

# Monkeypox - clinical picture

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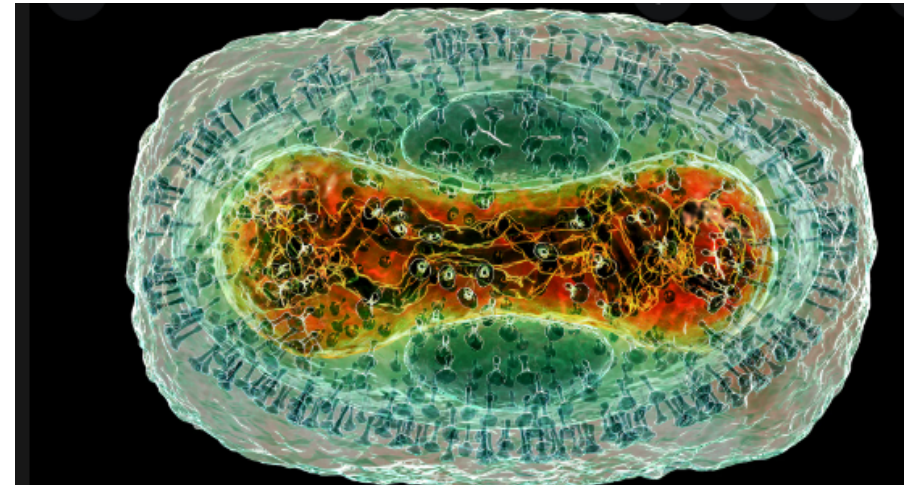
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# Epidemiology at a glance

- Orthopoxvirus (same genus as variola and vaccinia viruses)
- Natural reservoir: unknown (rodents/non-human primates)
- First isolated in Denmark in the '50s from Monkeys
- Identified in 1970 as a cause of disease in humans

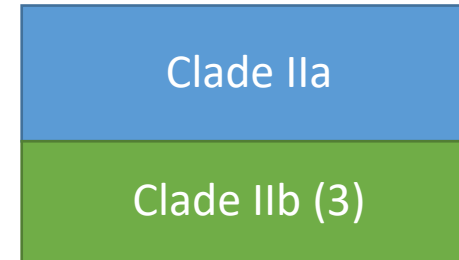


# Epidemiology at a glance

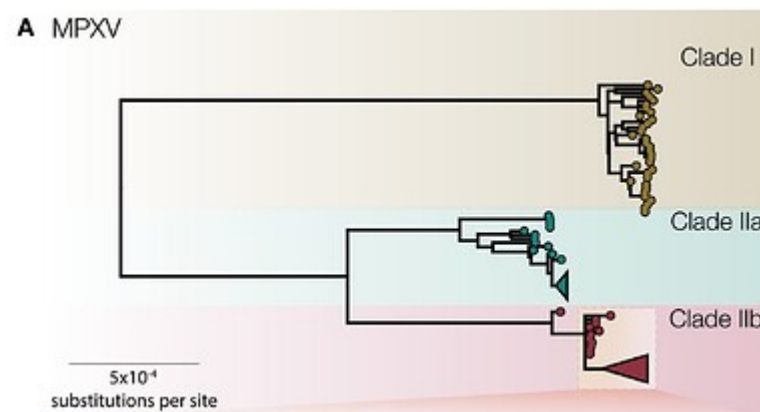


formerly «Central Africa» or «Congo Basin» clade  
(>10% CFR)

Aug 2022



Formerly « West Africa » (<1% CFR)



## Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus

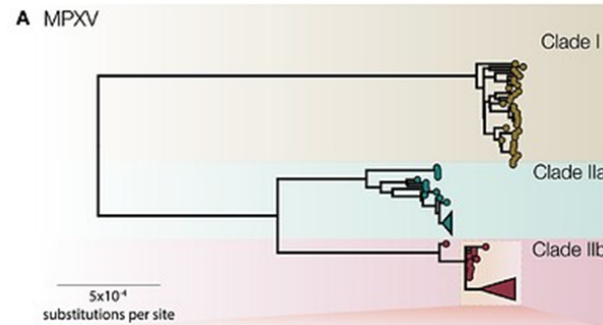
Joana Isidro<sup>1,6</sup>, Vítor Borges<sup>1,6</sup>, Miguel Pinto<sup>1,6</sup>, Daniel Sobral<sup>1</sup>, João Dourado Santos<sup>1</sup>, Alexandra Nunes<sup>1</sup>, Verónica Mixão<sup>1</sup>, Rita Ferreira<sup>1</sup>, Daniela Santos<sup>2</sup>, Silvia Duarte<sup>2</sup>, Luís Vieira<sup>2</sup>, Maria José Borrego<sup>3</sup>, Sofia Nuncio<sup>4</sup>, Isabel Lopes de Carvalho<sup>4</sup>, Ana Pelerito<sup>4</sup>, Rita Cordeiro<sup>4</sup> and João Paulo Gomes<sup>1,5</sup>

