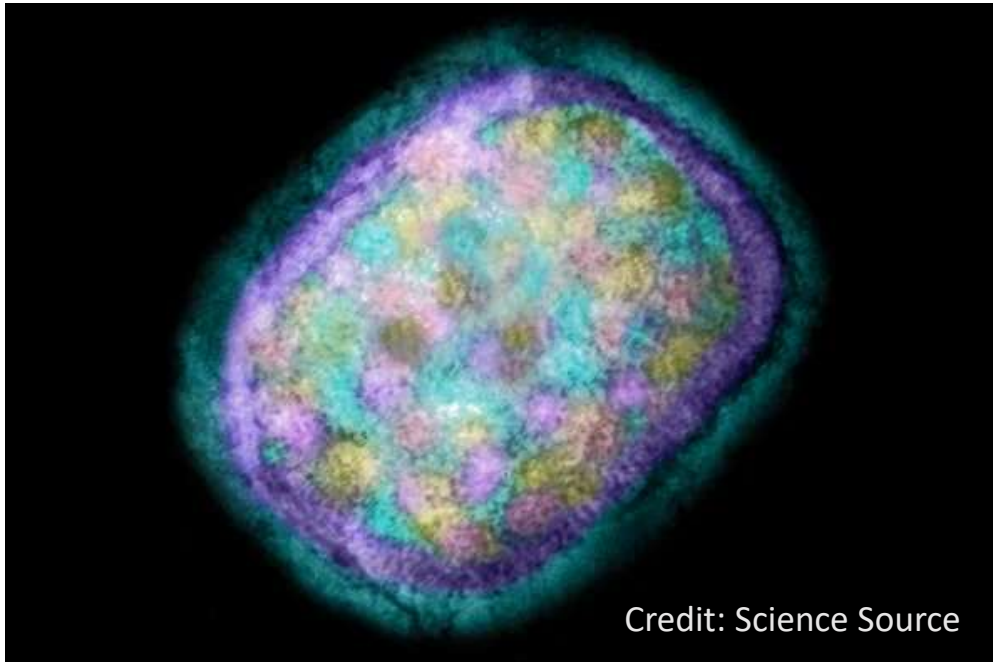
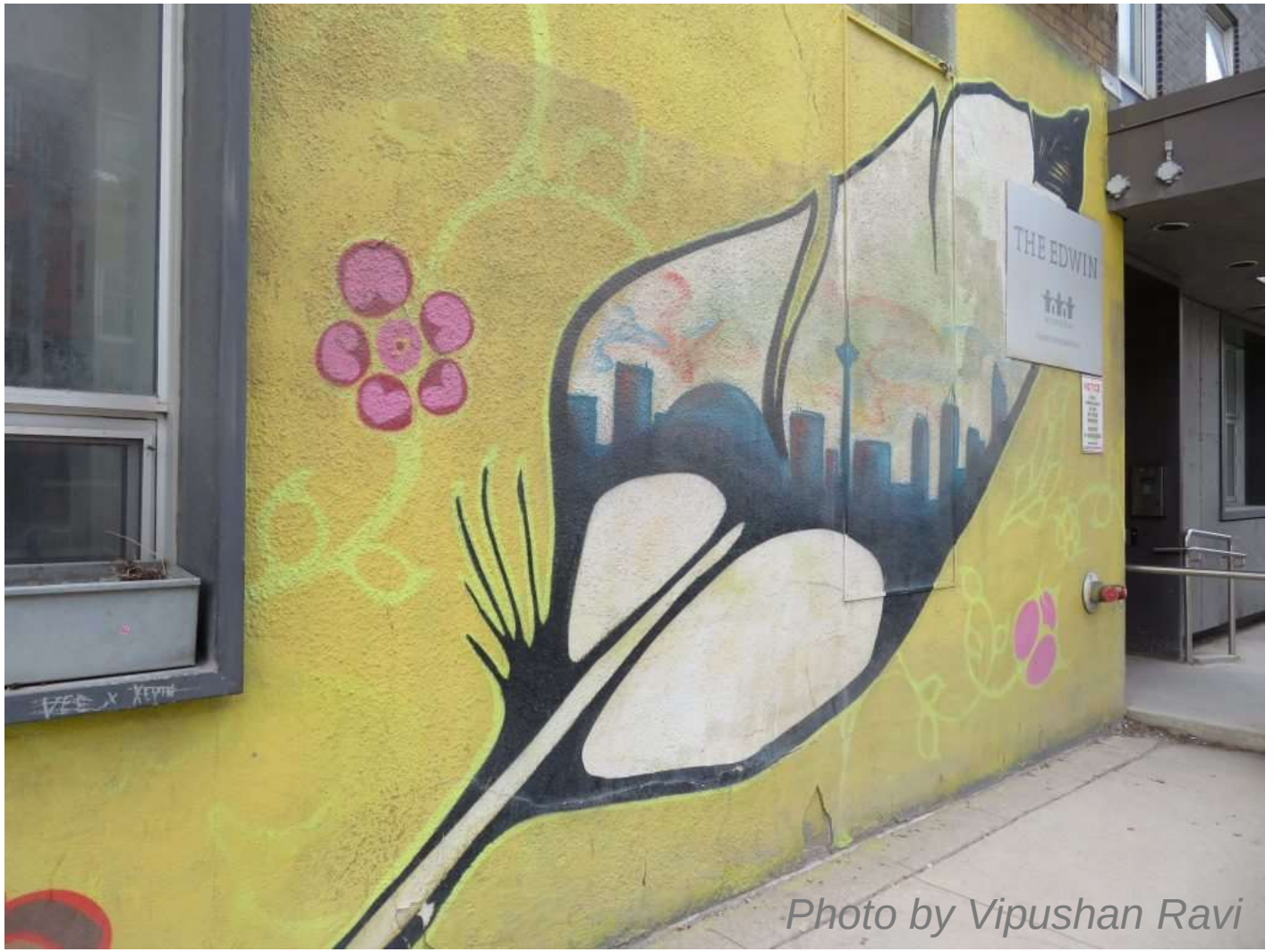
Monkeypox: Clinical Diagnosis For Primary Care



Adrienne K. Chan MD MPH FRCPC

July 22, 2022

We live and work on the traditional territories of the Mississaugas of the Credit, Anishnabeg, Chippewa, Haudenosaunee and Wendat peoples.



Tkaranto Past/Tkaranto Future (2017)
Artists: Odinamaad, Chief Lady Bird, Dave Monday Oguorie, Philip Cote
Woodgreen Services Mural

