Clinical Presentation of Monkeypox occurring outside endemic areas

What is different in the current worldwide outbreak

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Disclosures

Industry

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- Consultant: ViiV, Gilead Sciences, Abbvie

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- CIHR
- FRQS-Réseau sida/mi
- CTN
- NIH

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Acknowledge my colleagues: Luke Harrision
Sapha Barkati

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Classical features of endemic Monkeypox

- Clinical syndrome characterised by fever, rash, and lymphadenopathy.
- Rash then begins as maculopapular and proceeds to pustules to more classic ulcerative / "pox" like lesions.
- Lesions typically progress starting on face then body and are frequently found on hands and soles
- Complications can include pneumonitis, encephalitis, keratitis, and secondary bacterial infections
- Reported mortality rates variable from 1-10%
- Higher rates reported from outbreaks in Congo basin and lower rates < 3% with variant found in West Africa
- Risk factors for more severe outcomes include young age and HIV infection
- Person-to-person transmission well documented but not felt to be efficient
- Spread through droplets and direct contact with infected lesions

Clinical features and management of human monkeypox: a retrospective observational study in the UK

Hugh Adler, Susan Gould, Paul Hine, Luke B Snell, Waison Wong, Catherine F Houlihan, Jane C Osborne, Tommy Rampling, Mike BJ Beadsworth, Christopher JA Duncan, Jake Dunning, Tom E Fletcher, Ewan R Hunter, Michael Jacobs, Saye H Khoo, William Newsholme, David Porter, Robert J Porter, Libuše Ratcliffe, Matthias L Schmid, Malcolm G Semple, Anne J Tunbridge, Tom Wingfield, Nicholas M Price* on behalf of the NHS England High Consequence Infectious Diseases (Airborne) Network†*

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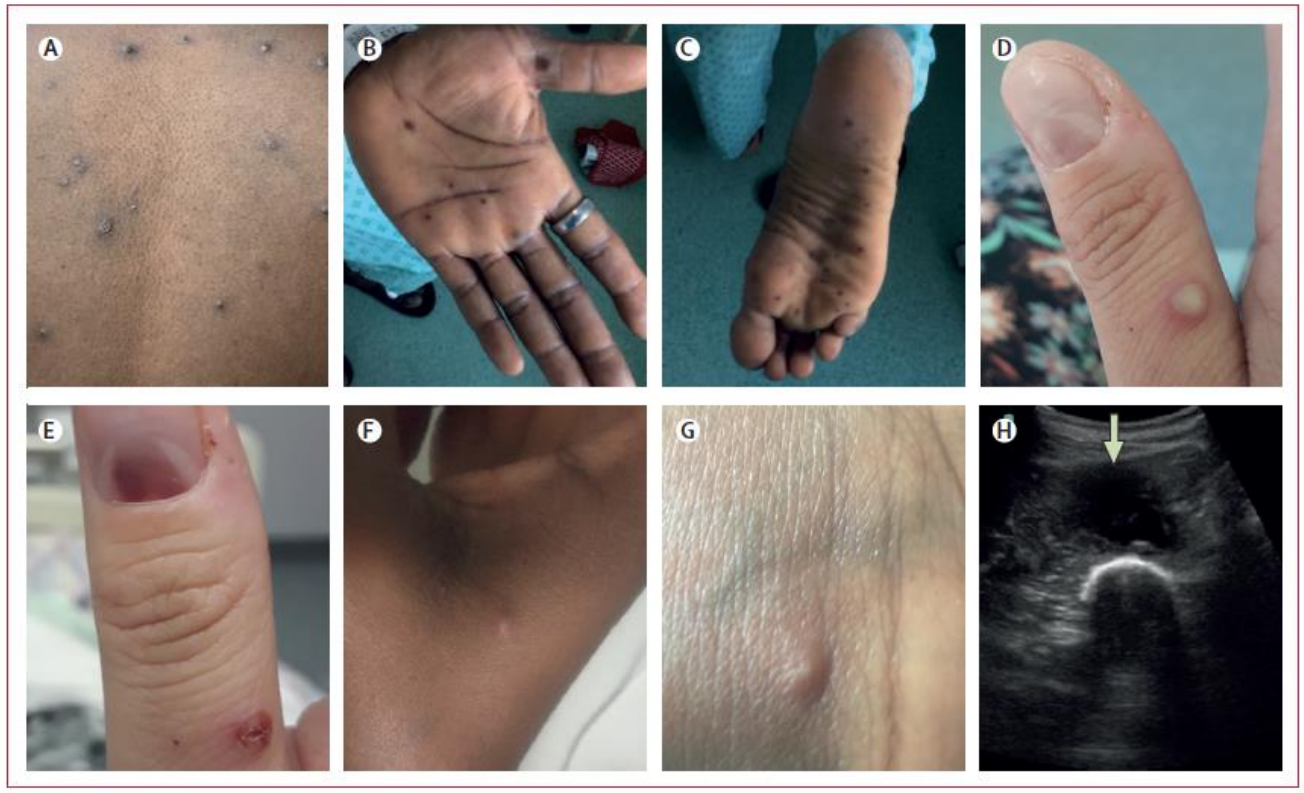

