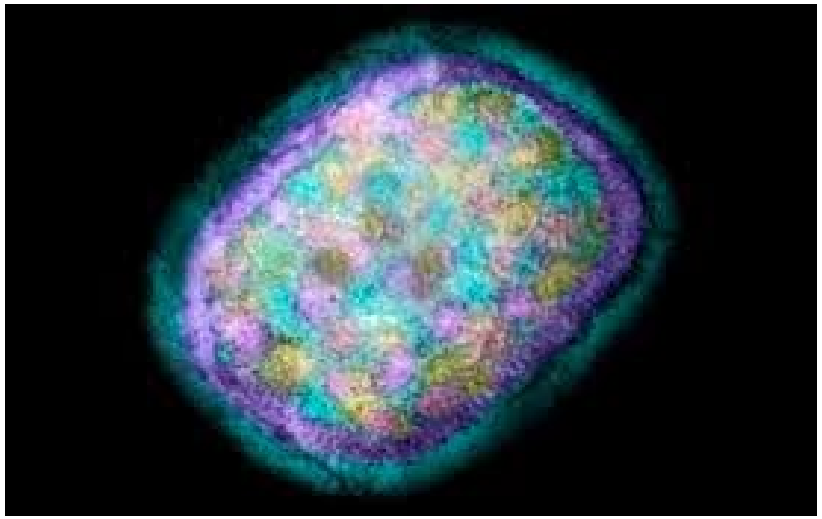
Monkeypox



2023-12-7

Owen Tsang

Infectious Disease Centre

Princess Margaret Hospital

Pox viruses

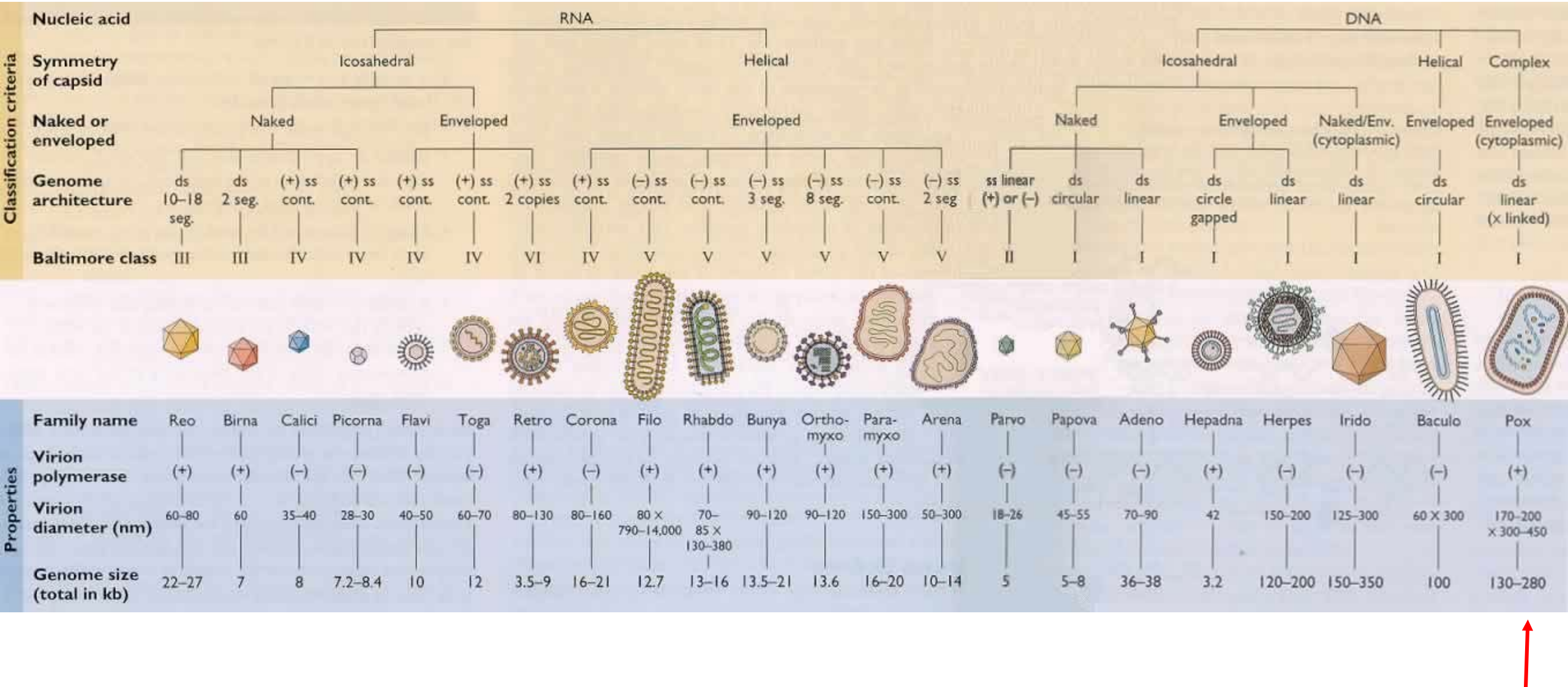

Classification criteria
Nucleic acid
RNA
DNA
Symmetry of capsid
Icosahedral
Helical
Icosahedral
Helical
Complex
Naked or enveloped
Naked
Enveloped
Enveloped
Naked
Enveloped
Naked/Env. (cytoplasmic)
Enveloped
Enveloped (cytoplasmic)
Genome architecture
ds 10–18 seg.
ds 2 seg.
(+) ss cont.
(+) ss cont.
(+) ss cont.
(+) ss cont.
(+) ss 2 copies
(+) ss cont.
(–) ss cont.
(–) ss cont.
(–) ss 3 seg.
(–) ss 8 seg.
(–) ss cont.
(–) ss 2 seg.
ss linear (+) or (–)
ds circular
ds linear
ds circle gapped
ds linear
ds linear
ds circular
ds linear (x linked)
Baltimore class
III
III
IV
IV
IV
IV
VI
IV
V
V
V
V
V
V
II
I
I
I
I
I
I
I
Properties
Family name
Reo
Birna
Calici
Picorna
Flavi
Toga
Retro
Corona
Filo
Rhabdo
Bunya
Ortho-myxo
Para-myxo
Arena
Parvo
Papova
Adeno
Hepadna
Herpes
Irido
Baculo
Pox
Virion polymerase
(+)
(+)
(–)
(–)
(–)
(–)
(+)
(–)
(+)
(+)
(+)
(+)
(+)
(+)
(–)
(–)
(–)
(+)
(–)
(–)
(–)
(+)
Virion diameter (nm)
60–80
60
35–40
28–30
40–50
60–70
80–130
80–160
80 × 790–14,000
70–85 × 130–380
90–120
90–120
150–300
50–300
18–26
45–55
70–90
42
150–200
125–300
60 × 300
170–200 × 300–450
Genome size (total in kb)
22–27
7
8
7.2–8.4
10
12
3.5–9
16–21
12.7
13–16
13.5–21
13.6
16–20
10–14
5
5–8
36–38
3.2
120–200
150–350
100
130–280

Table 1. Zoonotic poxviruses

Virus	Genus	Geographic location	Clinical features	Reservoir host
Cowpox	Orthopoxvirus	UK, Europe, adjacent USSR	Cutaneous inoculation. Short 7-day incubation. Systemic flu-like malaise and pyrexia. Lesions solitary or few, mainly face and hands. Localized firm oedema, erythema and regional adenopathy. Initial erythematous papule/blister later forms crusted eschar, which heals slowly leaving deep pock-like scar	Small rodents, particularly wood mice and wood voles
Monkeypox	Orthopoxvirus	West Africa: Zaire, the Congo	Cutaneous inoculation or inhalation. Twelve-day (range 7–17 days) incubation. Severe flu-like prodrome with high fever. Two-thirds have respiratory symptoms. Multiple small firm umbilicated blisters in centrifugal distribution. Resembles smallpox with marked adenopathy. Facial pock marks	Several species of tree and rope squirrels and probably other small mammals
Buffalopox	Orthopoxvirus similar to vaccinia virus	Indian subcontinent	Cutaneous inoculation. Mild illness, usually few lesions on hands and arms. Similar to cowpox but less severe. Leaves minor pock-like scars	Water buffalo
Cantagalo and Araçatuba	Orthopoxvirus similar to vaccinia virus	South America, mainly Brazil	Cutaneous inoculation. Mild illness similar to cowpox or buffalopox	Cattle and probably rodents
Vaccinia	Orthopoxvirus	Smallpox vaccine	Probable precursor of Cantagalo and Araçatuba viruses and possibly buffalopox virus	
Orf	Parapoxvirus	World-wide	Cutaneous inoculation. Three- to seven-day incubation. Mild illness, lesions solitary/few, usually hands. Minor scars	Sheep and goats
Paravaccinia	Parapoxvirus	World-wide	Clinically similar to orf	Cattle
Bovine papular stomatitis	Parapoxvirus	World-wide	Clinically similar to orf	Cattle
Deerpox	Parapoxvirus	Deerherds	Clinically similar to orf	Various deer
Sealpox	Parapoxvirus	Seal colonies	Clinically similar to orf	Harbour and grey seals
Tanapox	Yatapoxvirus	Africa, Kenya	Solitary or few umbilicated lesions, legs and trunk. Systemic malaise and adenopathy. Slow healing with cicatricial scar	Monkeys and ? insects

Lewis-Jones S. ***Curr Opin Infect Dis*** *2004;17:81–89.*

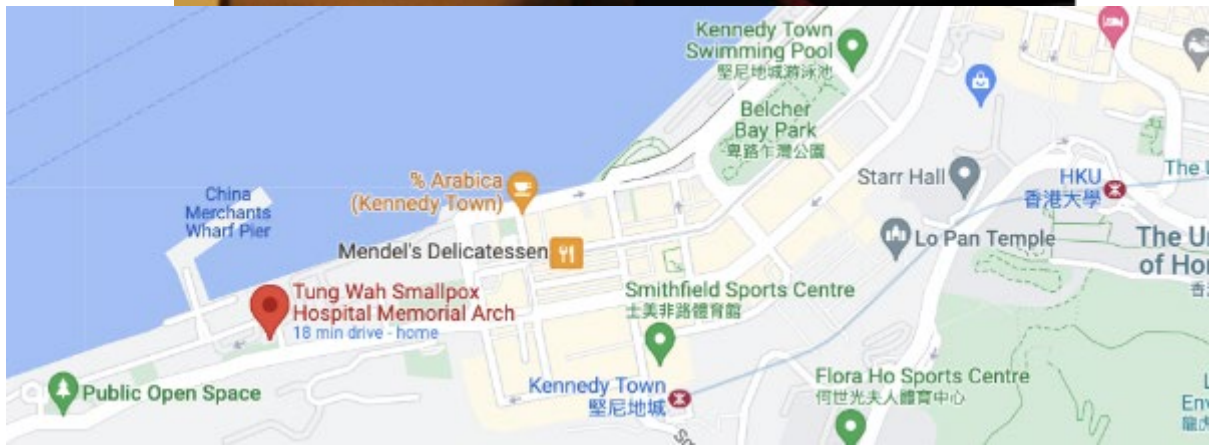
The discovery of cowpox vaccination by Edward Jenner in 1796