Disclosures

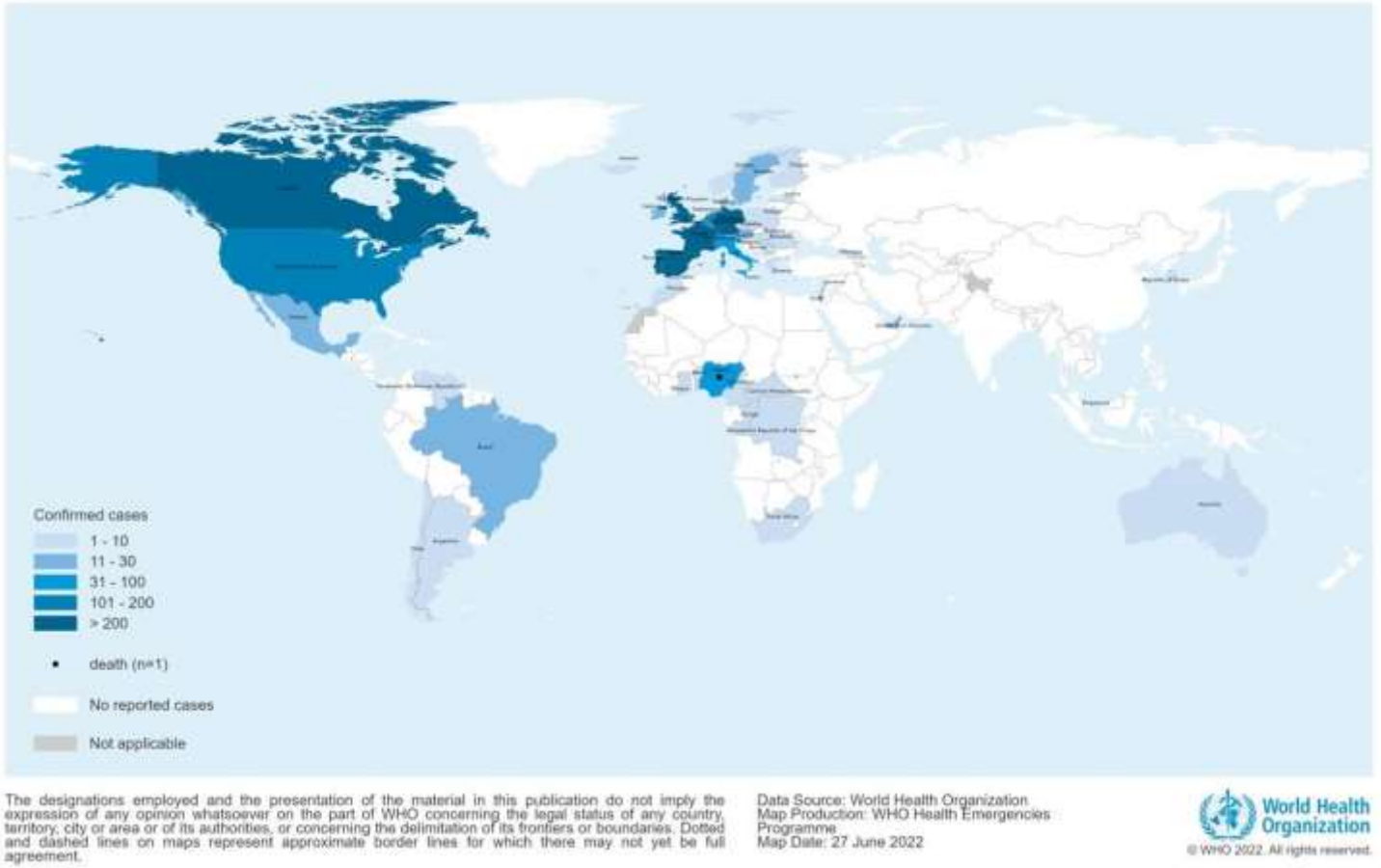
- Dr. Adrienne K. Chan has nothing to declare

Objectives

- A brief update on the current epidemiology
- An update on lessons learned from the clinical features of cases presenting in Canada
  - A review of a small collection of suspect and confirmed cases
- Provide an approach to the diagnosis of monkeypox in the primary care setting
- Further resources on NCCID Website (with AMMI/PHAC)
  - https://nccid.ca/webcast/
  - Monkeypox IPAC – Yves Longtin
  - Monkeypox in Canada What Clinicians Need to Know – Geneviève Cadieux, Geneviève Bergeron (Public Health Response and Case Management), Darrell Tan (Clinical Presentation and Community Engagement) , Jean Longtin (Tecovirimat)

Background: Global Epidemiology Update

- Poxviridae - Orthopoxvirus
- Endemic to Africa (zoonotic primary infections)
- Clusters outside of endemic area since April 2022
  - >14000 cases worldwide
    - ~8000 cases in EU/EEA
    - >2000 cases in UK and US each
    - 5 deaths (Africa)
  - >600 cases in Canada
    - 230 Ontario
    - 320 Quebec
    - BC, Alberta and Saskatchewan



WHO heat map of confirmed MPX cases Jan 1 – 22 Jun 2022

Epi updates available online: WHO, UKHSA, ECDC, CDC, PHAC as of July 21, 2022

WHO Epidemiology Update July 10, 2022

- 99.4% (6482/6519 cases identified as male)
- Median age 37 years (IQR 31-43)
- 98.1% self identified as MSM (2108/2149) and 0.8% BSM
- 41.4% HIV+ (no data on status of immunosuppression or on ART)
- 9.3% hospitalized primarily for pain management or isolation
- 0.3% ICU
- Exposure settings – social gathering with sexual contact, large events with sexual contact, social setting with no sexual contact, household
  - 95% associated with sexual contact

Available at: https://www.who.int/news-room/events/detail/2022/07/10/default-calendar/towards-the-development-of-a-global-core-protocol-for--evaluation-of-treatments-for-mpx-leveraging-the-congolese-experience

WHO Epidemiology Update July 10, 2022

- Incubation Period
  - Mean 8.5 days (4.2-17.3 95% CI) based on 18 cases in Netherlands[1]
  - Mean incubation period 9.22 days (90% CI 6.26, 15.8) WHO Data
  - Mean incubation period 7 days (range 3-20) SHARE-Net[2]
  - Used to justify the 21 day guidance for contact tracing

- Serial interval
  - Mean serial interval 9.8 days (95% CI 5.9-21.4), 17 case and contact pairs in the UK[3]
  - Suggest transmission occurs fairly early after onset of symptoms

1. Miura F, et al. Euro Surveill. 2022 Jun;27(24):2200448. doi: 10.2807/1560-7917.ES.2022.27.24.2200448.
2. SHARE-Net Clinical Group. NEJM 2022 Jul. doi 10.1056/NEJMoa2207323
3. UKHSA. Technical Briefing 2022 Available at: https://www.gov.uk/government/publications/monkeypox-outbreak-technical-briefings#full-publication-update-history

Clinical Presentation

Historical Presentation

- Incubation period, 5-21 d
- Febrile Prodrome, 8-12 d
  - 1-3 days before rash
  - Fever, chills, malaise
  - Myalgias, headache
  - Tender regional lymphadenopathy
- Rash, 2-4 w

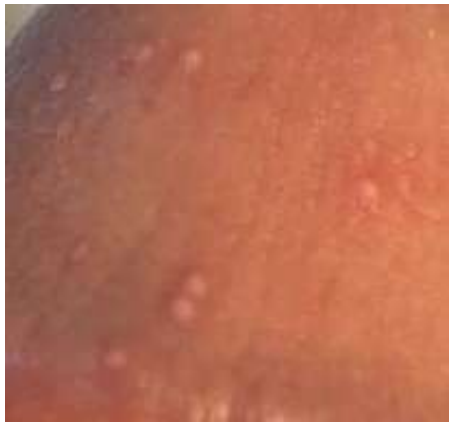
Observations in 2022

- The rash may occur before, with, or after the onset of the febrile illness
- May be secondary waves of lesions
- Developmental polymorphism of secondary lesions
- Anogenital and oral lesions more predominant as primary lesions and may be solitary
- May present with proctitis (+/- peri-anal lesions) of which a subset will have debilitating pain

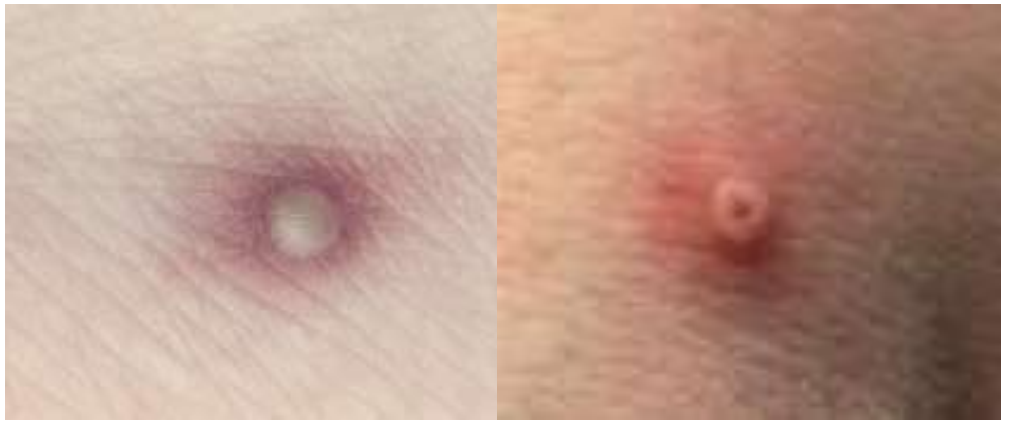
SHARE-net Clinical Group. NEJM July 2022; DOI: 10.1056/NEJMoa2207323