# Epidemiology at a glance

- MPXV detected in 2022 outbreak has a **genetic linkage** to the virus that caused the **2017–2018 Nigeria outbreak** potentially representing the continuous circulation and evolution
- Current scenario: one introduction from a single origin with superspreader event(s) (i.e. sauna events for sexual encounters)

# Epidemiology at a glance

- the 2022 MPXV diverges from the related 2017–2018 viruses by a mean of 50 single-nucleotide polymorphisms (**roughly 6–12-fold more of the substitution rate** expected for **Orthopoxviruses**)
- Accelerated evolution potentially due to “hyper mutation signature” (**APOBEC3** enzymes of the host)

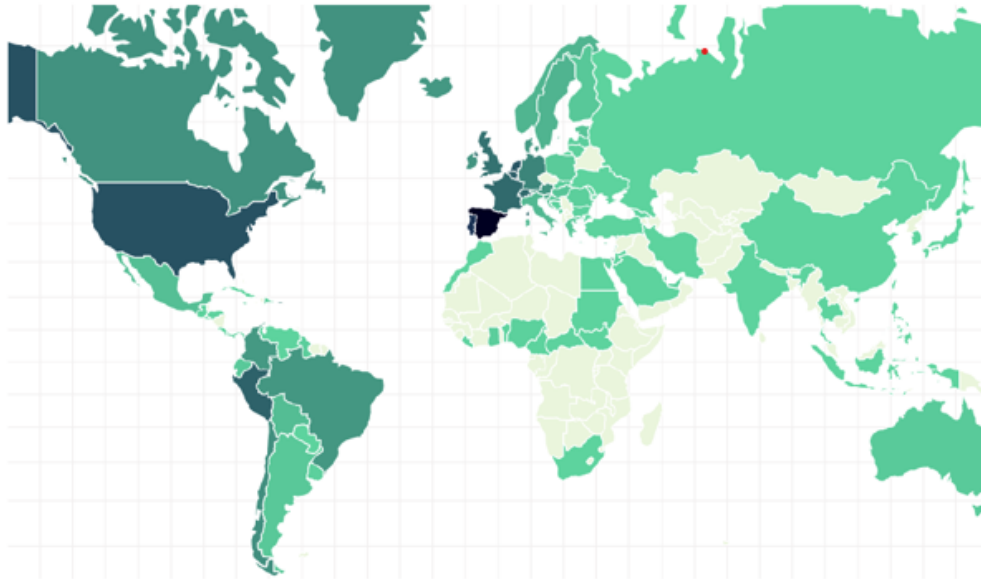


# Geographic distribution

# Geographic distribution

Global confirmed Monkeypox cases

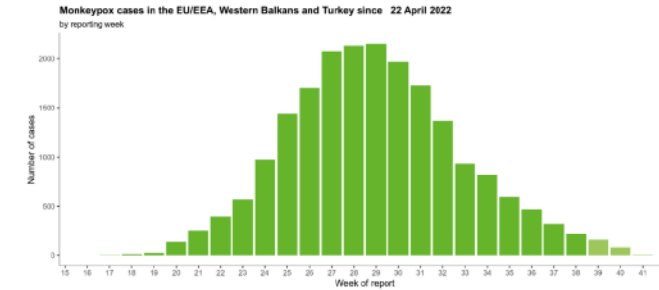
Click on a country to view more details



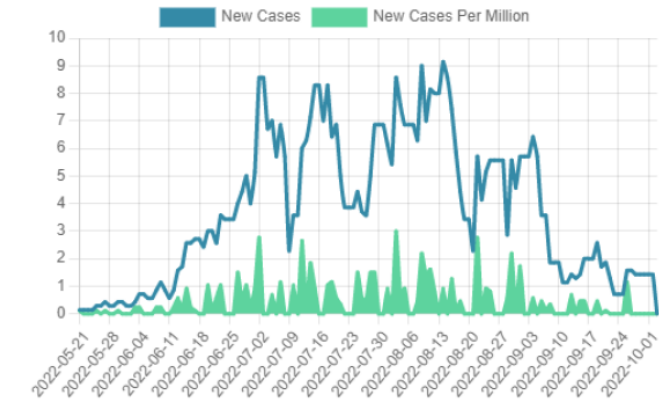
12.10.22

- Confirmed cases: 72198 in 109 countries, 32 deaths
- 87.9% self-identified as MSM
- 48% HIV +