Milk lady was immune from Smallpox

Jenner vaccinated his servant's son

Jenner vaccinated his own son

Smallpox vaccination in Hong Kong



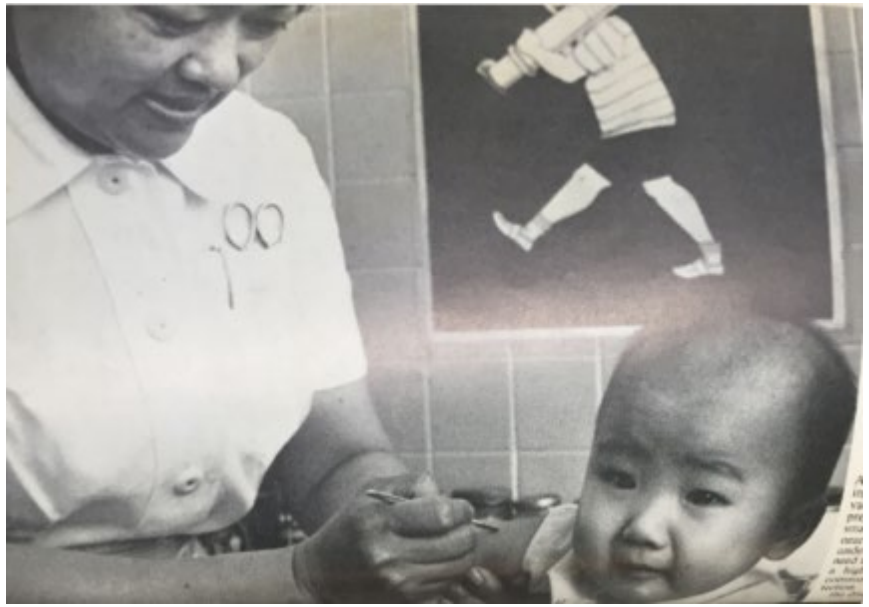
Wong S, ***HKMJ*** *2017;23(1):101-3*

Smallpox vaccination in Hong Kong

總督部昨公布
下月起開始種痘
天氣漸燥居民種痘預防天花
如無種痘証不許在市面往來

（本報特訊）總督部衛生當局，爲確保居民健康，對於公共衛生及防疫工作不遺餘力，今年雷風疫症發生減少，亦賴衛生當局防範適宜，及居民協力施行種痘之故。最近季節天氣漸燥，居民飲食極宜小心，衛生當局，并爲預防天花症流行，作有備無患計，決定由十一月一日起施行免費種痘，總督部昨日發表布告第一五號通告實行。

茲此次實施種痘運動，純爲保護居民健康而設，故免費施種，指定免費施種場所，計香港方面十二處，九龍方面十處，新界方面六處。凡不願在免費場所接種者，亦經指定衛生醫香港九龍兩診療所，博愛會香港九龍兩診療所，香港婦孺會，東華醫務兩診療所，一般居民屆時宜前往指定場所接受施種，并領回證明書，以備檢查，倘記明不接受施種，將禁止其在市內交通及貿易，各宜協力維護公共健康。茲將布告第一五號及各區指定種痘場所錄下：



醫藥署昨貼街招
警告居民速種痘
謂免致一世有痘皮
今年肺癆死亡千餘

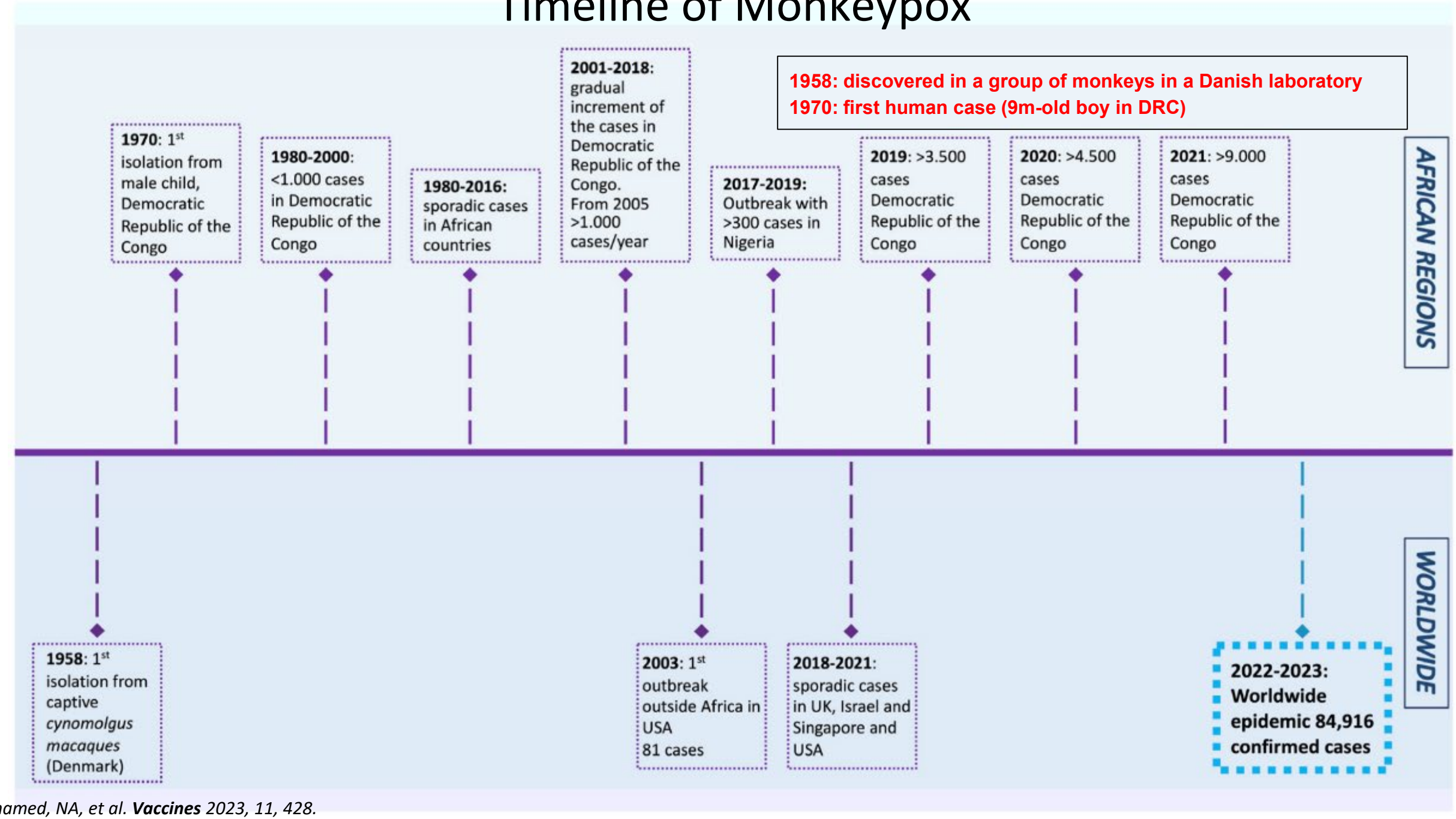
本港發生痘症，蔓延甚厲，衛生當局，週來舉行防痘大運動，醫藥署長奇勒克，爲促起居民種痘預防天花起見，昨特印就中西文街招，滿貼於通衢大道上，警告居民速種洋痘，其中警語有謂「如不種痘，即患天花」，該街招云，「勸君快種痘，勸君快同你的兒女種痘，免致染着了痘症，一世有痘皮，或者毀盲了雙眼，甚或至到死，種痘好容易，下列各地方，處處有得種，不費半文錢，若到醫生處，所費亦無多，君你要知到，雖然係種痘，五年須再種，勿話不知到，因爲無人言，勸君須注意，大衆得安全，」