Figure 2: **Skin and soft tissue manifestations of monkeypox**
Skin and soft tissue features included: (A and D) vesicular or pustular lesions; (B and C) macular lesions involving the palms and soles; (D and E) a sub-ungual lesion; (F and G) more subtle papules and smaller vesicles; (H) and a deep abscess (arrow, image obtained during ultrasound-guided drainage).

Review of 7 cases occurring in UK between Aug 2018-Sept 2021

3 cases acquired in the UK (one nosocomial transmission to a HCW and 2 via household transmission from imported case)

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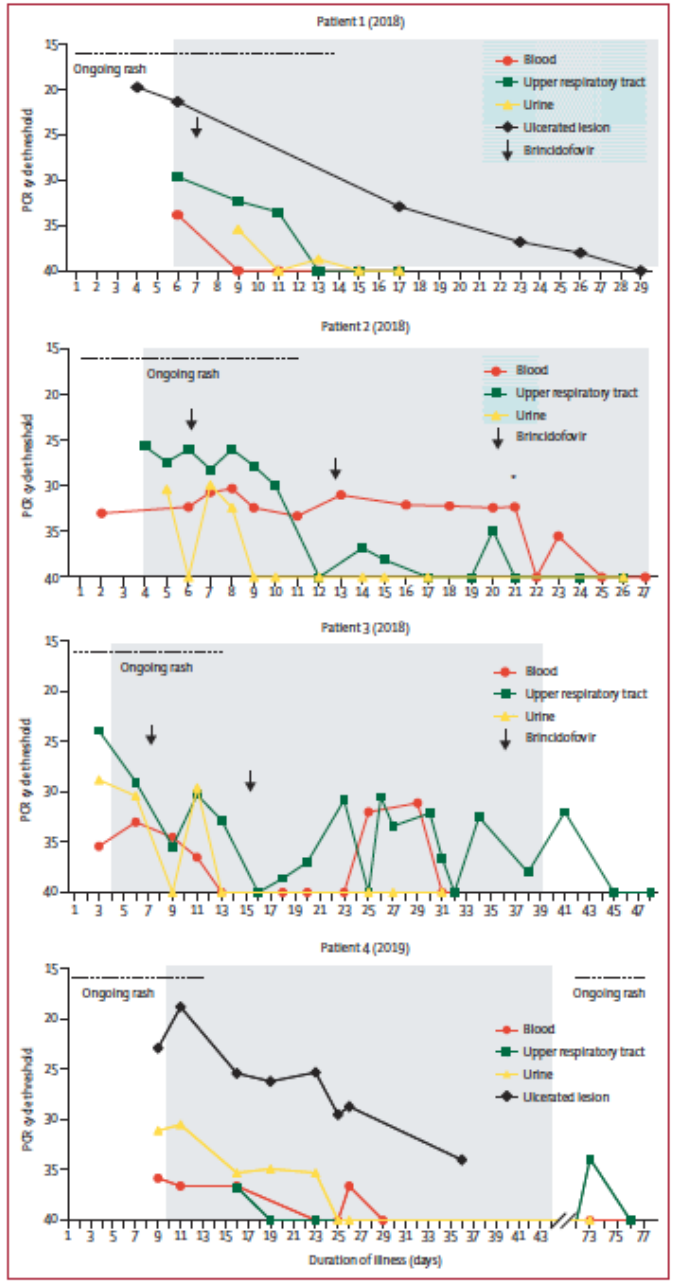
Clinical Features