Slide from Sharon Sukhdeo

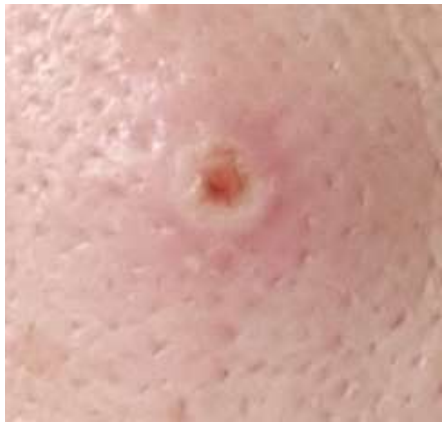
Lesion stages progress over 2 to 4 weeks



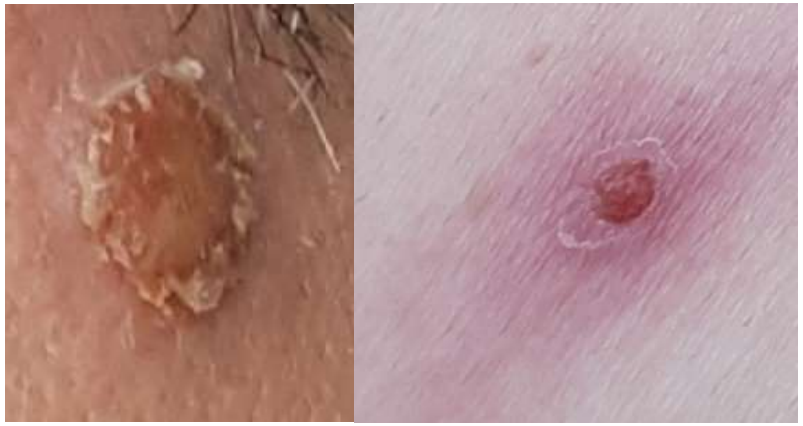
Macule & Papule



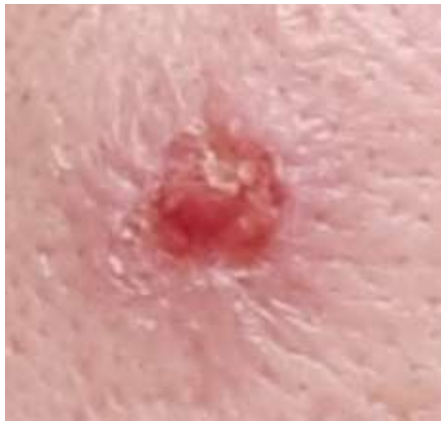
Pustule **Umbilicated**



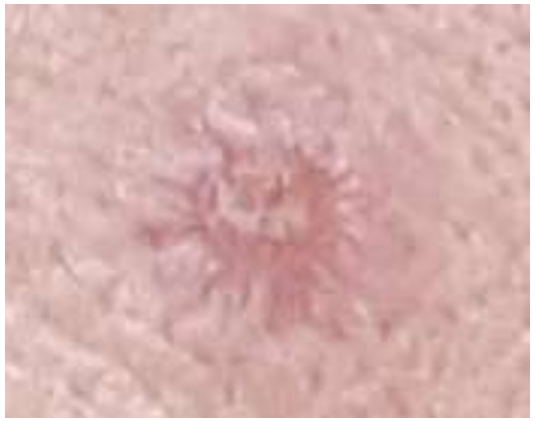
Ulcer



Crust



Desquamated

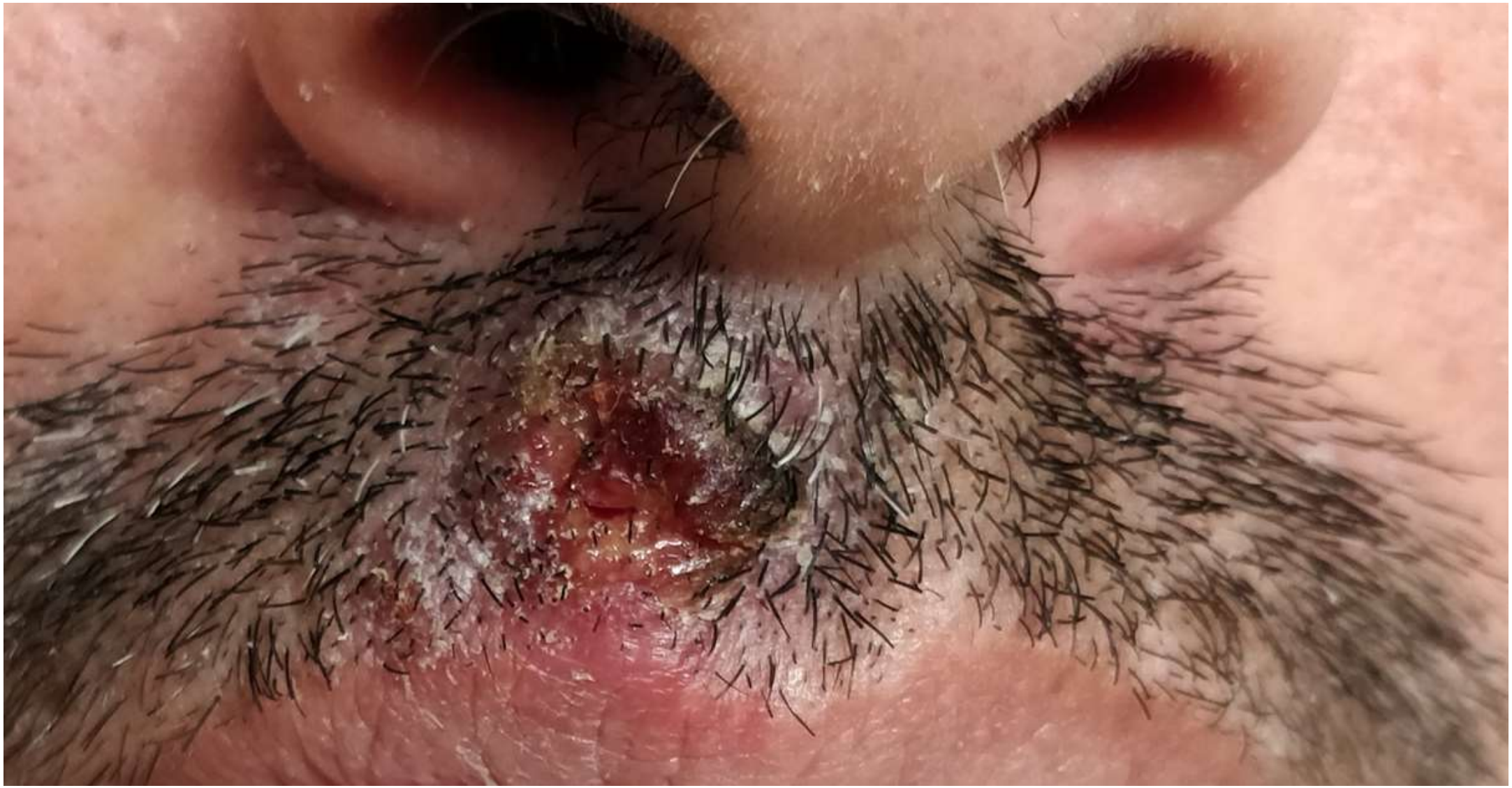


Re-epithelialized Scar

Slide from Sharon Sukhdeo

Case 2

- 40M no PMHx on PrEP (Truvada)
- Recent treatment for rectal chlamydia March 2022
- Sexual contact (mutual oral, rimming, insertive anal) with new partner about 21 days and then again 13 days prior to presentation to ED
- Developed “bumps” on genital area, lip around 10 days prior to presentation
- Then developed fever, headache, malaise and adenopathy 4 days prior to presentation
- Presents to ED with new crop of lesions and chest pain