免費種痘（香港之公共汽車前往，（一）中約公立醫局，（二）中環鴨巴甸街第三號皇后醫院，可由統利一碼頭搭第四號路線，（三）東約公立醫局

Vaccination stopped in 1973

Monkeypox

Timeline of Monkeypox

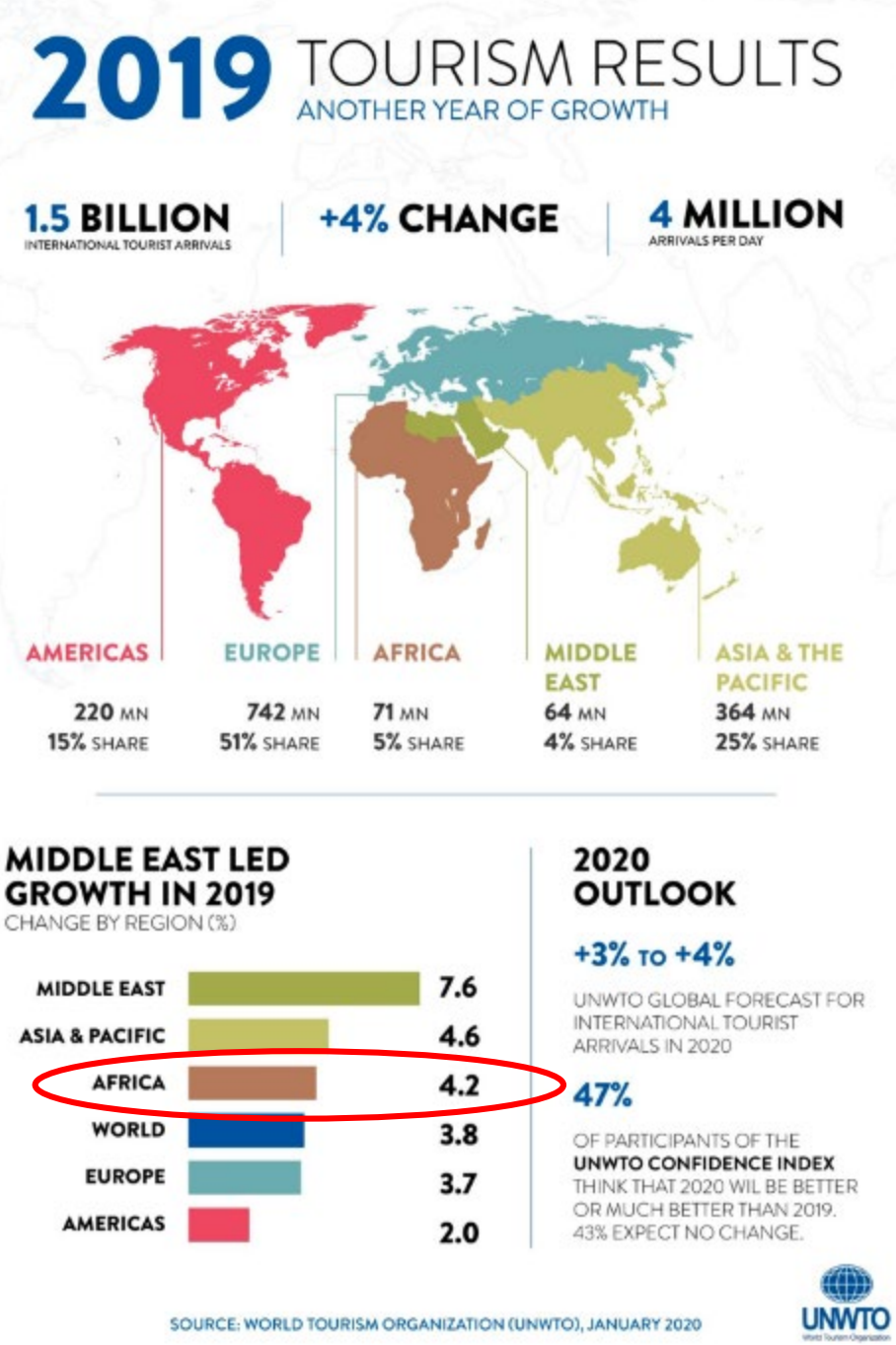


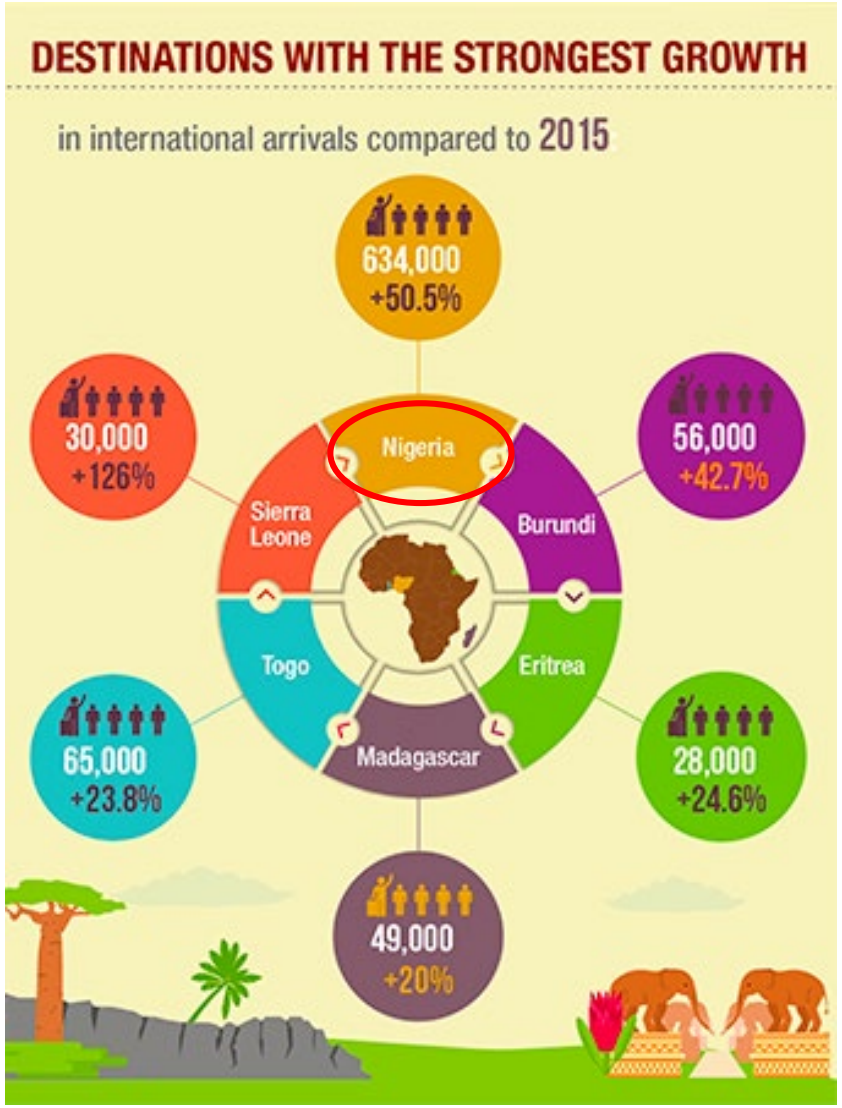
Mohamed, NA, et al. ***Vaccines*** *2023, 11, 428.*

Key questions of the current global outbreak

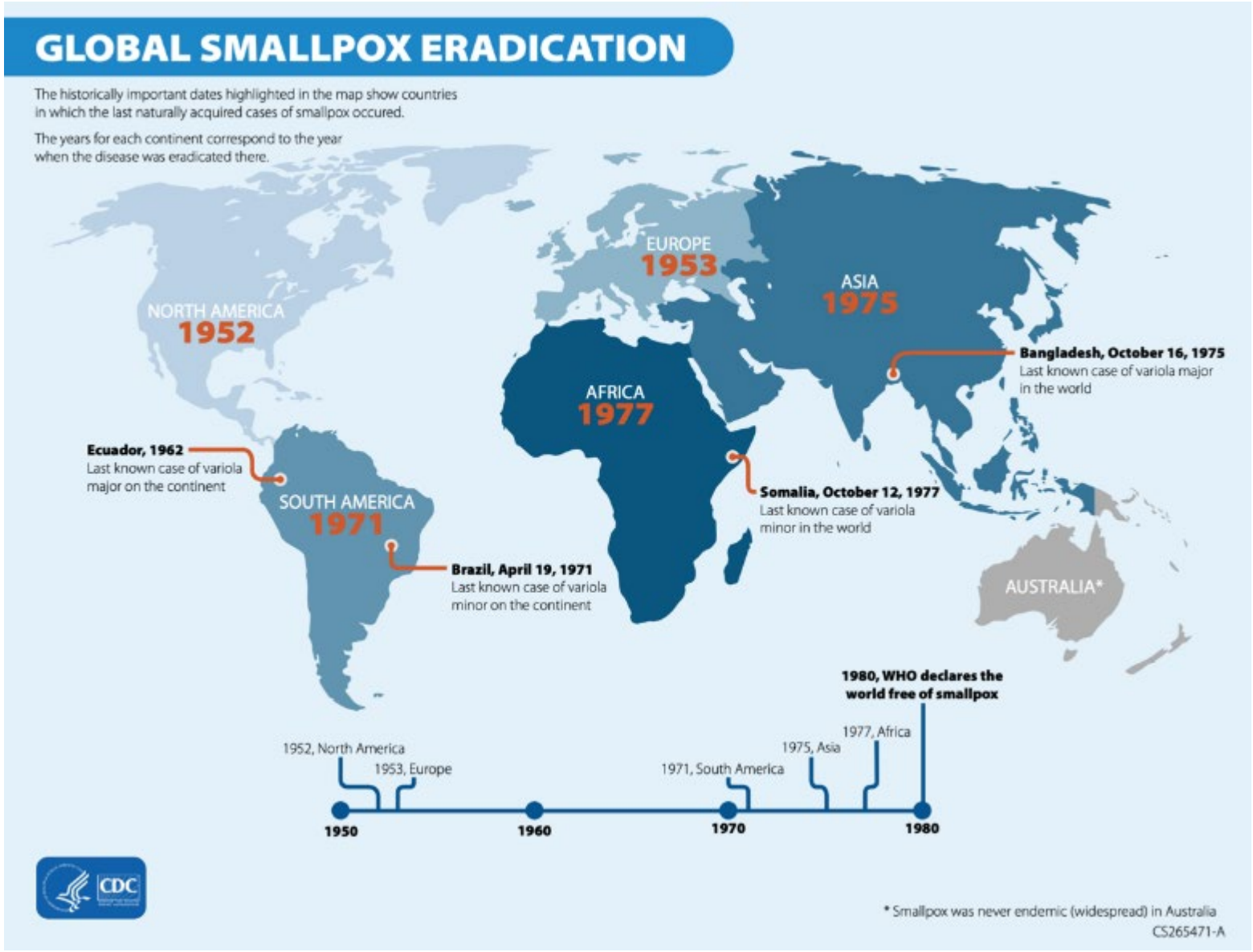
- Why now for a DNA viral disease of over 50 years old?
- Atypical Clinical characteristics?
- Sexual transmission?
- Needing antivirals?
- Needing vaccination?

Why Now:
increasing international travelers to Africa





Why now?
decreasing vaccination rate

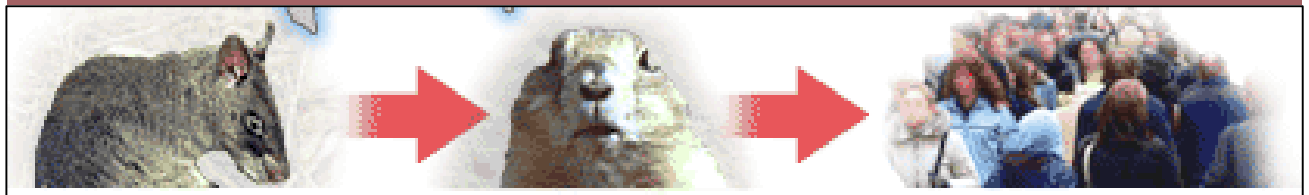


- WHO declared eradication of smallpox in 1980
- Smallpox vaccination **confers 85% cross protection against monkeypox**
- Most countries stopped SP vaccination in the 1970s

Why now?
Animal trade

2003 outbreak in US

Monkeypox: Suspected trail of infection



GIANT GAMBIAN RAT
Disease carried into US by rats imported from Africa as exotic pets

PRAIRIE DOG
Disease spreads to prairie dogs captured in Texas for use as pets

HUMANS
Contract disease when scratched or bitten by infected prairie dogs

SOURCE: CDC

TABLE 2. Disposition of African rodents* imported from Ghana to the United States on April 9, 2003, associated with monkeypox infection of prairie dogs

Rodents	Dead	Alive	Lost to follow-up	Total
Gambian giant rats	26	20	4	**50**
Dormice	~350	27	~135	**510**
Rope squirrels	49	4	—	**53**
Tree squirrels	24	20	3	**47**
Striped mice	14	50	36	**100**
Porcupines	2	—	—	**2**

