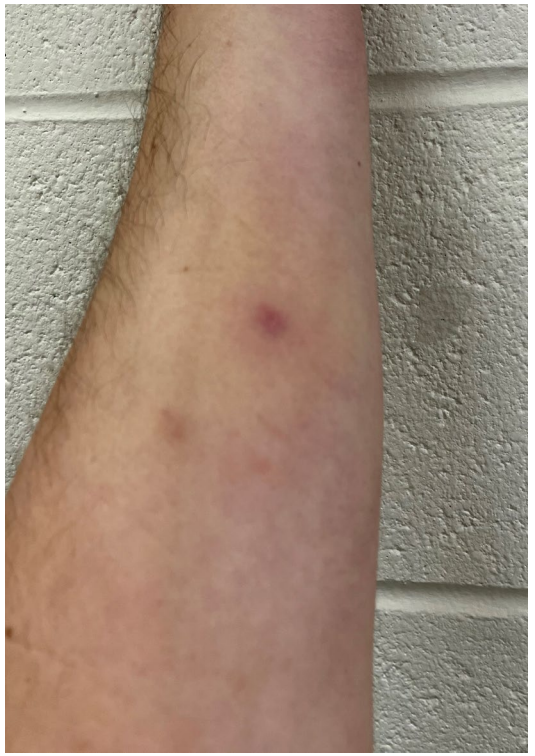
20 hours post dose 2



28 hours post dose 2



48 hours post dose 2

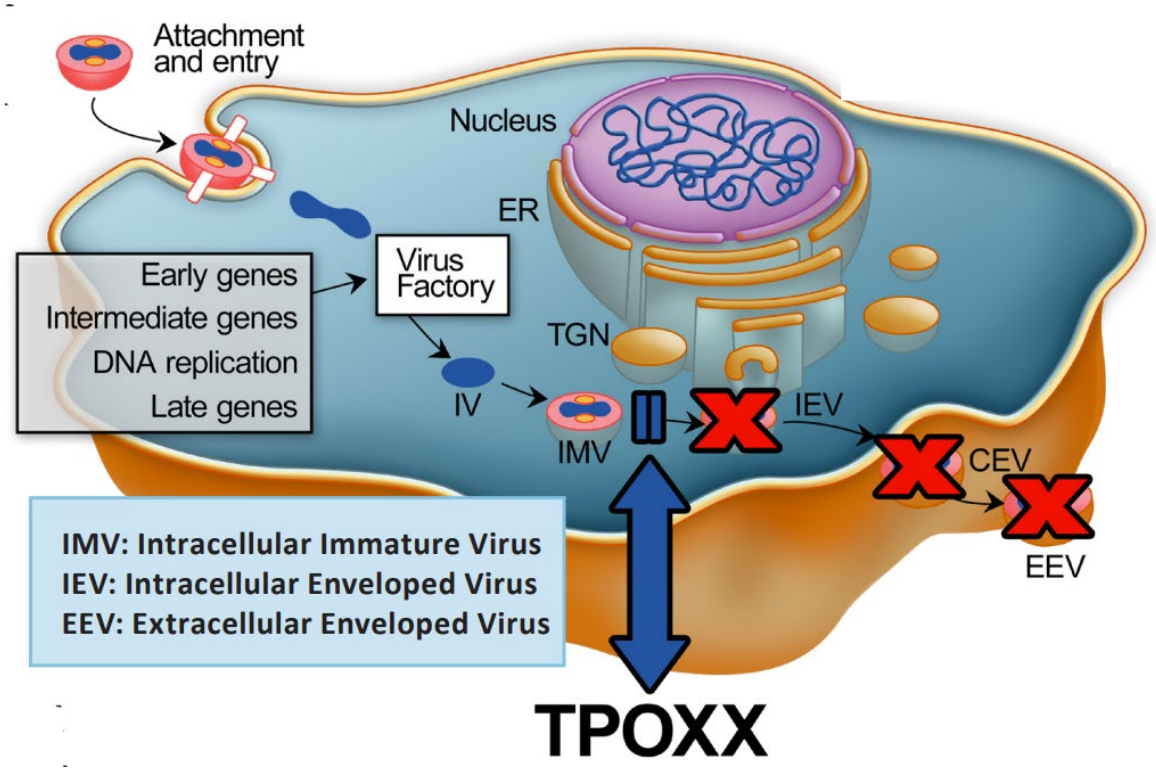


1 week post dose 2

**De-identified MGH patient**

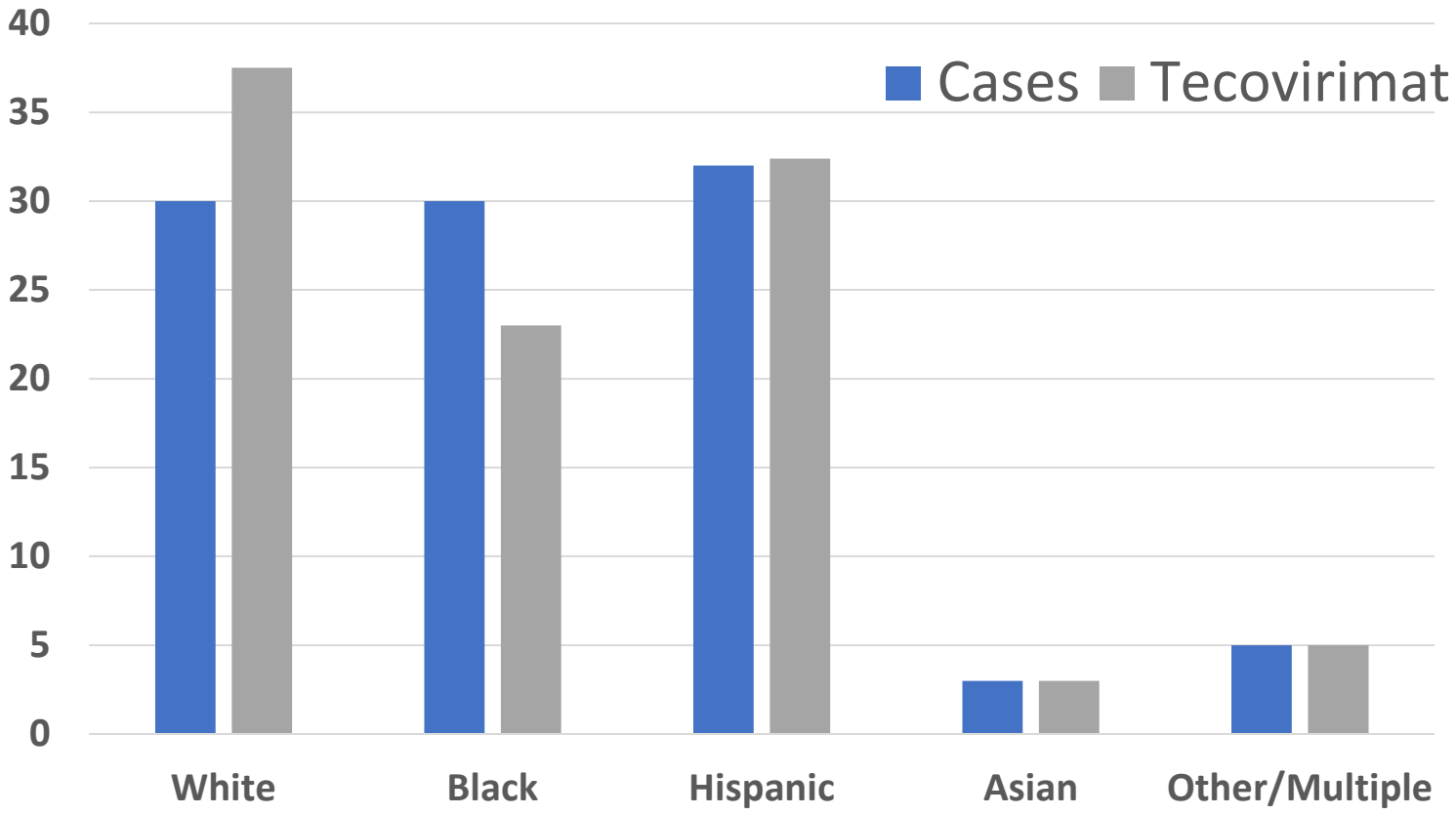
# Tecovirimat (TPOXX)

- Mechanism of action: Blocking secondary viral envelope formation
- FDA approved (under the “Animal Rule”) for the treatment of smallpox in adults and children
- Not FDA approved for monkeypox or other orthopoxviruses
- Available during this outbreak through an expanded access IND




https://www.siga.com/wp-content/themes/sigahba/TPOXX-Fact-Sheet.pdf

# Tecovirimat racial disparities



# Randomized controlled trials

In the United States: ACTG 5418 to evaluate tecovirimat or placebo (2:1) in 500 people with monkeypox.

Primary endpoint: Time to resolution of active lesions

In the United Kingdom: PLATINUM to evaluate tecovirimat or placebo (1:1) in 500 people with monkeypox.

Primary endpoint: Time to resolution of active lesions

# Looking forward to questions and learning from the audience

- What features of the outbreak have been different/similar to the US experience?
- What are the main differences between infection prevention and control approaches?
- How have you managed exposure in healthcare facilities?
- Have you seen shifts in sexual behavior in your patients?
- What’s your impression of Canadian monkeypox vaccination and antiviral use?