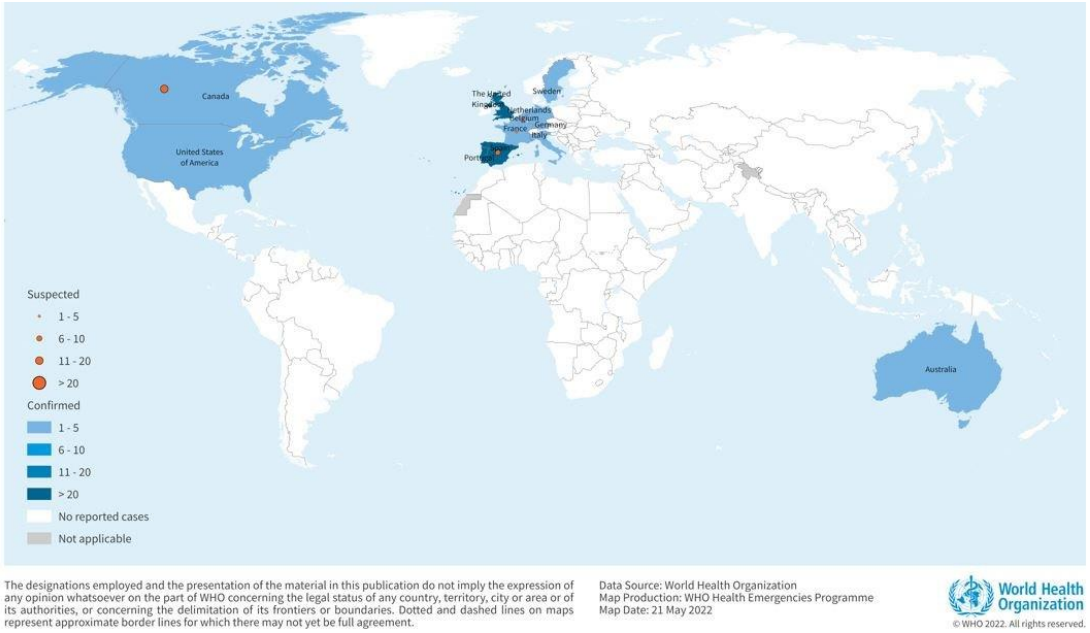
- Viremia detected in all
- Prolonged monkeypox virus DNA shedding in respiratory swabs even after resolution of rash
- Hospitalised and prolonged isolation period