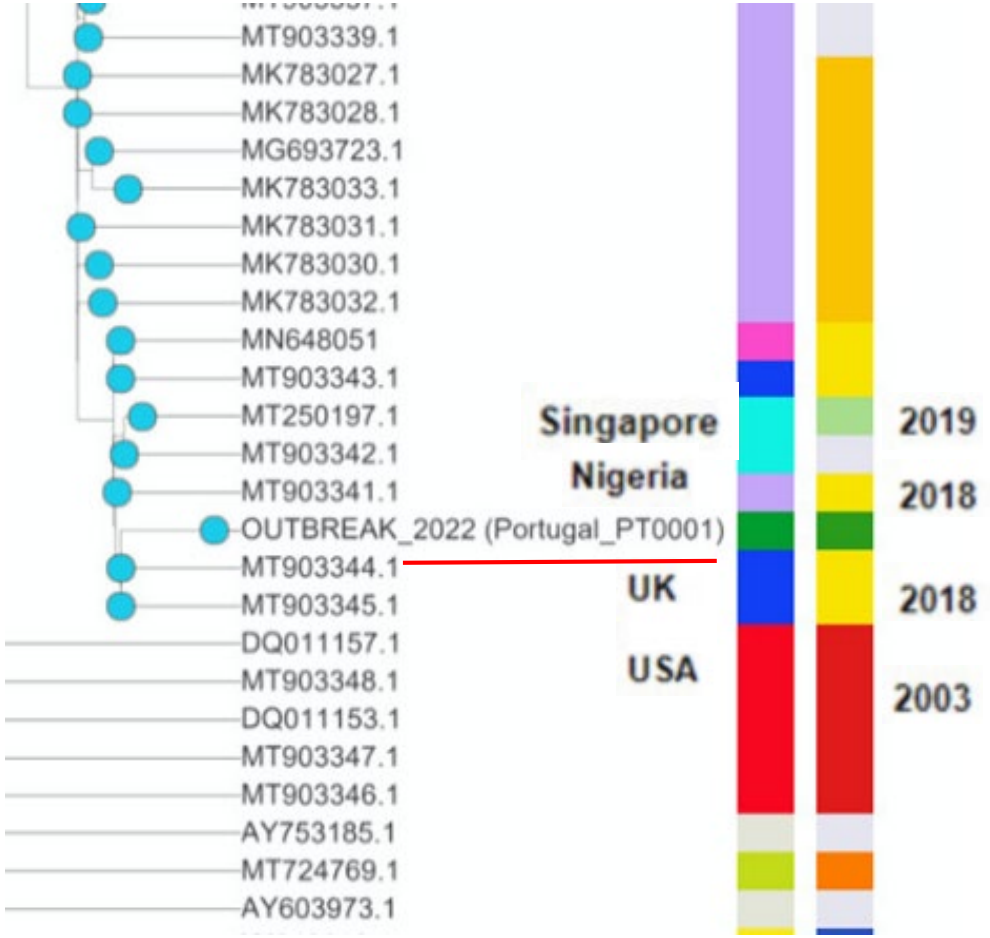
* N = 762.

TABLE 1. Number and percentage of laboratory-confirmed monkeypox cases, by selected characteristics — United States, 2003

Characteristic	No.	(%*)
State		
Illinois	8	(23)
Indiana	7	(20)
Kansas	1	(3)
Missouri	2	(6)
Wisconsin	17	(49)
Age group (yrs)		
6–18	11	(31)
19–51	24	(69)
Sex		
Female	18	(51)
Male	17	(49)
Possible sources of monkeypox exposure		
Prairie dog(s)	14	(40)
Prairie dog(s) and human case(s)	14	(40)
Premises housing prairie dogs	6	(17)
Premises housing prairie dog(s) and human case	1	(3)
Clinical features		
Rash†	34	(97)
Fever	29	(85)
Respiratory symptoms§	27	(77)
Lymphadenopathy	24	(69)
Hospitalized¶	16	(46)
Previous smallpox vaccination**	8	(33)

CDC. ***MMWR Morb Mortal Wkly Rep.*** *2003 Jul 11;52(27):642-6.*

Origin of the 2022 outbreak

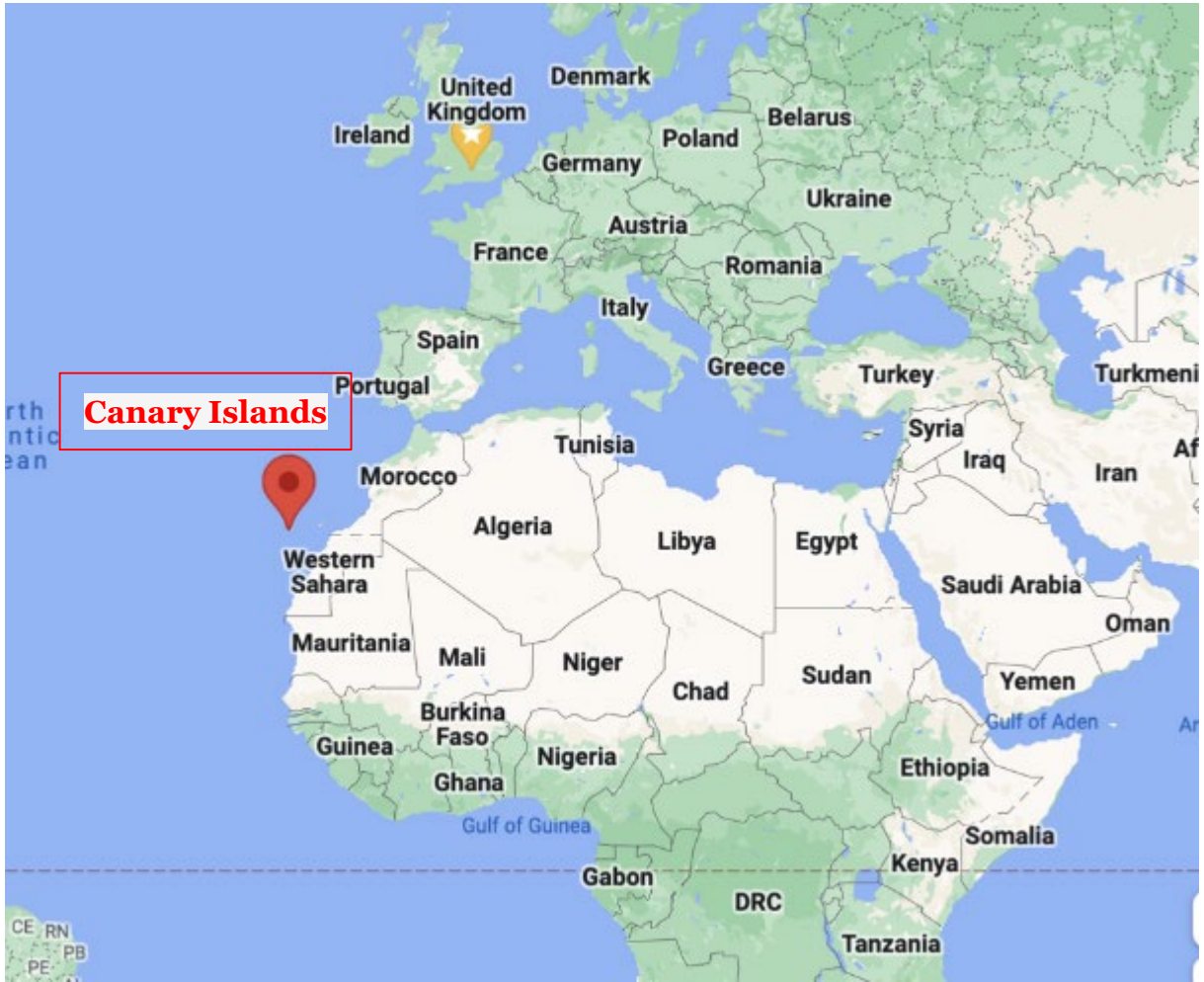


Genome

- The 1st sequence of the 2022 outbreak by Portugal
- Closely resemble that of UK and Nigeria in 2018, and Singapore in 2019
- West African clades
- ? circulating in animal and human since 2018

https://virological.org/t/multi-country-outbreak-of-monkeypox-virus-genetic-divergence-and-first-signs-of-microevolution/806

Sexual transmission?

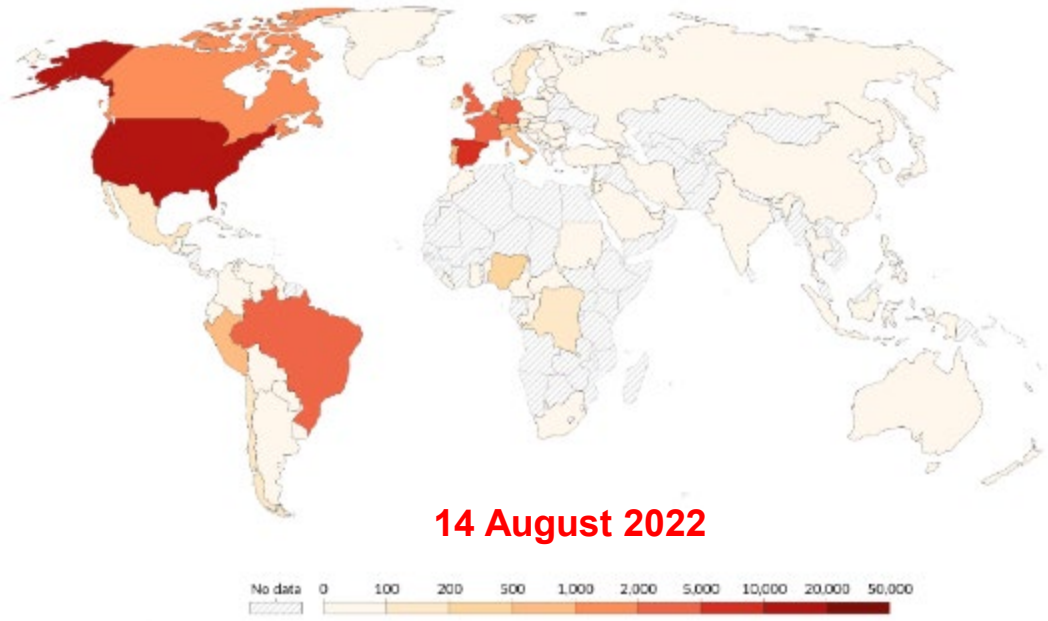


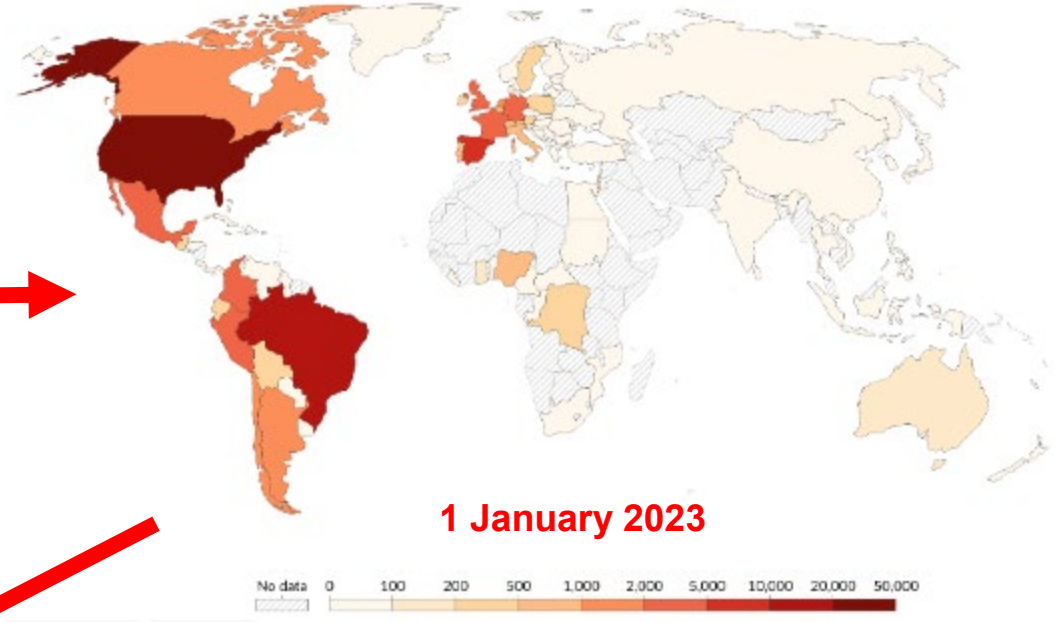
Pride festival in Gran Canaria that was attended by 80,000 people is linked to Spanish monkeypox cases as well as two cases in Italy - while European reaches a total of 100 known cases