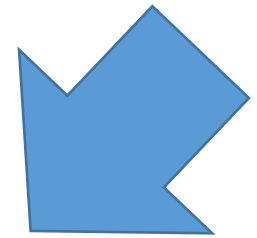
Monkeypox Cases in the EU/EEA



Switzerland: New Monkeypox Cases



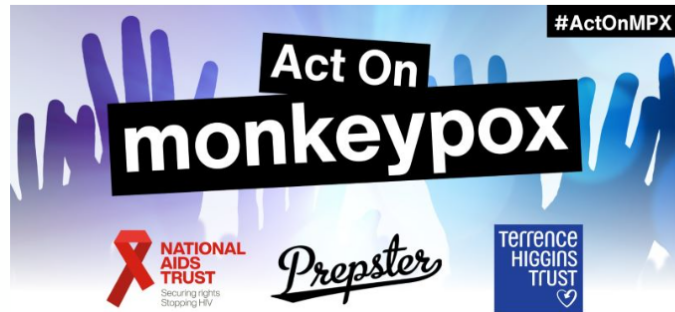
- Behavior Change
- Vaccination



From F.Jacquierioz, point EPI



Public health education that's gone out to the MSM and the LGBTQ community primarily affected





Transmission

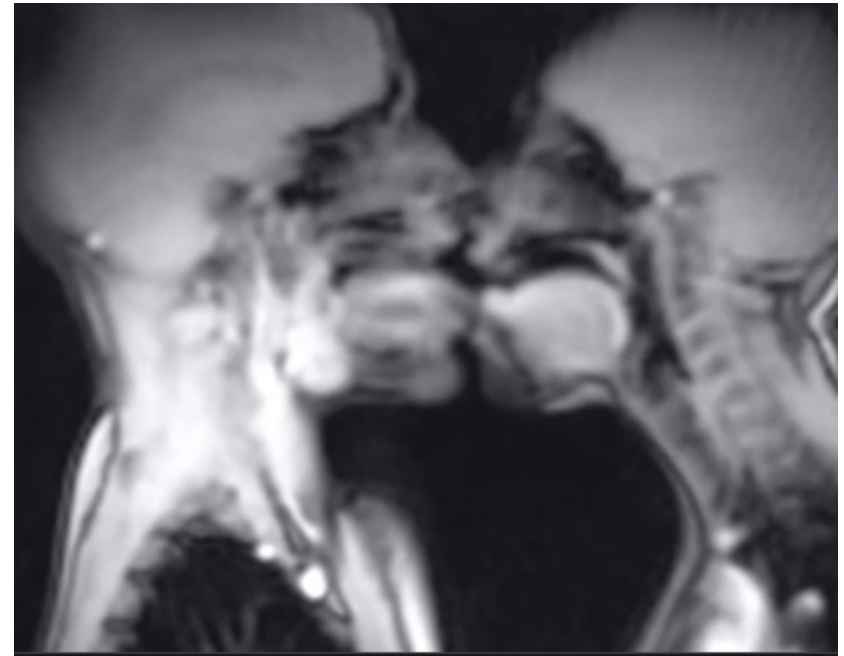
# Transmission from human to human

- Close contact with lesions
- Body fluid
- Respiratory droplets
- Contaminated materials

## SEXUALLY TRANSMISSABLE?



Swiss statement paraphrase:  
'must for now be considered and STI and should be treated as such... but can  
be transmitted outside of sex'



# Association with sexual activity

- Most patients diagnosed with Monkeypox reported high-risk sexual behavior
- Concomitant STDs (16 to 29 %)
- More than 40% HIV-coinfected

HIV infection affects a person's risk for acquiring Monkeypox?