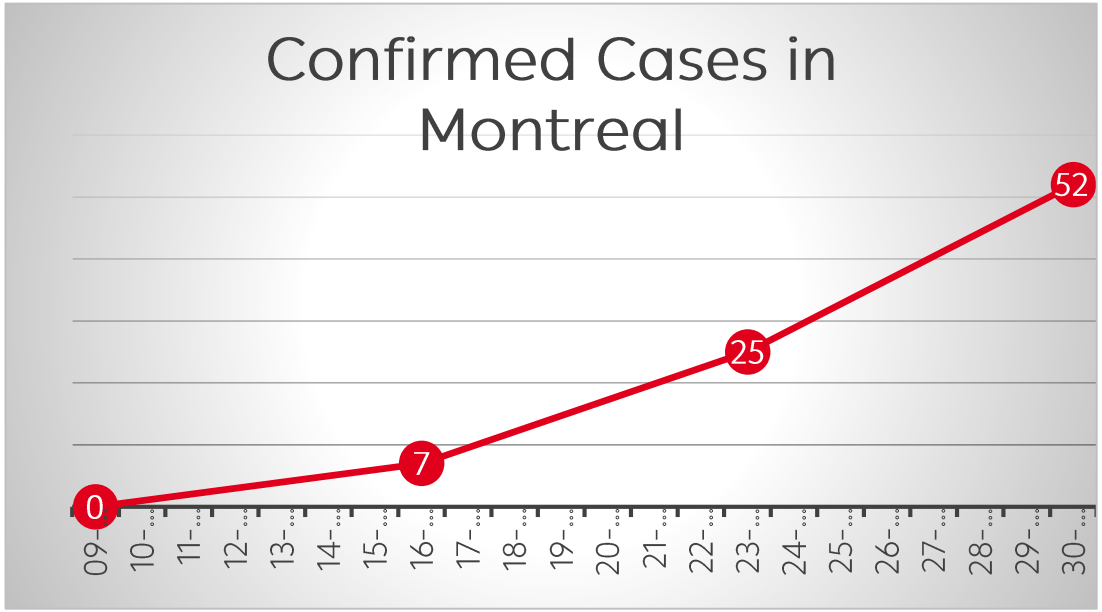


(Figure 1 continues on next page)

Current Outbreak

- Among people with no travel history to endemic regions although travel between/within Europe and between countries now reporting cases
- >95% male and mostly among gay, bisexual, or other men who have sex with men (GBMSM).
- Aged 20 to 49 years old





Case 1

- 32y/o male
- GBMSM
- HIV+, well controlled on Bictegravir/emtricitabine/tenofovir alafenamide
- CD4 550 cells/ul, HIV VL < 20 copies/ml