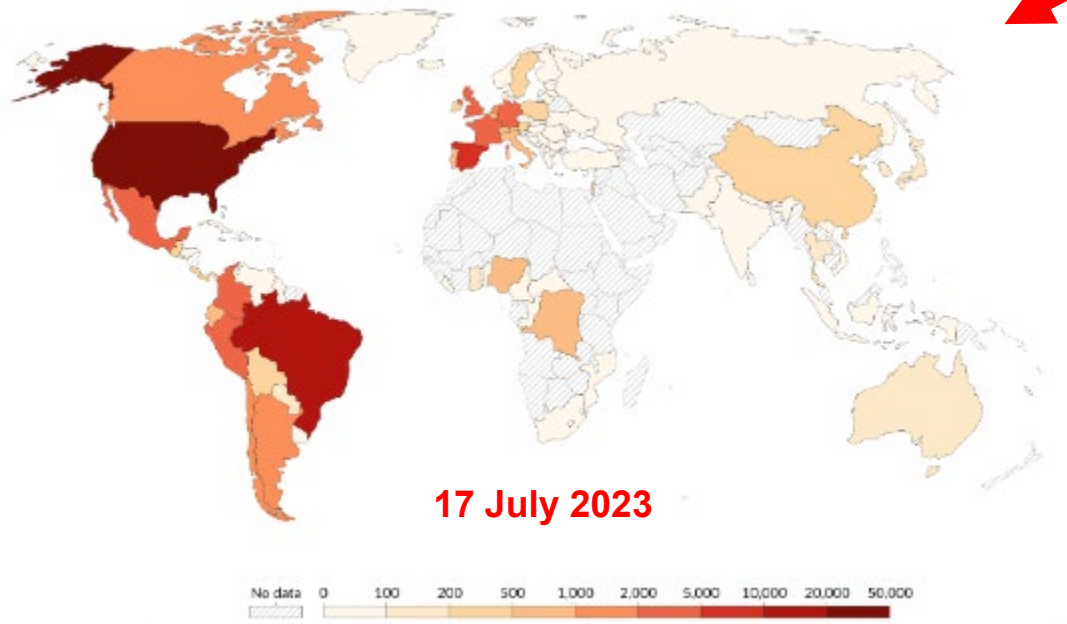
By Jessica Warren For Mailonline
07:01 EDT 21 May 2022 , updated 14:21 EDT 21 May 2022

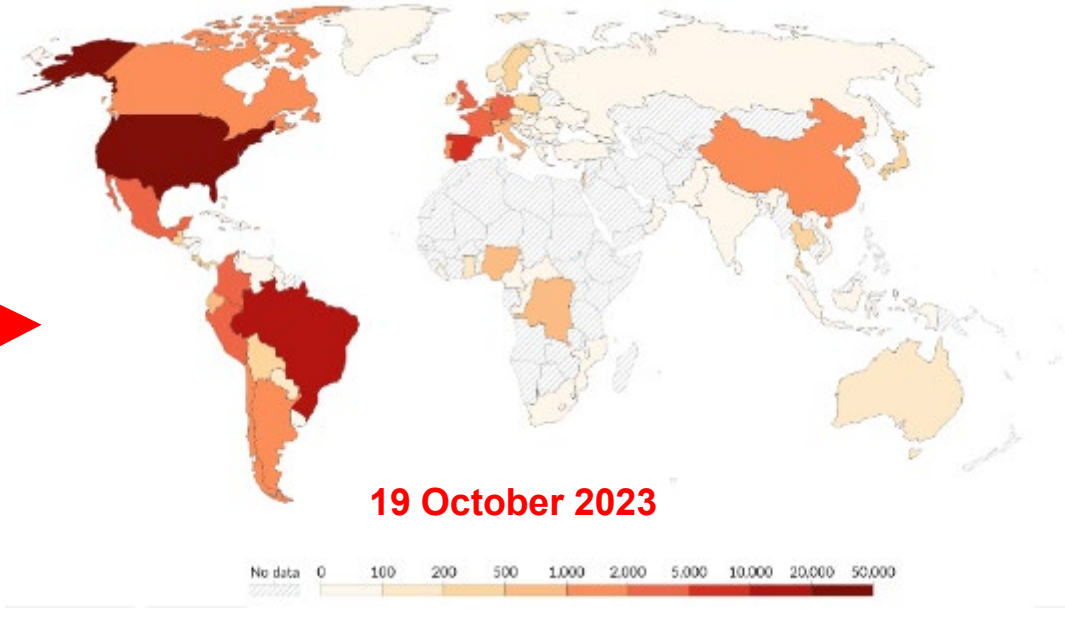
Situation update

Our World in Data









Mpox: Daily confirmed cases

7-day rolling average

Our World in Data

Table | Map | Chart

Settings

As of 1 Dec 2023, there were total of 92,182 cases

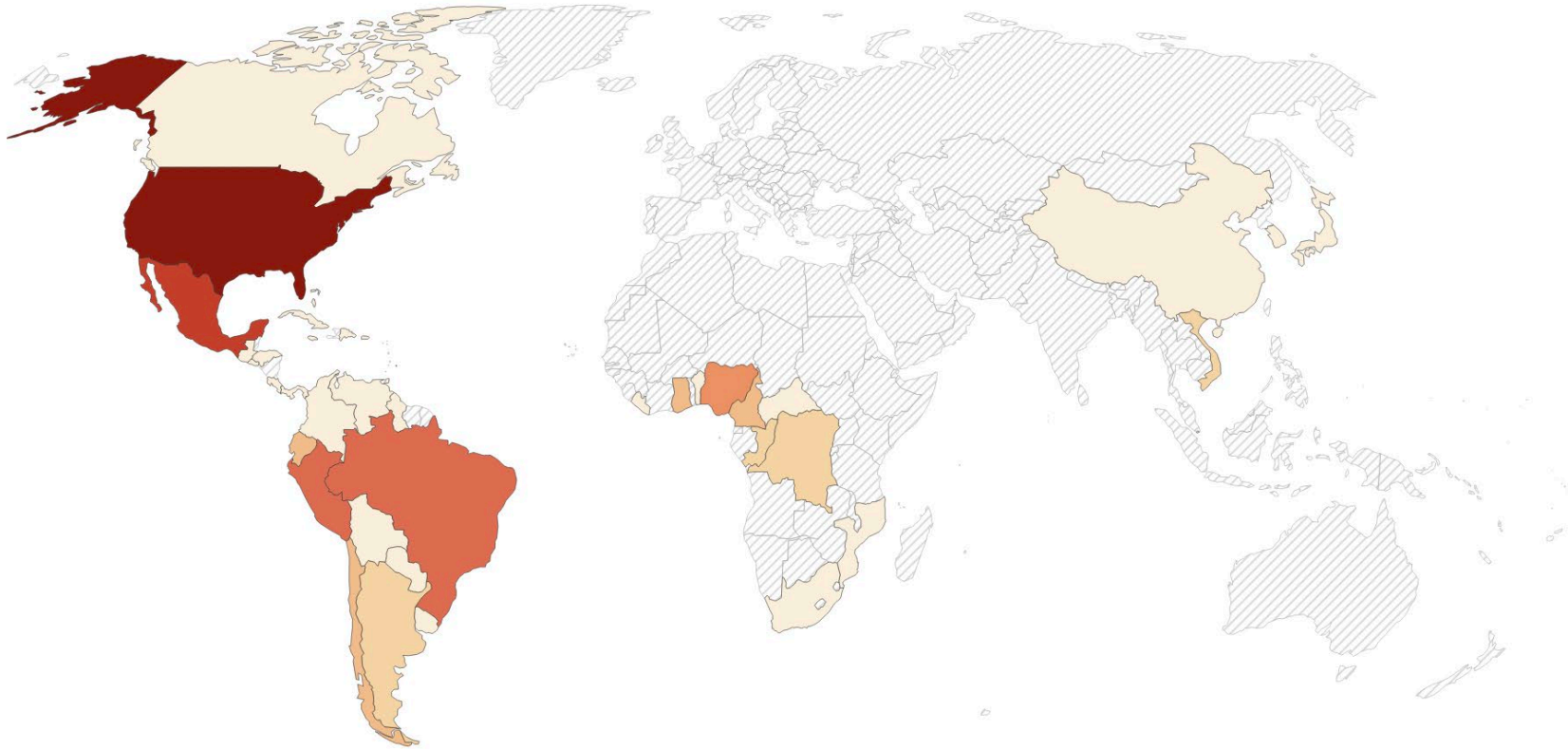
Mpox: Cumulative confirmed deaths, Dec 1, 2023

Our World in Data

Table | Map | Chart

World

171 deaths as of 1 Dec 2023 (0.18%)