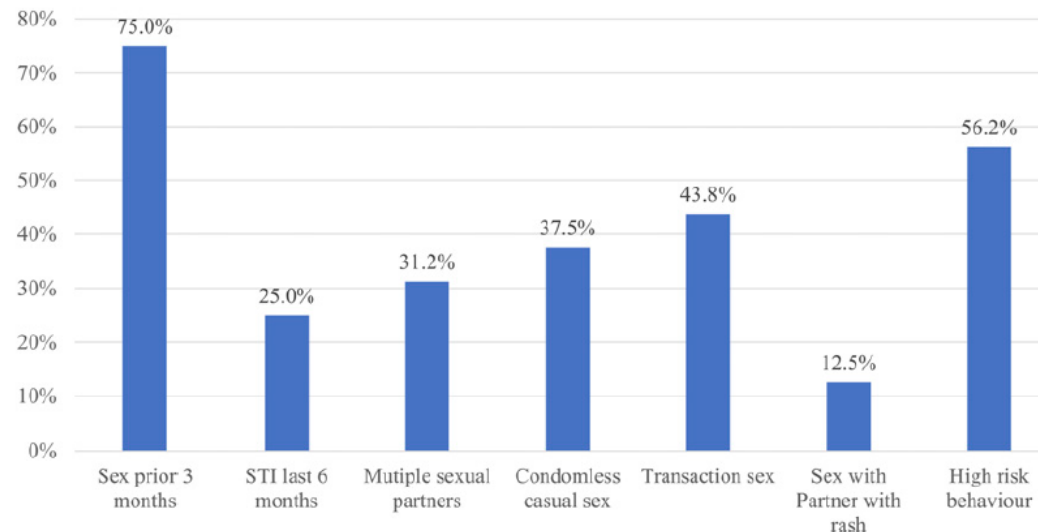
PLWH  
disproportionately  
affected

- Global case series : 41% (218) PLWH
- WHO dataset : 46.5% PLWH
- US dataset : 38%
- Why???
- (Ideas: behavioural, ascertainment bias, biological/microbiome)

# Association with sexual activity

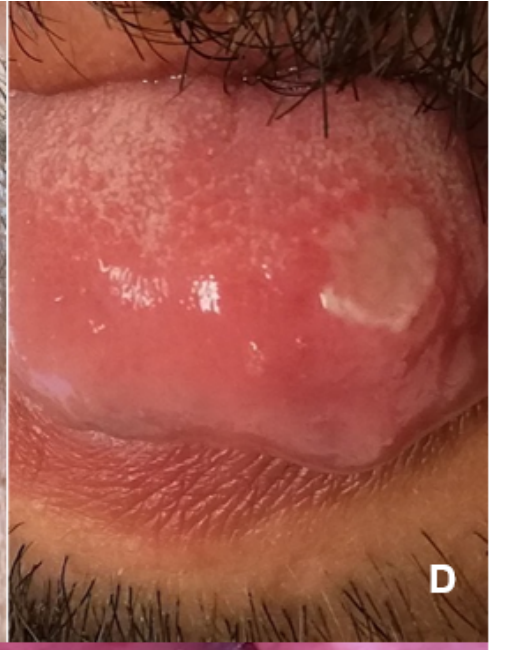
- 2017-2018 outbreak in Nigeria a role of sexual contact was already hypothesized (retrospective review)

While there is sufficient evidence to link MPX transmission with sexual contact and specific sexual behaviours, further confirmatory studies will be required before HMPX could be classified as a sexually transmitted disease



**Figure 1.** Self-reported sexual history of 16 human monkeypox cases seen at a tertiary hospital in Nigeria. 56.2% of study participants reported high risk behaviours, including condomless casual sex, transaction sex and sex with multiple concurrent partners.





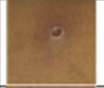
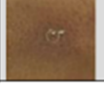
# Clinical presentation



# Clinical cutaneous and systemic presentation

- Incubation 7 days **(5-21 days)**
- **Prodromic symptoms**  
(fever, myalgia fatigue and headache) *(not always present)*
- Lymphadenopathy
- **Maculopapular rash (95%)**
- Lesions develop simultaneously  
(but this is **NOT** what we have been seeing)
- Contagiosity: from prodromal to **last crust fall off**