- Sexually active, multiple unprotected male partners
- One partner recently hospitalized in US with diagnosis of Monkeypox after travelling to Montreal

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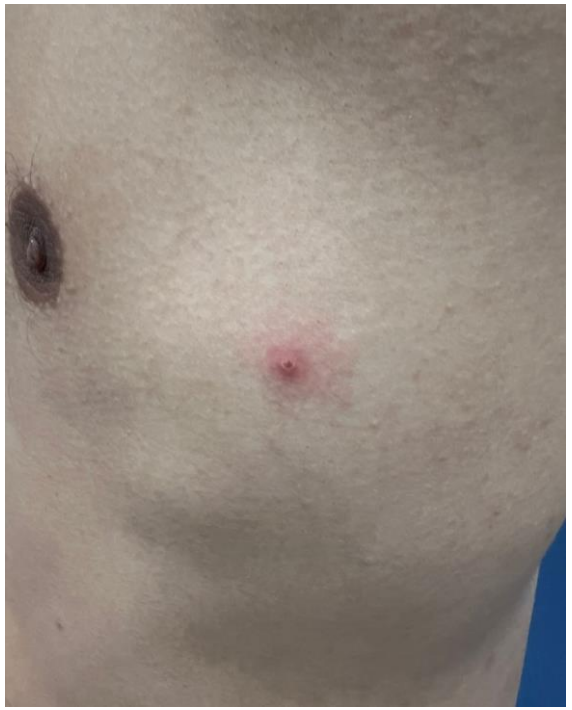
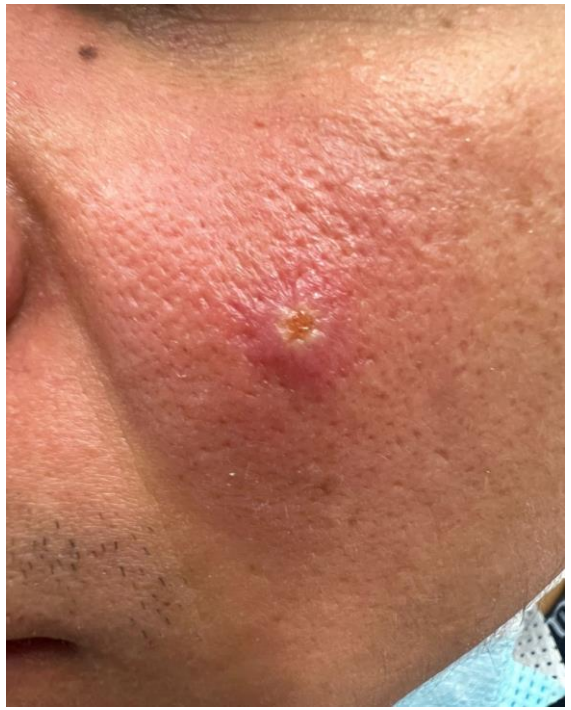
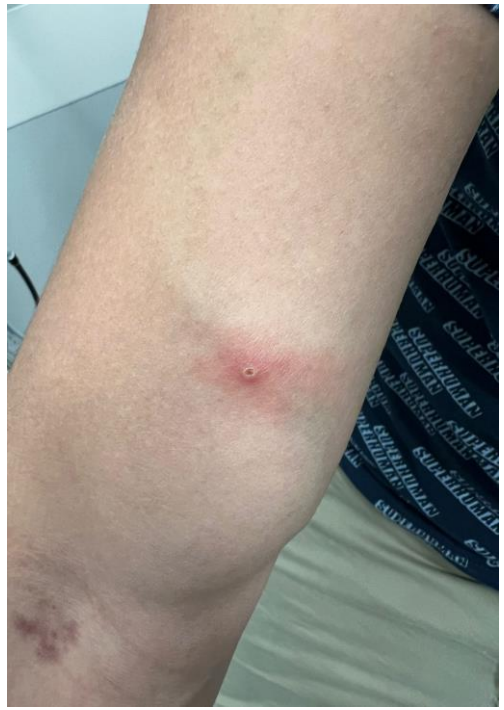
May 10th	May 13th	May 17th	May 18th
Sx of Proctitis	Onset of Rash	Sore throat and ongoing rectal pain	Progression of Rash
		STI screen+ rectal GC	