What is your suspicion for monkeypox?

a) Low
b) Medium
c) High

Case 2 Conclusion

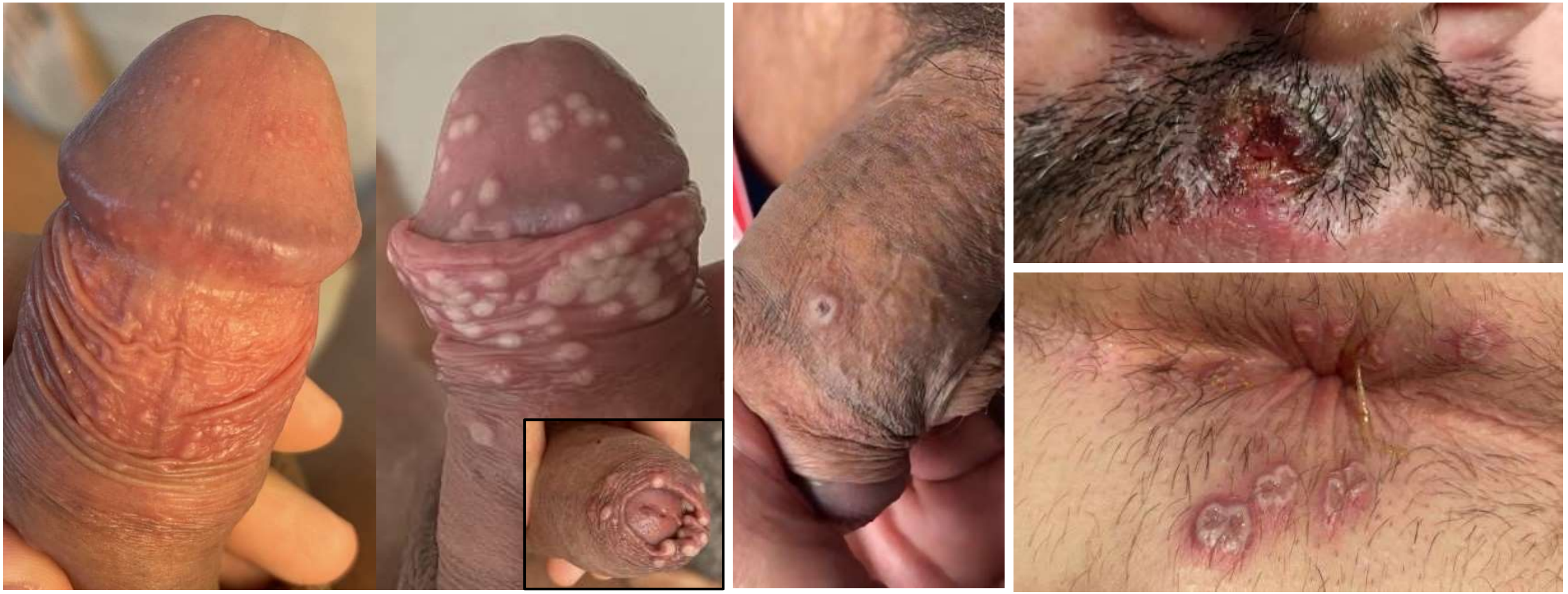
- Admitted to hospital due to myocarditis
- Lesions swabbed: **Positive for MPX all lesions**
- GC and Chlamydia +ve throat and rectal
- Discharged with resolution of symptoms

Comments on Case 2

- At the time Tecovirimat was not available but would be a candidate for treatment now
- Myocarditis has been described in at least 3 cases
- Other complications of note:
  - AKI
  - Ocular lesions
  - Pharyngitis and Epiglottitis
  - Severe Proctitis
  - Bacterial superinfection
- STI co-infection is common
  - Reported in 29% of patients tested in the SHARE-Net series
  - 2 newly diagnosed cases of HIV in SHARE-Net series
  - 2 newly diagnosed cases of HIV in Toronto patients
- Test for STI in separate bag from tests for MPX
  - Label that the patient is suspected MPX
  - HSV PCR testing can be done off of MPX samples after extraction

SHARE-net Clinical Group. NEJM July 2022; DOI: 10.1056/NEJMoa2207323

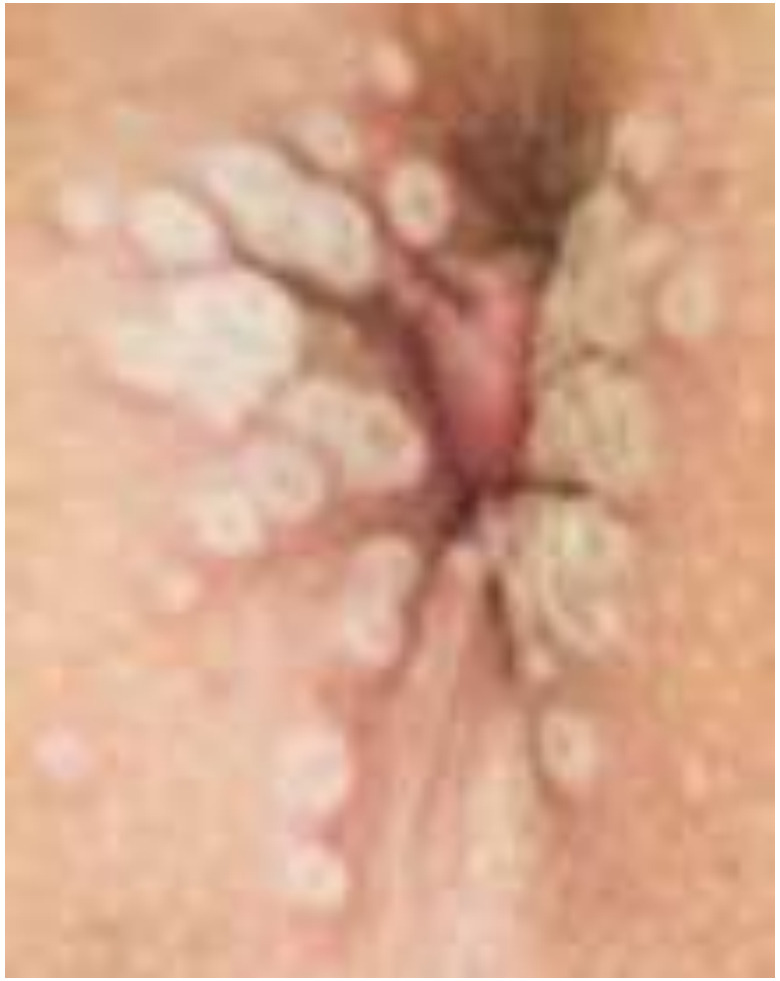
MPX: Primary Lesions Occur at Sites of Inoculation