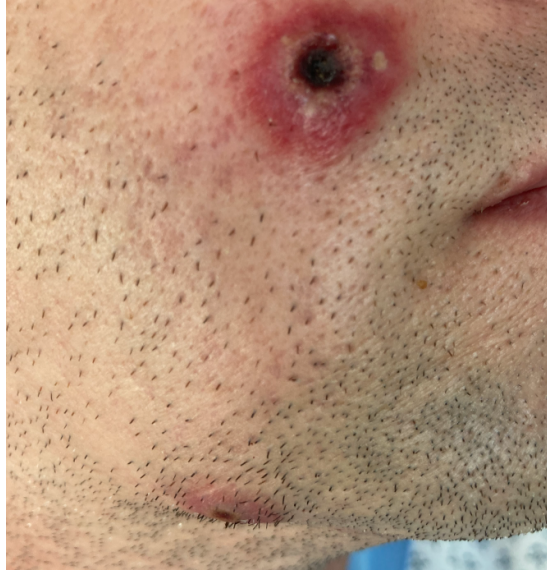
## Clinique

LE PATIENT EST CONTAGIEUX PENDANT TOUTES LES PHASES CLINIQUES		
Délai approximatif	Phase clinique (source CDC)	Illustration (source gov.uk)
J0	Phase prodromique non spécifique : fièvre >38°C, poly adénopathie, myalgies, asthénie	
J1-2	Enanthème 1 <sup>ère</sup> lésions = bouche / langue	
J2-3	Macules Rash centrifuge débutant sur la face et se répandant vers les membres en 24h, puis les paumes des mains et plantes des pieds	
J3	Papules	
J4-5	Vésicules (liquide clair) ∅ ≈ 3mm	
J6-7	Pustules (liquide opaque) pointues, fermes ∅ ≈ 2mm	
	Pustules ombiliqués ∅ ≈ 3-4mm	
	Pustules ulcérés ∅ ≈ 5mm	
J12	Formation de croûte sur lésion mature	
A partir de J14	Croûte en cours de cicatrisation <i>A noter : le patient reste contagieux jusqu'à la cicatrisation complète après chute des croûtes</i>	

# «Classic» vs «New» Form

**Table 1.** Features of the Classic Form of Monkeypox and the New Clinical–Epidemiologic Form.

Variable	Classic Form, 1970s to the Present	New Clinical–Epidemiologic Form, 2022
Location	Central and West Africa	Countries where monkeypox is not endemic (Europe, North and South America, Middle East, Australia)
Affected population	Children and young adults (age at diagnosis increasing since 1980)	Young men who have sex with men (age, 31–40 yr)
Epidemiologic features	Sporadic cases and epidemics	Pandemic under way since May 2022
Transmission	Contact with infected animal reservoir (probably rodents), followed by human-to-human transmission	Exclusively human-to-human transmission
Dissemination	Mostly intrafamilial and limited nosocomial dissemination	Mostly sexual networking, condomless sex with multiple male partners
Clinical phase	Incubation, prodromal stage, eruption phase with skin lesions	Incubation, prodromal stage (not always present), eruption phase with lesions in an unusual distribution, especially on the genitals
Symptoms	Lesions on the face and extremities, with centrifugal distribution, often associated with cervical or axillary lymphadenopathy	Penile rash, perianal lesions, ulcerative lesions and vesicular rash, painful inguinal lymphadenopathy, pharyngitis, proctitis
Viruses	Central African and West African clades (clades 1 and 2, respectively)	West African variant (clade 3)
Case fatality rate (%)	1–15	0.025



13.5 unprotected sexual intercourse ➡ 19.5 systemic symptoms ➡ 21.5 skin lesions





25.5 unprotected sexual intercourse



31.5 systemic symptoms



3.6 skin lesions

Is that all?

# Genital and perianal lesions

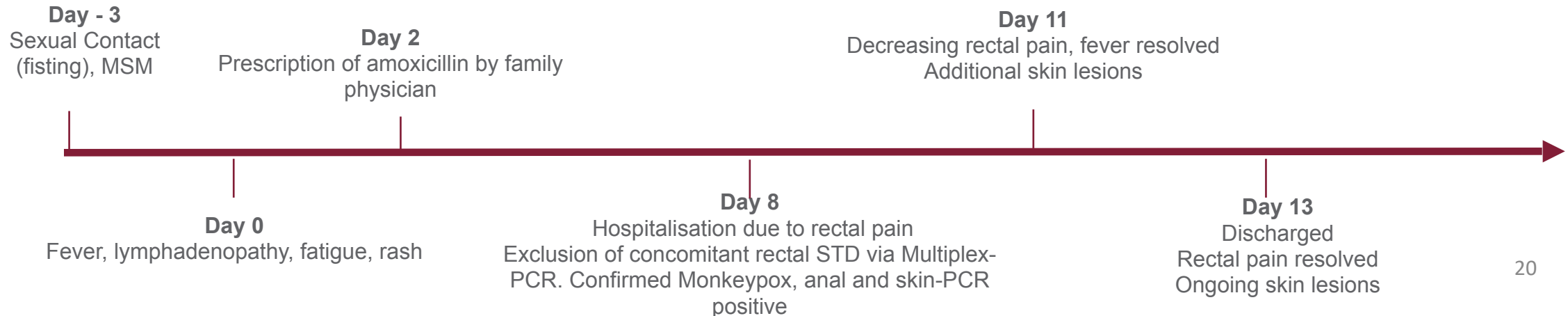
- Lesions frequently present in the anogenital region
- Genital lesions are commonly accompanied by surrounding edema
- Lesions in the perianal region are often associated with rectal pain or pain on defecation
- Proctitis