Blood: PCR- on serum
Roof of lesion: PCR+
Dry swabs: PCR + at NML







Case 2

- 25 y/o male
- GBMSM
- No significant PMH
- Not on PreP
- Sexually active, multiple unprotected male partners at sauna
- No travel

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Seen in ER Rx **Pen / Doxy**

Blood: not sent,
Swabs: PCR +

Case 3

- 50 y/o male
- No hx of smallpox vaccine
- GBMSM
- HIV+ x 20 years on dolutegravir/lamivudine
- CD4 741 cells/ul, HIV VL not detected
- Sexually active, multiple unprotected encounters, visited bathhouse around 05/04-05/08
- No travel

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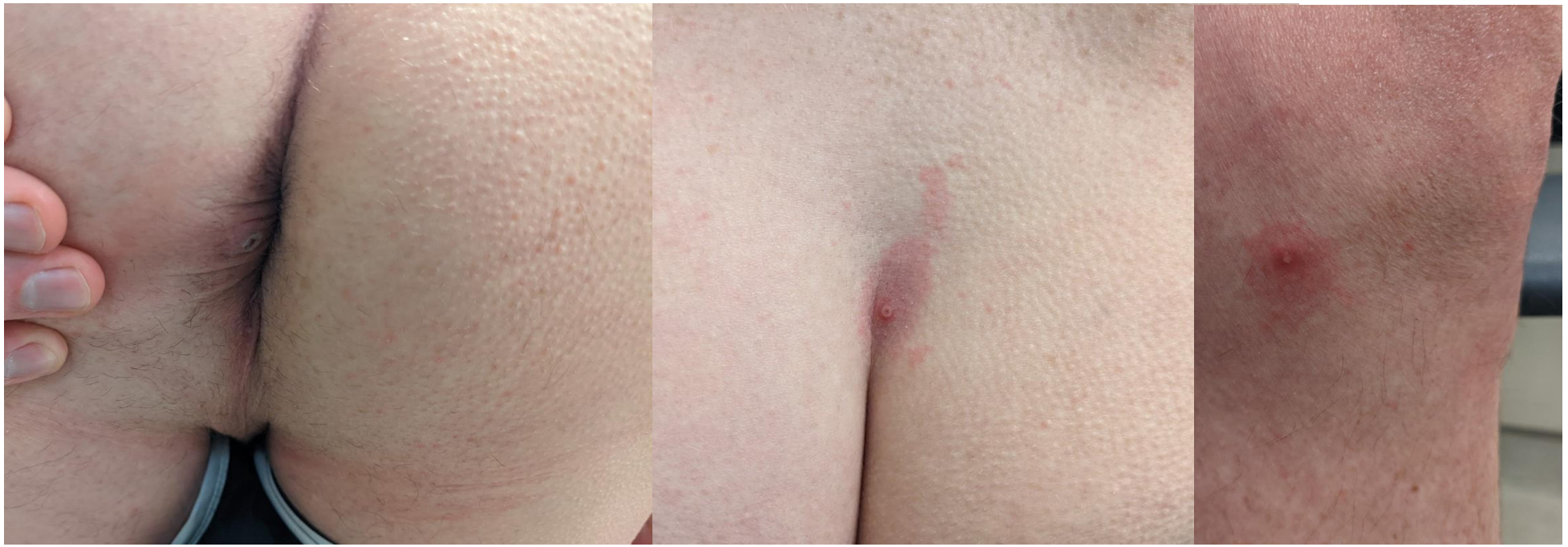
May 9th	May 15th	May 16th	May 17-18th
No Symptoms, routine visit	Myalgias, malaise and fever	painful perianal lesion, Sx of proctitis	multiple papular → papulopustular lesions (face, abdomen, legs)

Blood: PCR +
Swab: PCR +



Case 4

- 36 y/o male
- GBMSM
- HIV+ elite controller on dolutegravir/lamivudine
- CD4 741 cells/ul, HIV VL not detected
- Sexually active, multiple unprotected encounters, visited bathhouse around 05/04-05/08

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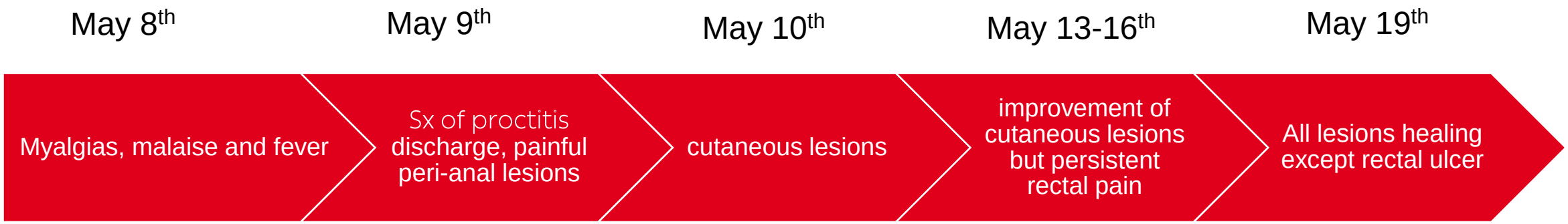

STI clinic →
Pen/CTX/Azith/Doxy
Testing neg

ER →
? Disseminated GC
Rx: Ceftriaxone
Rectal G/C PCR -ve

ID clinic →
? Chancroid
Rx: Ciprofloxacin
G/C PCR –ve x 3

Trop Med→
? Monkeypox
rectal ulcer → +PCR
Blood PCR negative

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Key take home points: Not "classic" Need high index of suspicion

- Presentation is very variable (order of onset and extent of dissemination)
- Anal or genital lesions common feature, often painful
- Initially quite non-specific and not classic
- Often multiple points of contact with health system and dx not entertained
- Masquerading as other STIs, co-occurring with other STIs
- Sampling lesions had high diagnostic yield
- Most relatively mild and resolved without specific treatment
- Time course fairly long so possible extended period of infectivity

What samples to take?