No data | 0 | 1 | 2 | 5 | 10 | 20 | 50 | 100

▶ Play time-lapse | May 1, 2022 | Dec 1, 2023

Western vs central clades

Difference between Western & Central clades

1–3%
Death Rate

West African Strain

The West African strain is the detected strain currently spreading beyond Africa

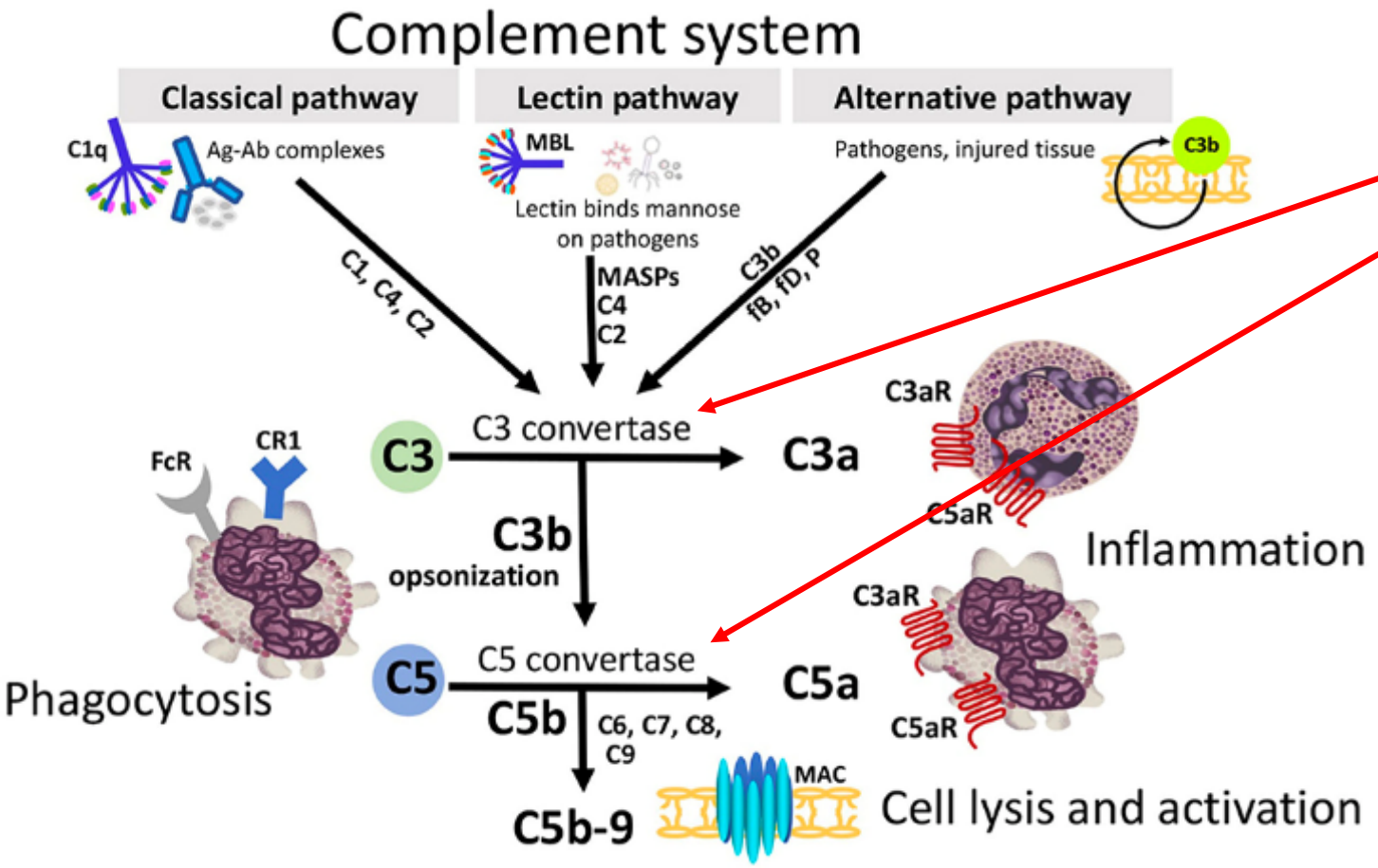
10%
Death Rate

Central African Strain

◀ Despite its name, monkeypox is actually a misnomer since it most commonly infects small African mammals and rodents.

Monkeypox got its name after being discovered in 1958 when two outbreaks of a pox-like disease were discovered in colonies of **crab-eating macaques** that were being used for research purposes.

Western vs Central clades

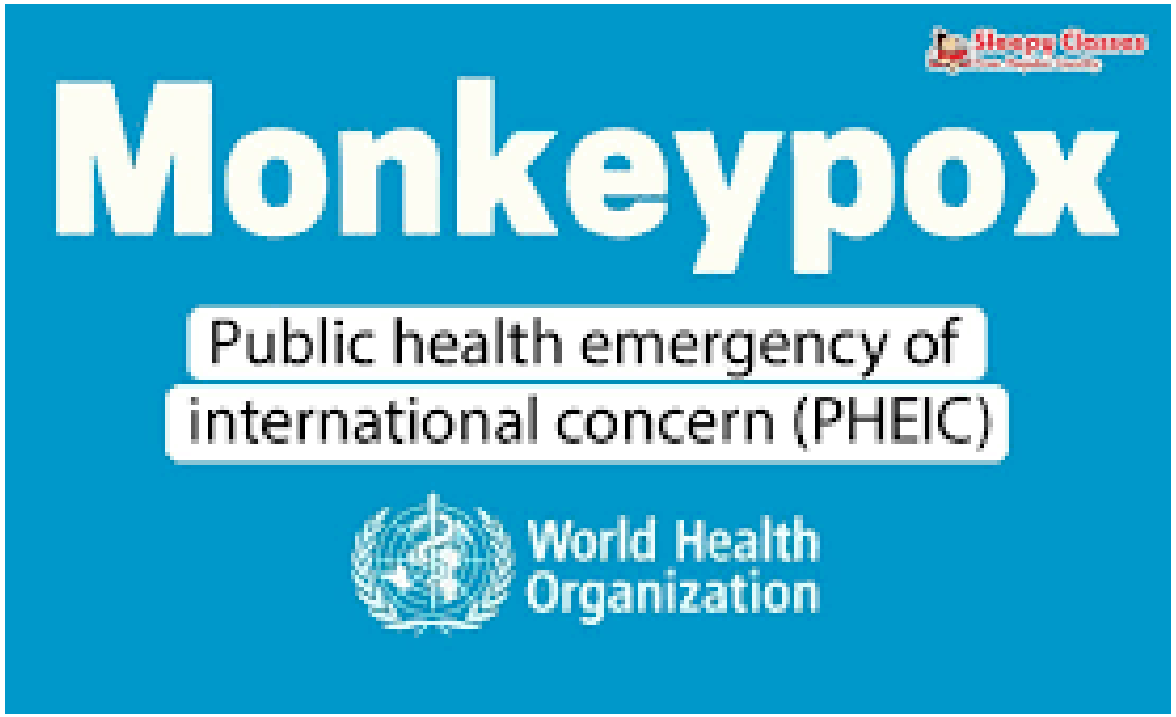


MOP inhibitor of complement enzyme (MOPICE)

- One of the virulence factors
- Gene encoding the inhibitor is present in the Central Congo clades
- Absent in Western clades