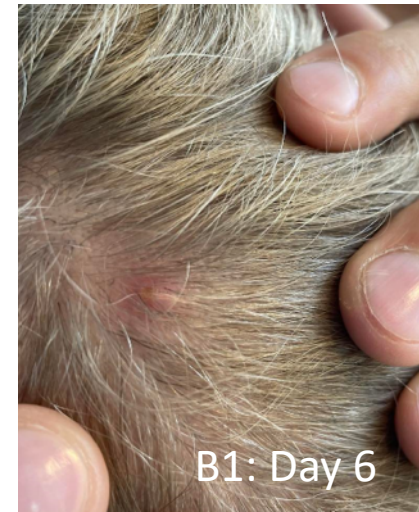
From Chloé Orkin, ECDC webinar, August 16th, 2022

**Figure 14:** Evolution of clinical signs in a single individual with Human Monkeypox infection. A shows a CT scan of a severe MPX-related proctitis. B and C show additional skin lesions. PCR status is indicated where available.

A: Day 8, PCR positive



**Figure 6:** Anal/perianal and cutaneous lesions in an individual with Human Monkeypox infection first presented with fever and one perianal lesion. A shows Anal/perianal lesions. B1-B3 show cutaneous lesions of the scalp arm and leg respectively.



**Day -6**  
Sexual  
Contact, MSM  
Condomless

**Day 0**  
Fever, lymphadenopathy,  
one lesion (perianal)

**Day 2**  
Confirmed Monkeypox, perianal lesion-  
PCR positive. More severe rectal pain,  
initially treated as outpatient

**Day 6**  
Admitted as inpatient due to very severe rectal pain,  
has a few perianal lesions, and anoscopy reveals  
many vesicular lesions in the anal canal

**Day 8**  
Developed 10 cutaneous  
lesions on limbs, face and  
scalp





Day 6

31yo, good general health  
PreP (no medical follow-up)  
Multiple sexual partners

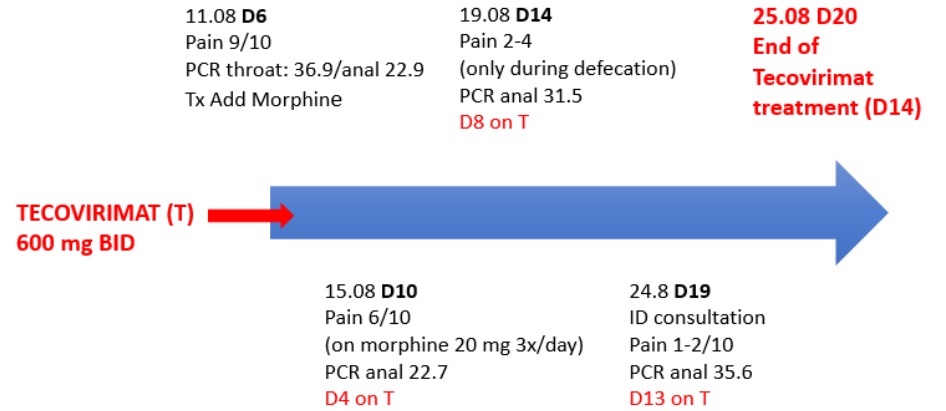
30.07: unprotected sexual intercourse

02.08: Imvanex® as PEP (UK)