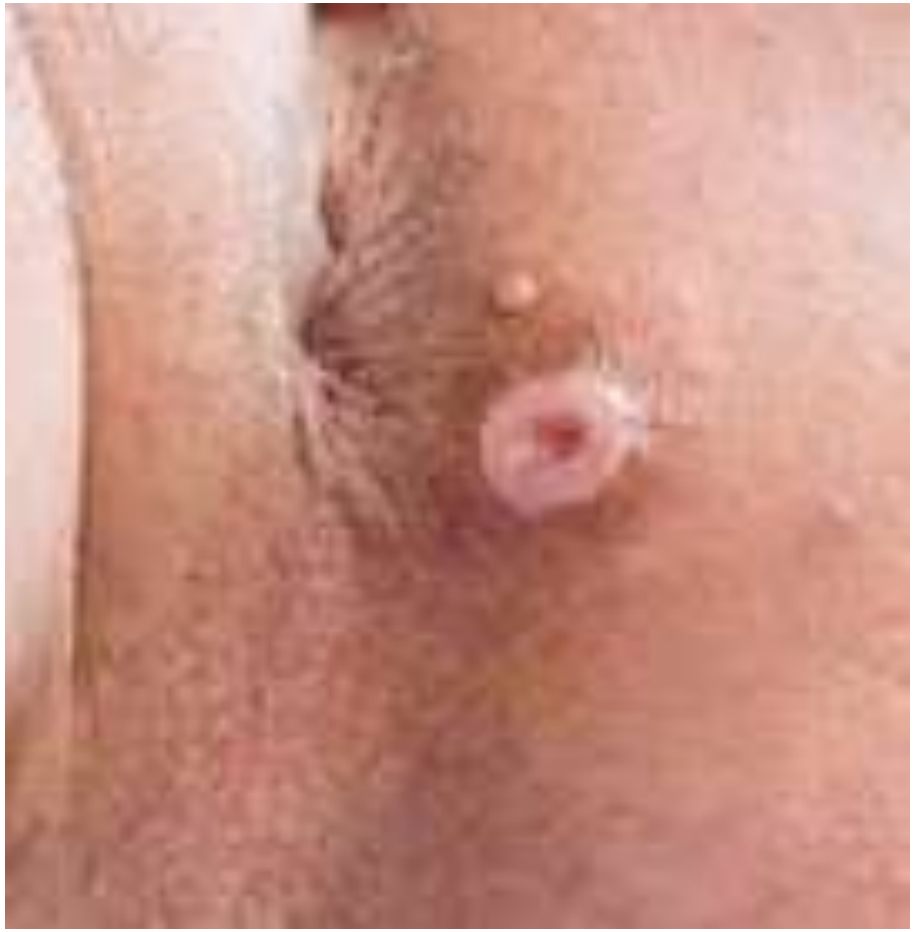


Slide from Sharon Sukhdeo

Perianal MPX Lesions:

73% of patients in the SHARE-net case series had ano-genital lesions





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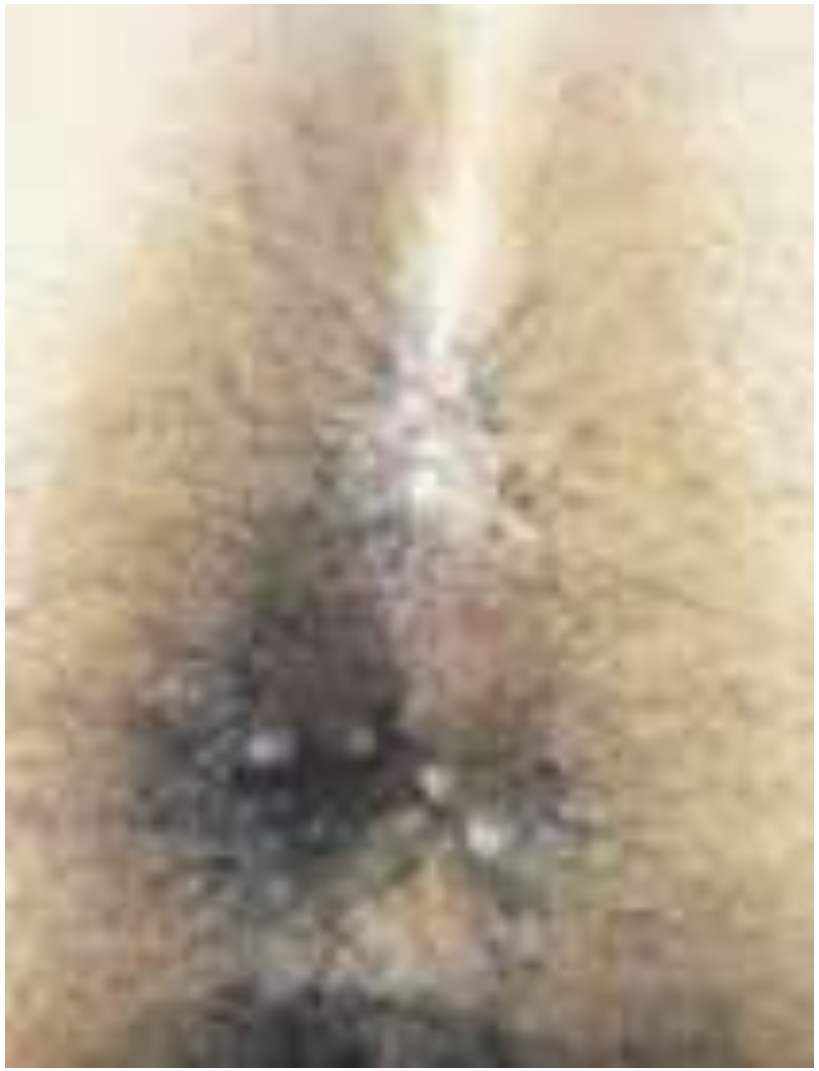
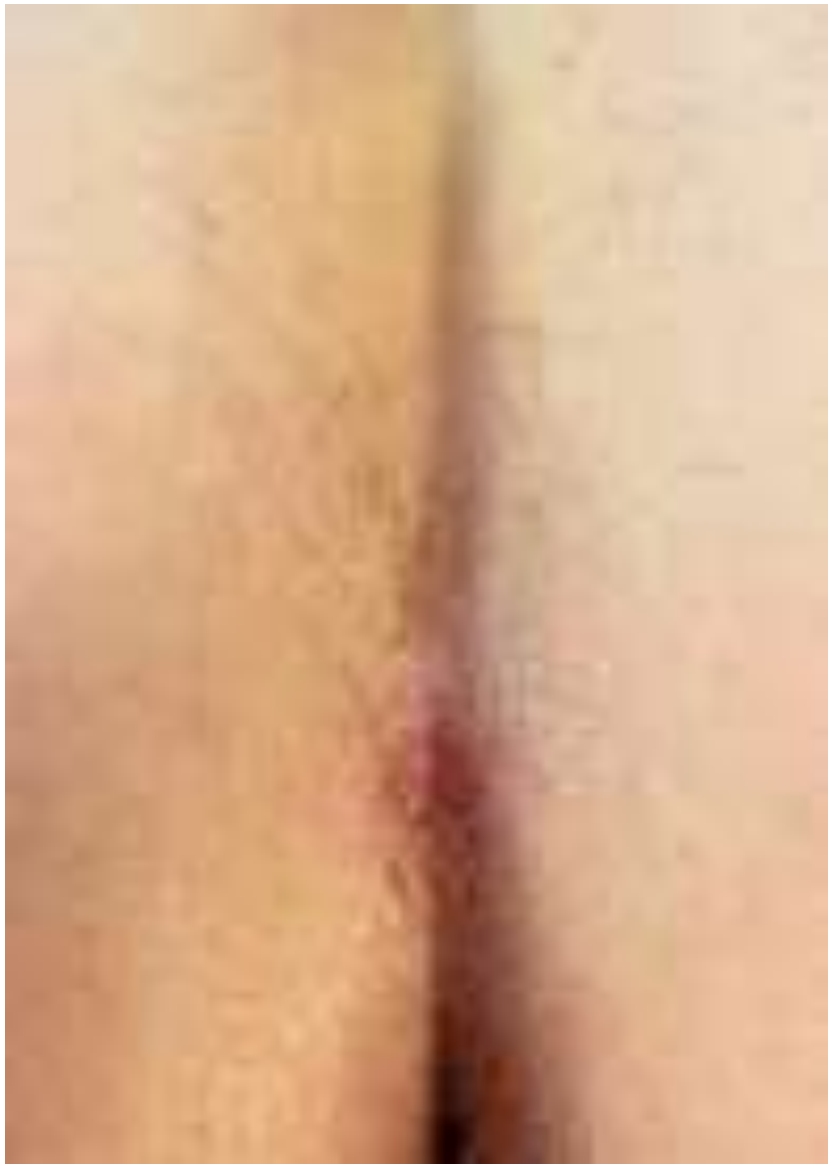
Perianal MPX