Liszewski MK, et al. ***J Immunol*** *2006; 176:3725-3734*

Declaration and stand-down of PHEIC
國際關注的突發公共衛生事件



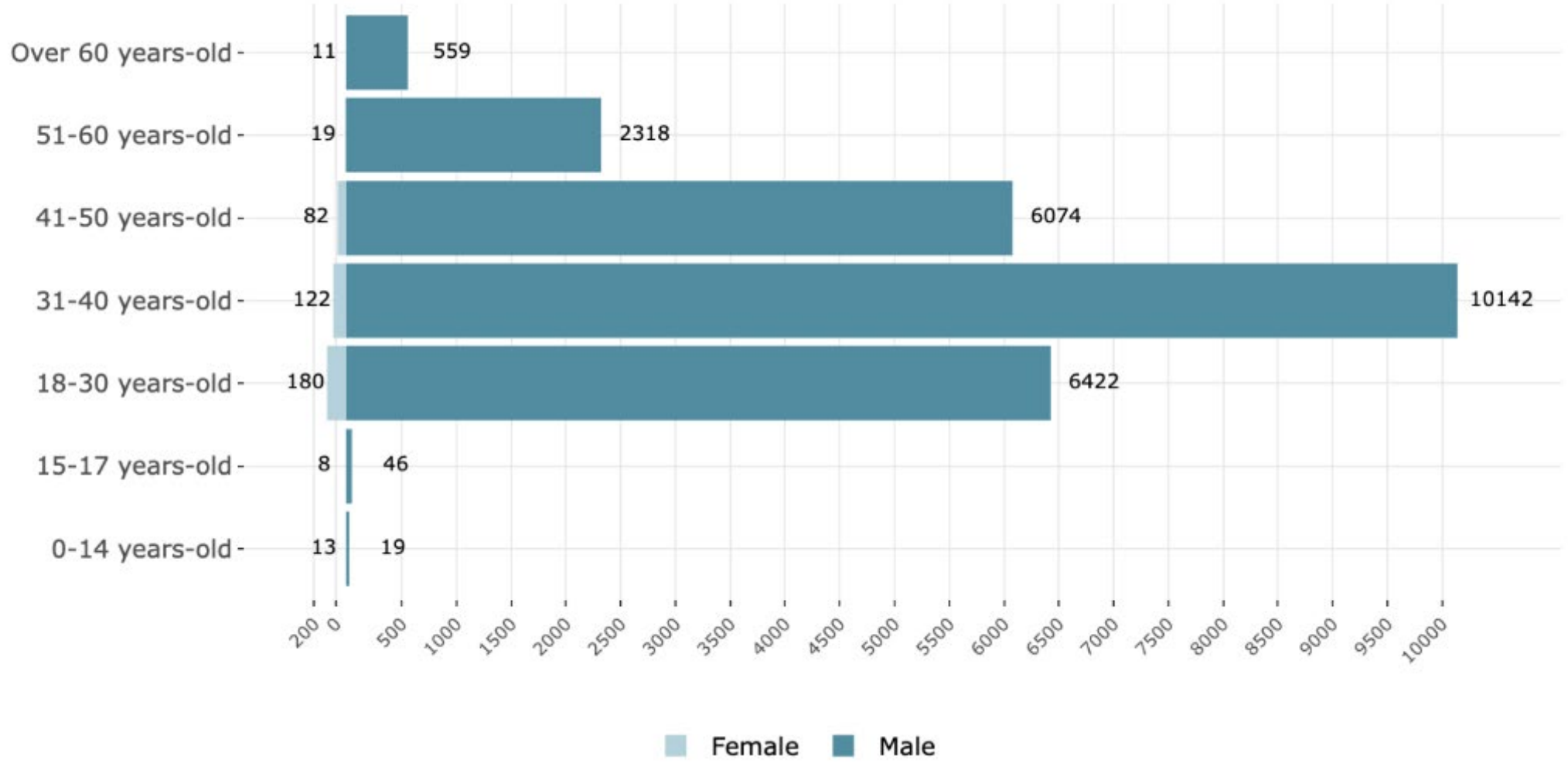
23 July 2022

11 May 2023

WHO changed the name from Monkeypox to **mpox** on 28 Nov 2022

Joint ECDC-WHO Regional Office for Europe Mpox Surveillance Bulletin

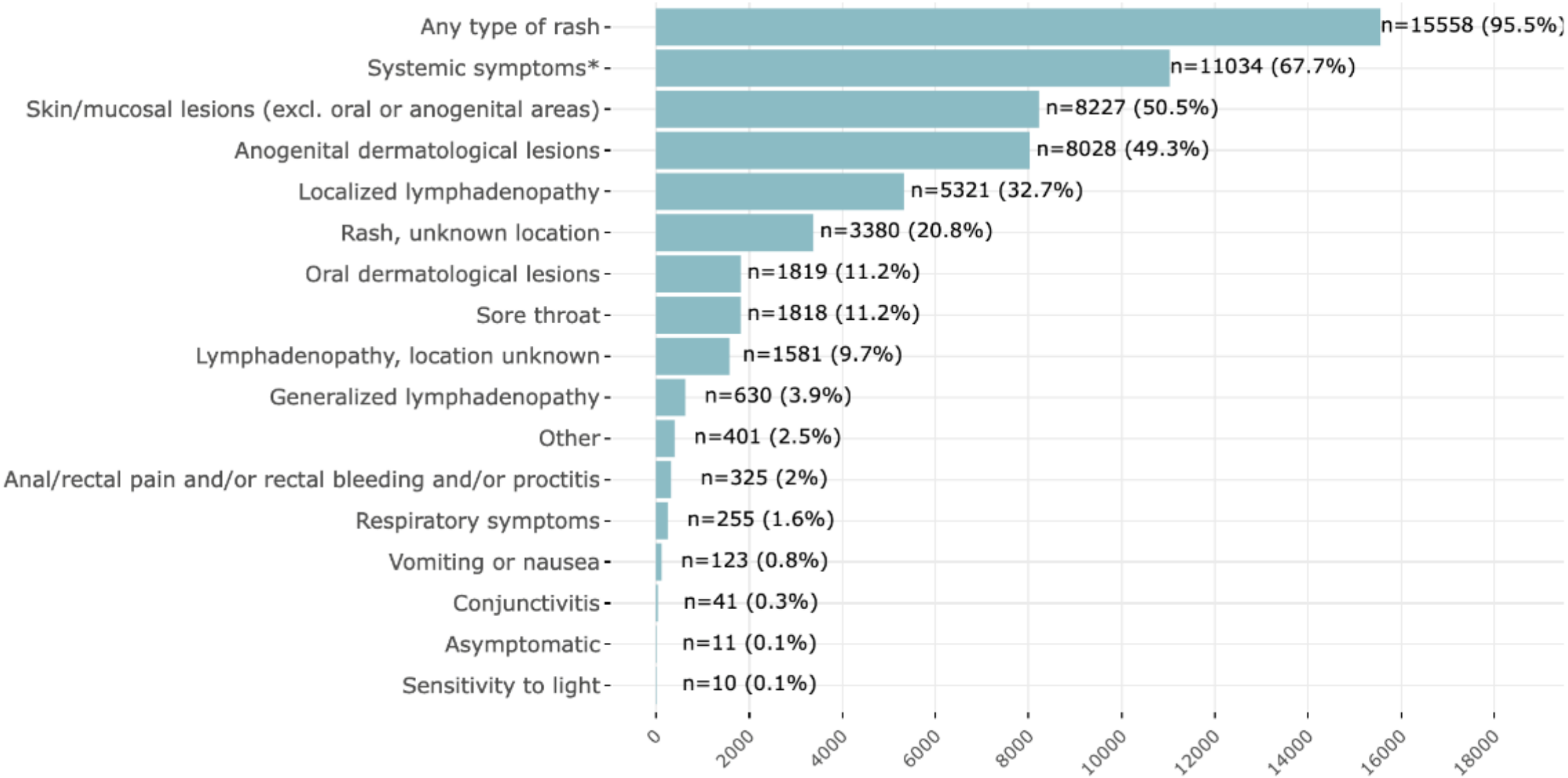
Produced on 09 October 2023, 12:00



Joint ECDC-WHO Regional office for Europe Mpox Surveillance Bulletin 9 Oct 2023

Distribution of symptoms among those reporting at least one type of symptom (N=16289), European Region, TESSy, 2022–2023

The median time between symptom onset and diagnosis was 7 days.



Summary of outcome of cases of monkeypox in the European Region, 2023

	Yes	No	Total
Admitted to ICU	8 (0.1%)	7,203 (99.9%)	7,211 (100%)
Hospitalized*	835 (6.7%)	11,673 (93.3%)	12,508 (100%)
Died	7 (0.0%)	18,231 (100%)	18,238 (100%)
HIV-Positive	4,125 (38.0%)	6,734 (62.0%)	10,859 (100%)

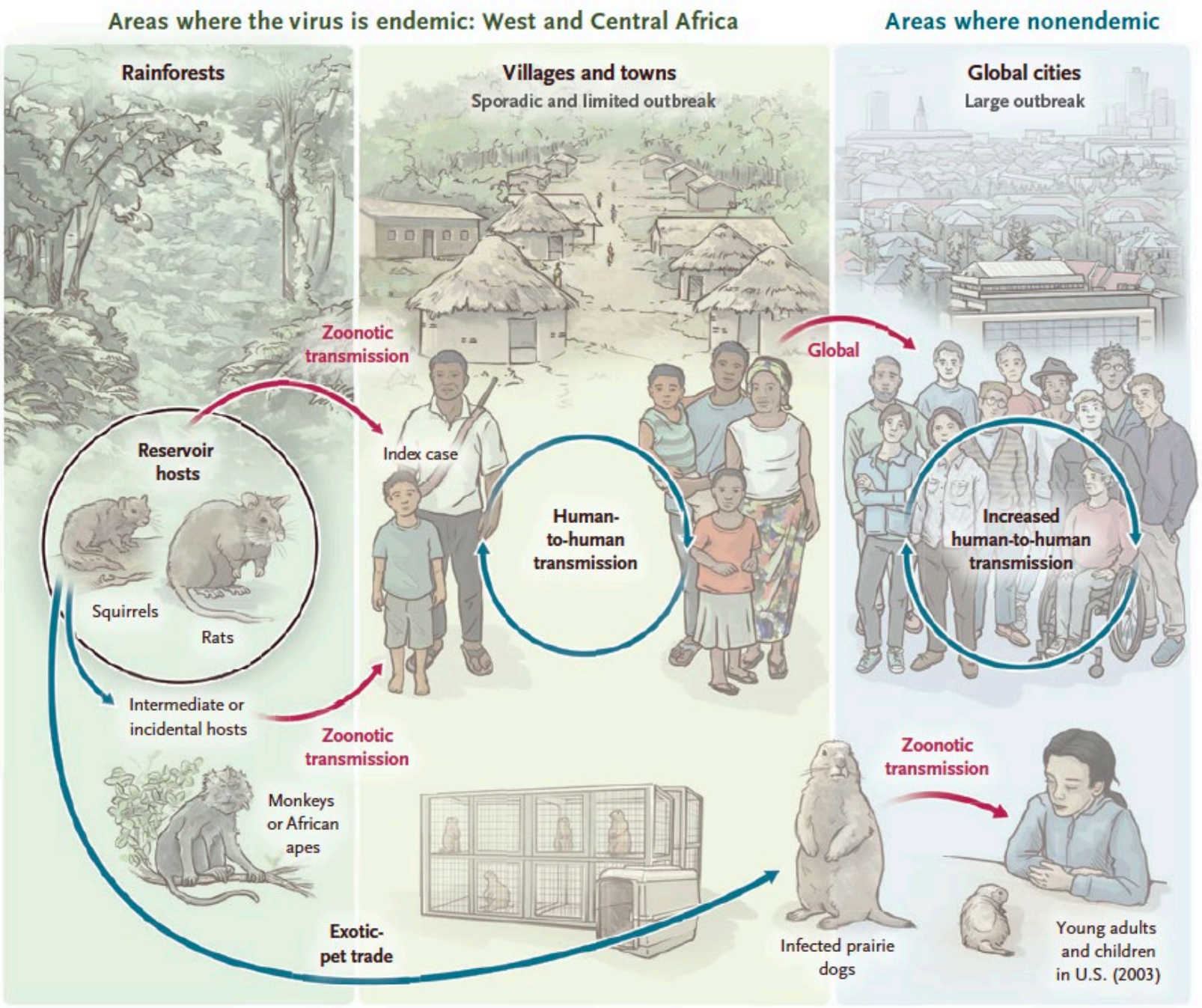
Joint ECDC-WHO Regional office for Europe Mpox Surveillance Bulletin 9 Oct 2023

Sexual orientations among male cases of mpox, European Region, 2022–2023

Sexual Orientation	Count (%)
MSM	10,958 (42.8%)
Bisexual	136 (0.5%)
Heterosexual	337 (1.3%)
Unknown or undetermined	2,858 (11.2%)
Not reported	11,313 (44.2%)
Total	25,602 (100%)

Joint ECDC-WHO Regional office for Europe Mpox Surveillance Bulletin 9 Oct 2023

Natural history of monkeypox



Gessain A, et al. ***N Engl J Med*** *2022;387:1783-93. DOI: 10.1056/NEJMra2208860*

Atypical presentation?

- Most cases have occurred in men aged 20–50 years who identify as **gay or bisexual or MSM**
- Do **not** have recent **travel history** to monkeypox endemic countries.
- Additionally, there does not appear to be links between these cases
- **Less likely** to have **prodrome** or have only **minimal prodrome**
- 1st sign of symptoms over **genital** or **perianal** regions

Otu A, et al. ***Lancet Microbe.*** *Published Online June 7, 2022*

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

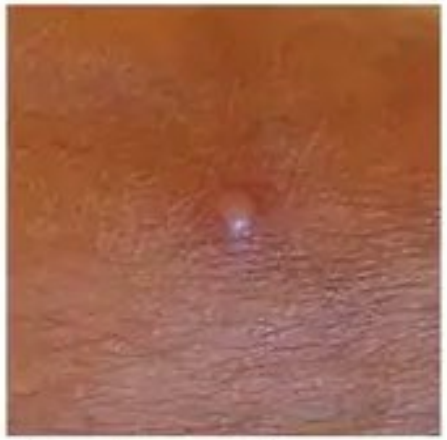
Gessain A, et al. ***N Engl J Med*** *2022;387:1783-93. DOI: 10.1056/NEJMra2208860*

Key Clinical Characteristics for Identification

- **Incubation period:** ~ 7−14d (range 5−21d)
- **First symptoms**: fever, malaise, headache, sometimes sore throat and cough, and lymphadenopathy
- **Lymphadenopathy** ~50%.
  - Occurs with fever onset, **1–2d before rash**, or rarely with rash.
  - Cervical 85.6%, inguinal 77.3%
- Lesions well circumscribed, deep seated, and often **umbilicated**
- Lesions are relatively the **same size & same stage** of development on a **single site of the body** (ex: pustules on face or vesicles on legs)
- Rash is **centrifugal** (more lesions on extremities, face)
- Lesions on **palms, soles** (vs chickenpox)
- **Painful** until the healing phase when they become itchy (crusts)
- **Mucosal lesions 28.7%**: Oral ulcers, Inflammation of the pharyngeal, conjunctival and genital mucosae