05.08 **D0** Severe rectal pain + local lesions

08.08 **D3**  
 CT: no abscess; PCR(anal)19  
 Tx: Augmentin/PCM/Irfen

10.08 **D5**  
 10/10 pain  
 Tx: Add Tramadol

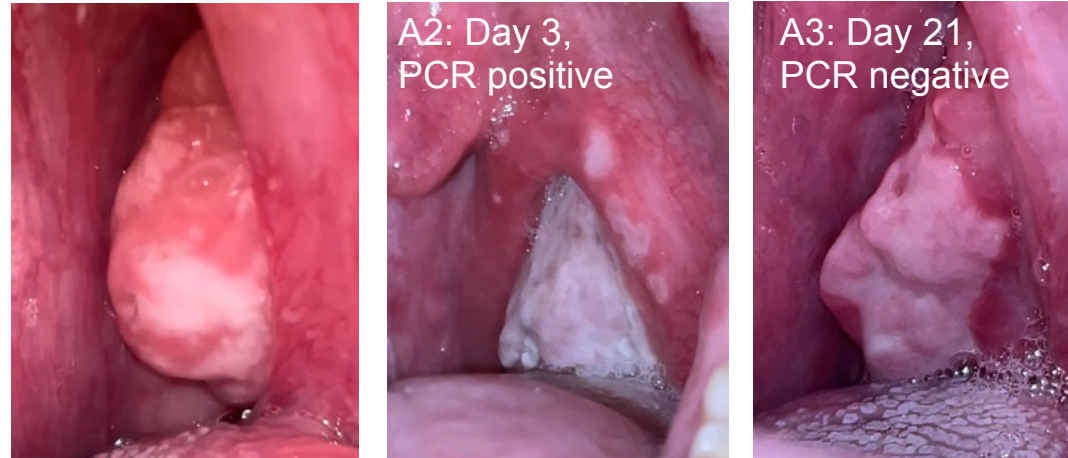


Day 19



# Pharyngeal lesions

**Figure 8:** Evolution of pharyngeal lesions in an individual with Human Monkeypox infection.



# STDs co-infection/Bacterial superinfection

- 56/178 (31.5%) participants had a **concomitant sexually transmitted infections**
- Bacterial superinfection may delay duration symptoms and complicate the clinical picture

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**Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: descriptive case series**



Aatish Patel, Julia Bilinska, Jerry C H Tam, Dayana Da Silva Fontoura, Claire Y Mason, Anna Daunt, Luke B Snell, Jamie Murphy, Jack Potter, Cecilia Tuudah, Rohan Sundramoorthi, Movin Abeywickrema, Caitlin Pley, Vasanth Naidu, Gaia Nebbia, Emma Aarons, Alina Botgros, Sam T Douthwaite, Claire van Nispen tot Pannerden, Helen Winslow, Aisling Brown, Daniella Chilton, Achyuta Nori



# Asymptomatic infection

- 13/200(6.5%) were **asymptomatic et positive for PCR Monkeypox virus** in a Sexual health clinic in France (Ferré et al.)
- The potential for transmission from an individual with asymptomatic infection is uncertain

## **Detection of Monkeypox Virus in Anorectal Swabs From Asymptomatic Men Who Have Sex With Men in a Sexually Transmitted Infection Screening Program in Paris, France** FREE

Valentine Marie Ferré, PharmD , Antoine Bachelard, MD, Meryem Zaidi, BSc, ... [View all authors](#) 

[Author, Article, and Disclosure Information](#)

## Complications

- Superinfection: : cellulitis, abscess - antibiotics/drainage
- Anorectal pain, ulcers, perforation
- Paraphymosis, urinary retention
- Oropharyngeal: tonsillitis, odynophagia, epiglottitis
- Dehydration, acute renal injury
- Ocular: keratitis
- Myocarditis
- Encephalitis, seizure, confusion, headache, depression (2%)
- Skin: Exanthem or disseminated lesions

# How do we treat monkeypox?

- Supportive care (pain relief medication, early detection and treatment of superinfection, empirical STDs treatment)
- PEP immunisation (up to D4?)
- Antiviral therapy (**Tecovirimat**, Cidofovir/Brincidofovir)



# How do we treat monkeypox?

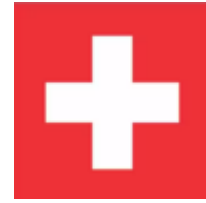
Girometti, WAIDS2022

## ANTIVIRALS

- Mostly reserved to treat severe cases (incl. individuals requiring hospitalization, with functional disabilities, severe pain, or at risk of severe disease - children < 8 years, pregnant women or immunosuppressed patients)
- **TECOVIRIMAT** (viral envelope protein VP37 inhibitor)
  - Effective in treating disease caused by orthopoxviruses on animal studies <sup>1 2</sup>
  - **In human: case reports (Ann Internal Med Lucar et al, August 16<sup>th</sup>, JAMA Desai et al, August 17<sup>th</sup>, 2022)**
  - May shorten the duration of illness and viral shedding
- **CIDOFOVIR / BRINCIDOFOVIR** (viral DNA polymerase inhibitors)
  - effective against orthopoxviruses in in-vitro and animal studies <sup>3</sup>
  - Brincidofovir has been approved by CDC for the treatment of human smallpox disease in adult and pediatric patients