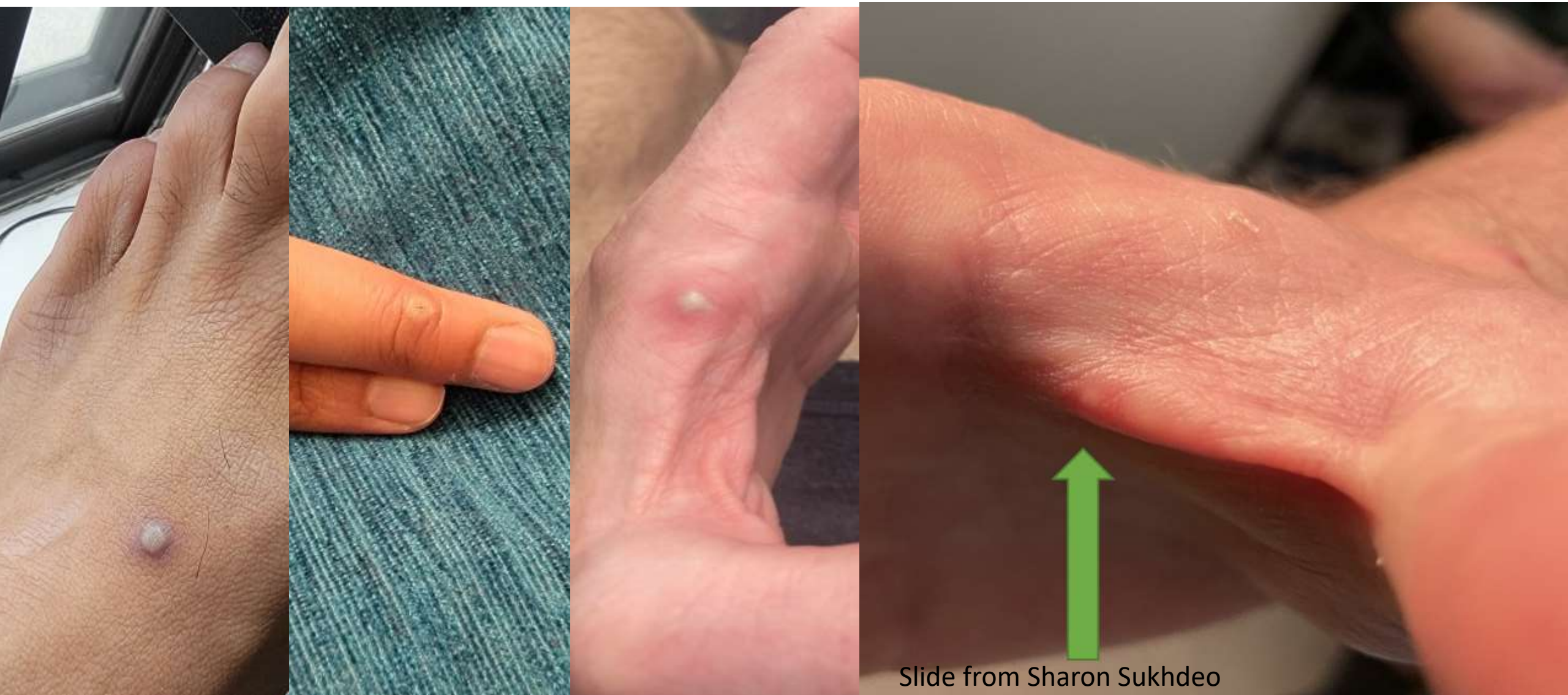




10% had a single genital lesion
(i.e. DDx other STIs)

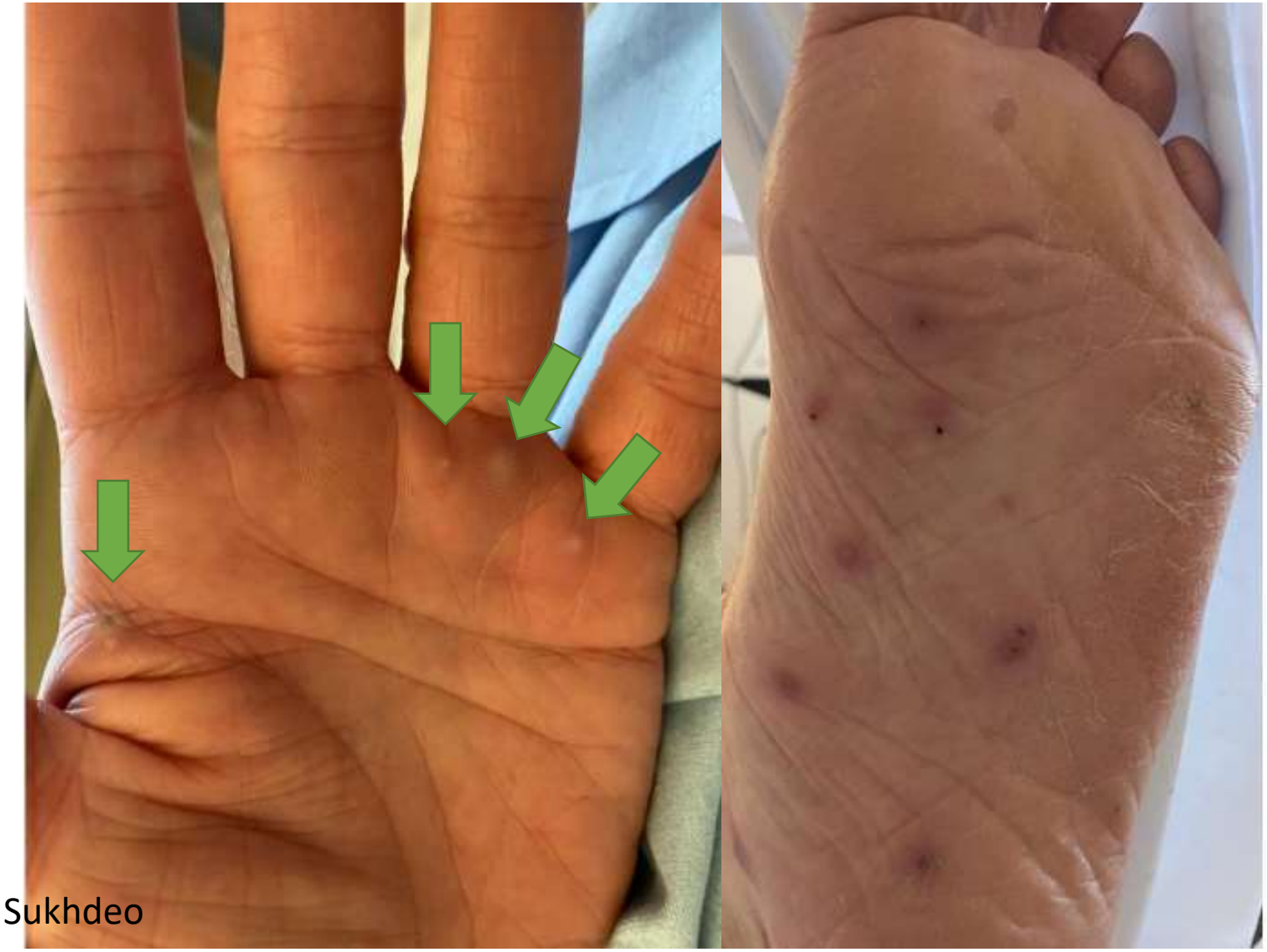
SHARE-net Clinical Group. NEJM 2022. DOI: 10.1056/NEJMoa2207323