Consult locally as may vary and evolve over time

Ideal samples

- Blood for DNA (EDTA or serum)
- Nasal swab / oropharyngeal swab
- Tissue (roof, crust, punch biopsy) -- dry in sterile (e.g. urine) container
- Swab of ulcer (dry flocked swab in UT

Testing

- Pan-orthopox PCR screen
- Confirm with simian orthopox PCR
- Sequencing

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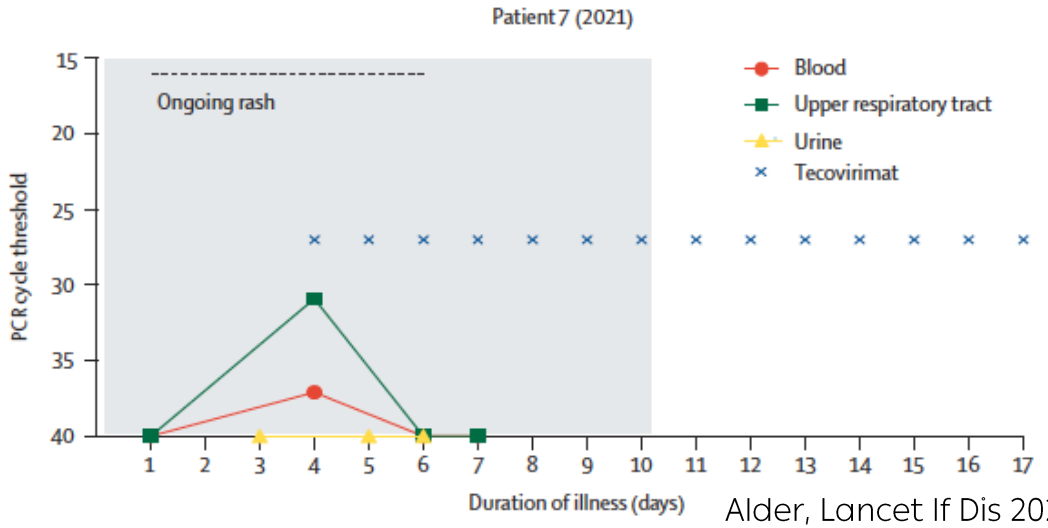
What about treatment and vaccination?

- Most will have a mild, self-limiting disease course without specific therapy
- Treatment may have a role in persons with sever presentation or at high risk for poor outcomes
  - hemorrhagic disease, confluent lesions, sepsis, encephalitis, or other conditions requiring hospitalization
  - Immunocompromised
  - Pregnancy
  - Young children
- Role of treatment to reduce viremia rapidly?
- MVA-BN vaccine (aka. Imvamune, Imvanex or Jynneos)
- Ring vaccination of close contacts, ideally within 4 days of contact to reduce secondary cases



Alder, Lancet If Dis 2022

Potential Treatment options

Tecovirimat (TPOXX) is an antiviral approved for smallpox treatment

Other antivirals may be active but are more toxic (Brincidofovir, Cidofovir)

Intravenous Vaccinia Immune Globulin

See details: Parker, Future Virol. 2008: 595–612.

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Conclusions and Research Gaps

- Variable presentation, from subclinical to more classic and long period of symptoms and potential transmission presents a challenge for case recognition and containment
- Population currently experiencing the greatest burden may have concomitant STIs, whether this alters disease course or presentation is unknown (e.g. HIV infection)
- Still many gaps in our understanding of the main modes of transmission driving the current outbreak and whether there is true sexual transmission
- Stigma related to the community is likely to impede the response
- The role of treatment and vaccination in managing infections and reducing spread needs to be urgently determined

Final Thoughts.....

"Because unfortunately, monkeypox is a disease that has traditionally caused outbreaks in Africa — and usually in very remote parts of Africa — and affecting populations that the world doesn't always care about."

Dr. Boghuma Titanji, Emory University
Source: CBC News · Posted: Jun 01, 2022