# Compassionate use of Tecovirimat in



1. Confirmed Monkeypox virus (MKPV) infection
2. Patient at risk for severe disease, immunocompromised or pregnant woman or children pending a specialized opinion
3. Patients with a severe disease presentation with extensive or coalescent lesions, leading to functional inability (throat or genital mucosal lesion, eyes) or uncontrollable discomfort and pain.
4. Patients hospitalized with organ dysfunction (encephalitis, sepsis) or hemorrhagic lesions

# Many unanswered questions

- Antivirals: To whom and when?
- Antivirals: At the beginning? Only for severe cases?
- Vaccination role, as cases are stagnant?
- Role of vaccinia Immune Globulin Intravenous (VIGIV)
- Good data needed

# MOSAIC cohort - Observational study

Promoter: Oxford



## Rationale of the study

As monkeypox is a rare disease and has only had sporadic cases reported before 2022 in Europe, there is a clear need to characterize the disease in countries where recent spread has been reported..



## Primary objective

To describe the clinical outcome in patients with monkeypox, whether or not treated with tecovirimat (or other antiviral).  
Measures: Time to resolution of active lesions. Defined as the first day that lesions are healed or scaly, with no complications up to 14 days post-diagnosis (or post-treatment)



## Visits

Inclusion criteria: PCR positive  
Clinical examination and throat smear and lesion for viral load on the 1st day, 14 days and 28 days post-diagnosis.  
Search for possible recrudescence 2 months and 6 months post-diagnosis

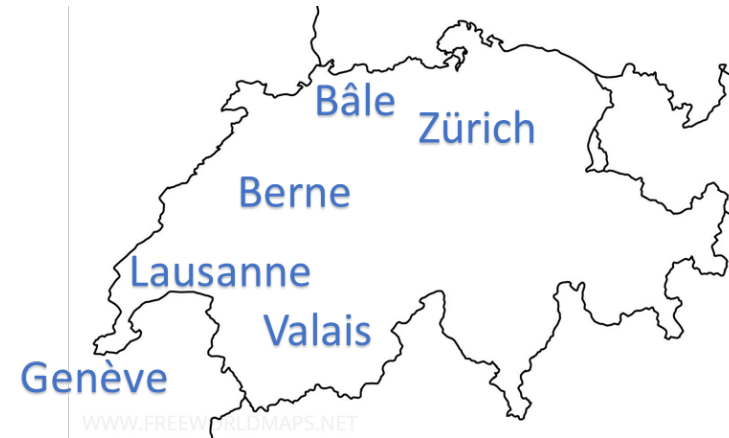
# MOSAIC cohort - Observational study

## Promoter: Oxford



### 11 countries involved

The MOSAIC cohort brings together many Western European countries such as the United Kingdom, Belgium, Spain and Norway. The countries where recruitment is active are the United Kingdom, France and Switzerland.



### 7 hospitals in Switzerland

With 35 patients included as of 24.10.2022, Switzerland was the first country involved in the cohort to recruit patients. The sites with the most participants are Geneva (12), Lausanne (11) and Zürich (8).





## Context and rationale of the study

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Adaptation of the WHO “CORE” protocol for Switzerland and Brazil: use of antivirals for the treatment of monkeypox.  
Tecovirimat, authorized in the USA (FDA) and in Europe (EMA) but not yet in Switzerland or Brazil.

## Objective

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Evaluating Tecovirimat in the treatment of monkeypox: efficacy and safety.  
Double-blind randomized trial against placebo, in patients over 14 years of age.  
The main criterion for judging the effectiveness of tecovirimat will be the time it takes for all visible lesions to resolve in patients who have contracted monkeypox.

## Visits

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Up to day 21:

- For hospitalized patients, clinical evaluation and sampling every 3 days.
- For non-hospitalized patients, clinical assessment and sampling every 7 days, with potential virtual visits between on-site visits.

Then follow-up at 1 and 2 months. 2-month visit possible by phone

Grazie  
Merci  
Grazcha  
Danke  
Thanks



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