MPX: Hand and Foot Lesions



Slide from Sharon Sukhdeo

MPX: Palms and Soles



Slide from Sharon Sukhdeo

Case 6

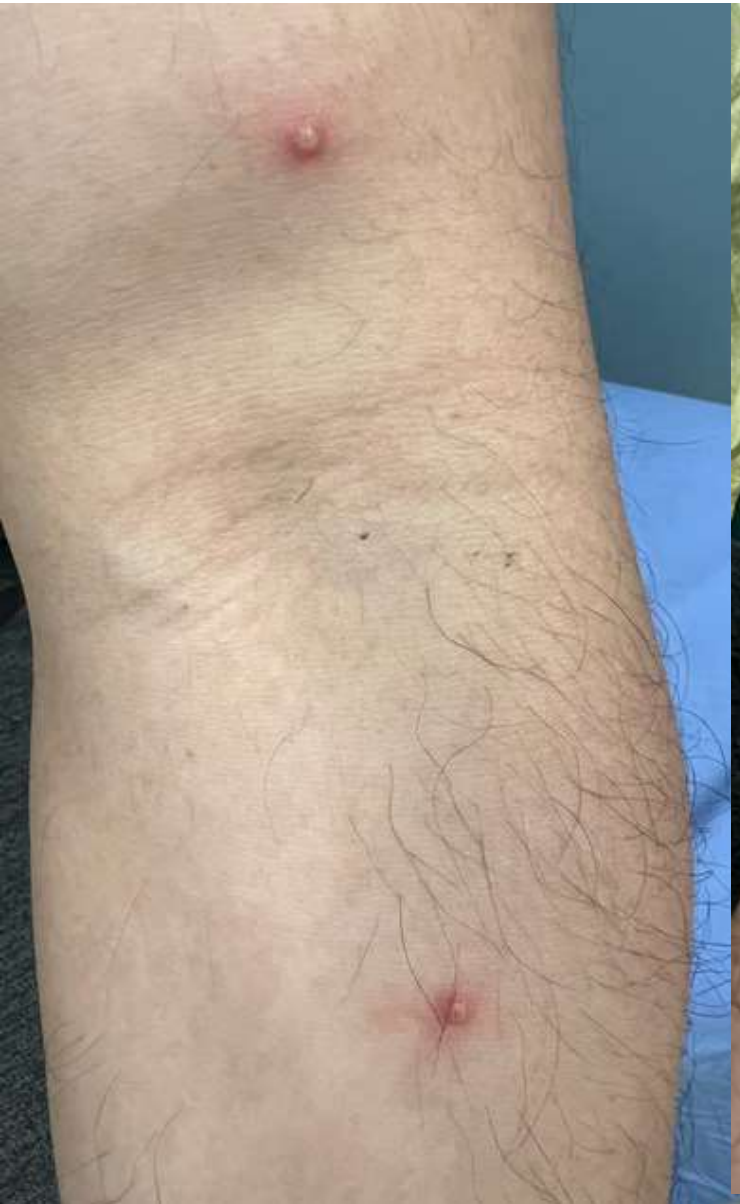
- 33 M presented to an ambulatory clinic with rectal pain and a pustular rash involving the face, extremities and torso.
- Twenty-one days before presentation (day 0), he had unprotected, receptive orogenital and oroanal intercourse with a new, anonymous male partner.
- On day 12, he developed enlarged, painful, tender inguinal and cervical lymphadenopathy, chills and night sweats.
- On day 13, he developed rectal pain and tenesmus, followed by the appearance of 4 pruritic, painless macules on his forearm and wrist on day 15, which became vesicular and then pustular over the subsequent 7 days.
- He presented to an emergency department and was prescribed valacyclovir for presumptive herpes simplex virus (HSV) infection.
- He subsequently developed similar lesions on the face, extremities and torso

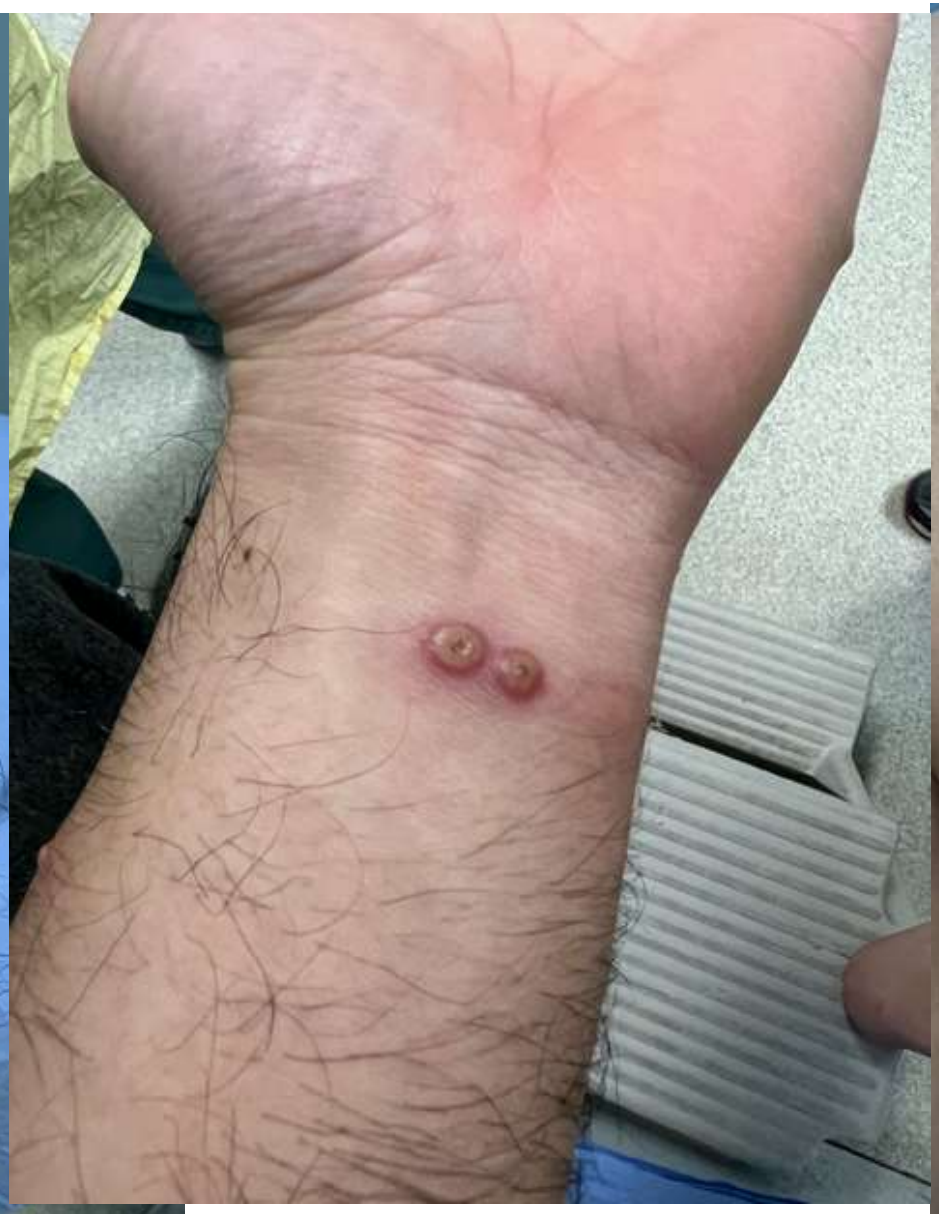
Case 6

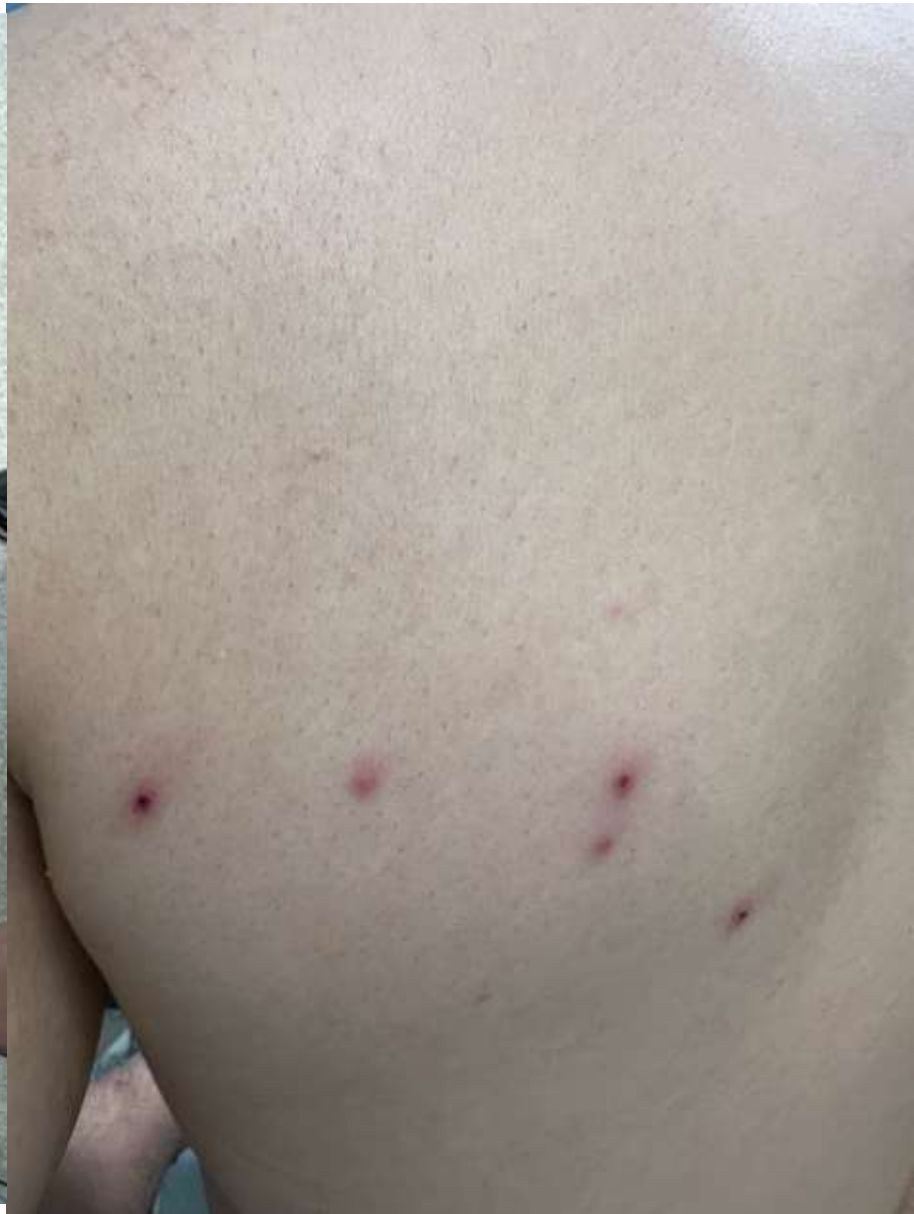
- On day 21, the patient presented to our infectious disease clinic, where we noted about 40 painless pustules on his face, scalp and extremities
- We did not observe any perianal or genital lesions
- We deferred digital rectal examination owing to pain.
- The patient had no palpable lymphadenopathy.

Sukhdeo et al. CMAJ 2022. doi: 10.1503/cmaj.220886; early-released July 6, 2022

Images on Day 21:







- What is your suspicion for monkeypox?

a) Low
b) Medium
c) High

Case 6 Conclusion

- Day 24: Diagnosis of monkeypox confirmed
  - NP swab – negative
  - Blood – negative
  - Skin lesion – invalid (issues with control test)
  - Lesion swab – Detected
  - Lesion swab – Detected
  - Vesicle roof – Detected

- Classical features can include the umbilication but does not happen in many cases
- Developmental polymorphism i.e. lesions in different stages is commonly observed
- ~10% of cases can develop severe anorectal pain due to proctitis with tenesmus and GI bleeding requiring narcotic analgesia
  - Patients with debilitating pain affecting function can be considered for Tecovirimat

Clinical Approach

At the point of first medical contact:

Clinical Approach

Apply appropriate precautions (notify PHU or institutional IPAC, notify lab)

History	Physical Exam	Diagnostics
• **Symptoms** • **In the 21 days prior to symptom onset, exposures** to a known case/location/event/ infected animal, sexual history • Risk factors • Housing & finances	Skin examination including scalp, palms, and soles, lymph nodes, oropharynx, ano-genital examination, DRE	• Lesions, lesions, lesions • Rectal, NP/pharyngeal • Serum • Other testing as appropriate (urine, vaginal etc)

For suspect and probable cases, send home if stable, isolate until PCR results

Goals

Case		Contact	
Isolation	Treatment	Tracing	Post-exposure prophylaxis

Infectious Differential Diagnosis

Disseminated Rash	Genital Lesions	Pharyngitis
• Chickenpox or herpes zoster • HSV-1 or HSV-2 • Secondary syphilis • HIV • Enterovirus (hand, foot, and mouth disease) • Molluscum contagiosum • Measles • Scabies • Disseminated gonococcal infection	• Primary syphilis • HSV-1 or HSV-2 • LGV • Chancroid (H. ducreyi)	• Group A streptococcus • Respiratory viruses including COVID-19 • EBV, CMV, or HHV-6

Coinfections

HIV, syphilis, chlamydia, gonorrhea, hepatitis

Diagnostics

- **Monkeypox PCR**
  - Skin lesions:
    - **Swabs of unroofed vesicle/pustule fluid**
    - Crusts
      - Into dry falcon tube
  - Rectal swab, pharyngeal/NP swab, serum, urine
- Serology unavailable currently
- More next from Dr. Gubbay….

Key lessons from the care of patients

- 1. Classic lesions appeared prior to onset of systemic symptoms
  - Differs from classical monkeypox in which fever/headache/malaise precede exanthem by 3-5d
  - Secondary crop of lesions appeared after the classic prodrome
  - Hypothesis: related to primary inoculation of organism via sexual activity → hematogenous → secondary crop of lesions *[?reminds us of syphilis*]
- 2. Subclinical/minimal symptoms are being seen/reported
- 3. Some new manifestations not previously reported
  - Myocarditis
  - Esophageal lesion
- 4. Empiric treatment for other conditions
  - Currently testing cannot be processed until monkey pox ruled out
  - Valacyclovir, Doxycycline, Ceftriaxone IM, Penicillin IM

Key lessons from the care of patients

- 5. Social considerations (barriers to isolation)
  - Economic (job security; food security)
  - Duration of isolation is not fixed
    - Jurisdictional guidelines are evolving with experience
      - https://www.toronto.ca/community-people/health-wellness-care/health-programs-advice/monkeypox/monkeypox-message-from-toronto-public-health/
      - https://www.gov.uk/guidance/guidance-for-people-with-monkeypox-infection-who-are-isolating-at-home#how-to-isolate-safely-at-home-if-you-have-monkeypox-infection
  - Re-implement resources/support (including financial) set up for COVID
- 6. Risk of stigma
  - Aware of news reports; HIV / PrEP;
  - Community-engagement and leadership in messaging and communication

Acknowledgments

- Patients and Community
- Colleagues at CBRC and GMSHA
- Unity Health: Darrell Tan and Sharmistha Mishra
- UHN: Sharon Walmsley
- Sunnybrook HSC: Phil Lam
- U of T: Sharon Sukhdeo, Emerging Pandemic and Infectious Consortium (EPIC)
- PHO, MOH Ontario, and TPH

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