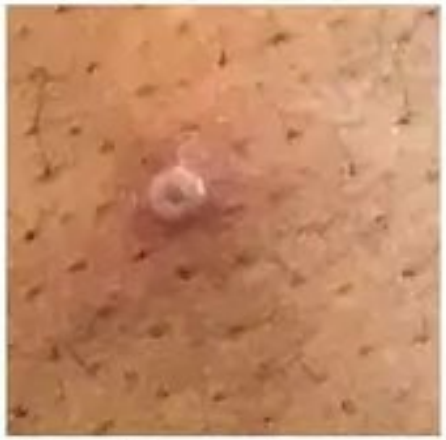
CDC, WHO

Stages of Monkeypox

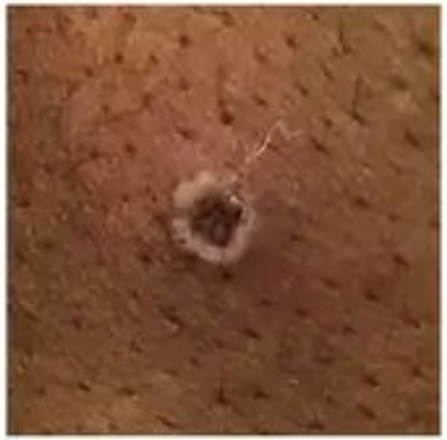


a) early vesicle, 3mm diameter

b) small pustule, 2mm diameter

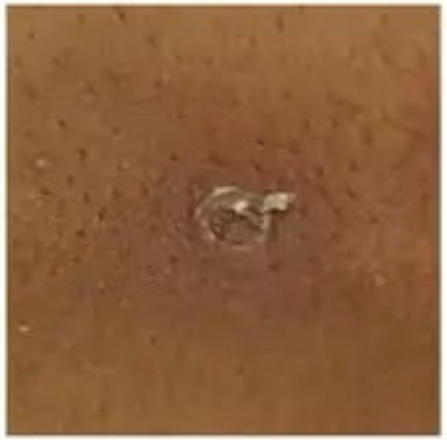


c) umbilicated pustule, 3-4mm diameter



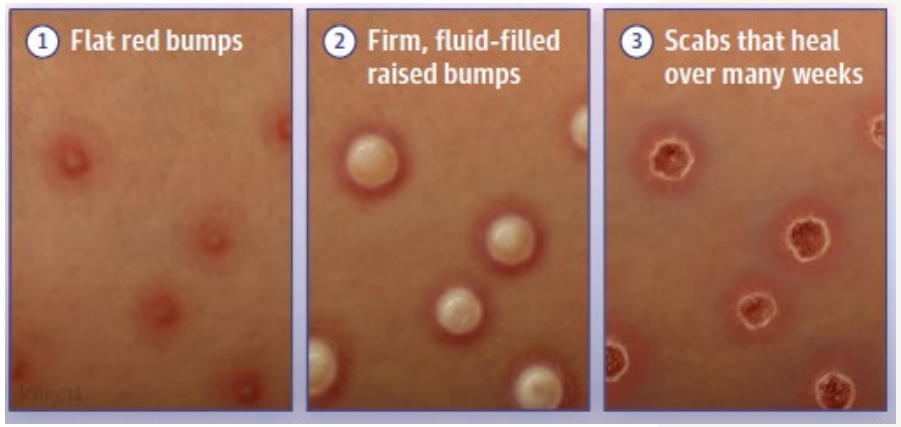
d) ulcerated lesion, 5mm diameter

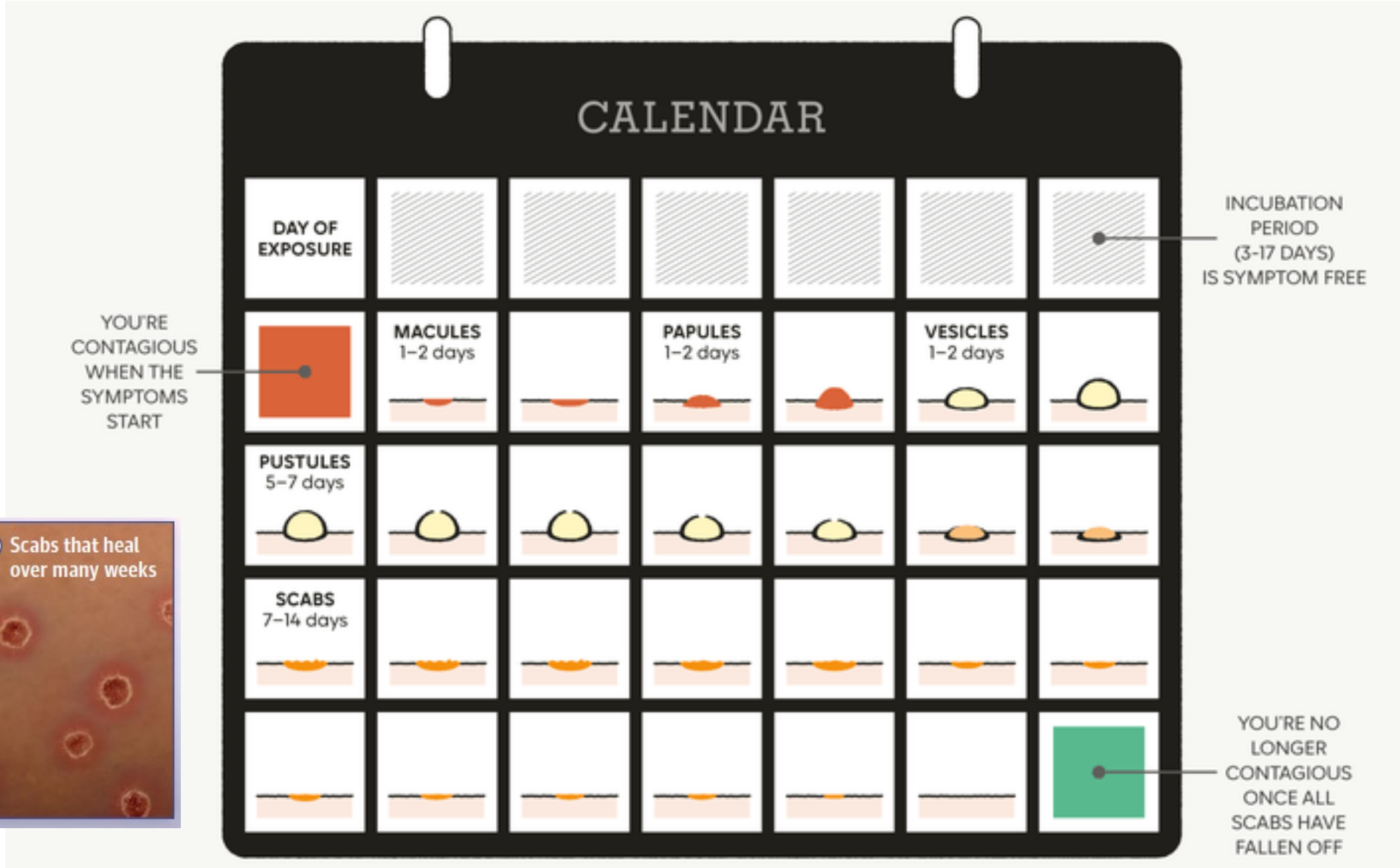
e) crusting of a mature lesion



f) partially removed scab

UK Health Security Agency





https://www.grxstatic.com/4f3rgqwzdznj/7l8ranOtUMpgO67GGDG1Cn/e89a96a5575dc0c6c26669b0a418085a/monkeypox-a-timeline_goodrx.png?format=png&auto=webp&width=704

Complications of Monkeypox

- **GI**: vomiting and diarrhoea, leading to dehydration & electrolytes imbalance
- **Eye**: conjunctivitis and corneal scarring, leading to blindness
- **Sepsis** from skin or LN infection
- **Encephalitis**
- **Bronchopneumonia**
- Permanent pitted **scarring** secondary to bacterial infection
- **Miscarriage** in pregnant women
- **CFR**: 0-11% in unvaccinated individuals
- **Immunocompromised individuals,** e.g. untreated HIV infections **more serious disease and higher risk of fatality**

Beer EM, et al. ***PLoS Negl Trop Dis.*** *2019 Oct 16;13(10):e0007791*
Reynolds MG, et al. ***Viruses*** *2017 Dec 12;9(12):380.*

CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 24-2022: A 31-Year-Old Man with Perianal and Penile Ulcers, Rectal Pain, and Rash

This article was published on June 15, 2022, at NEJM.org.

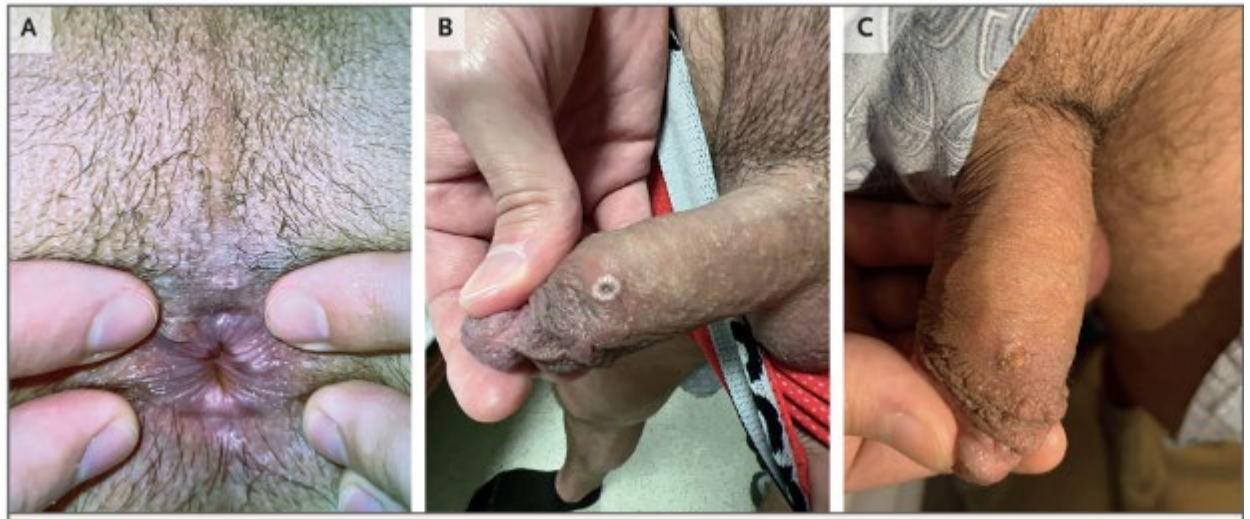


Figure 1. Photographs of Perianal and Penile Ulcers from 2 Days before Admission.

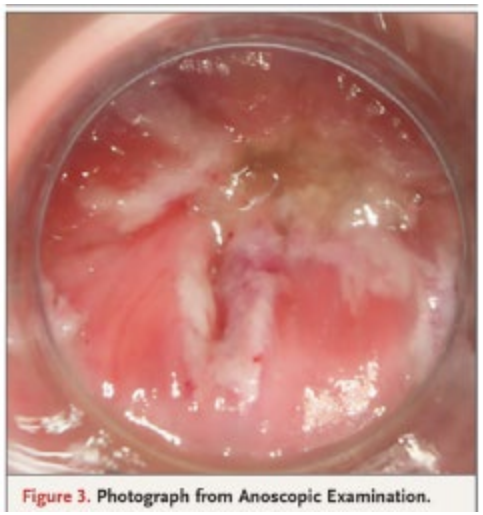
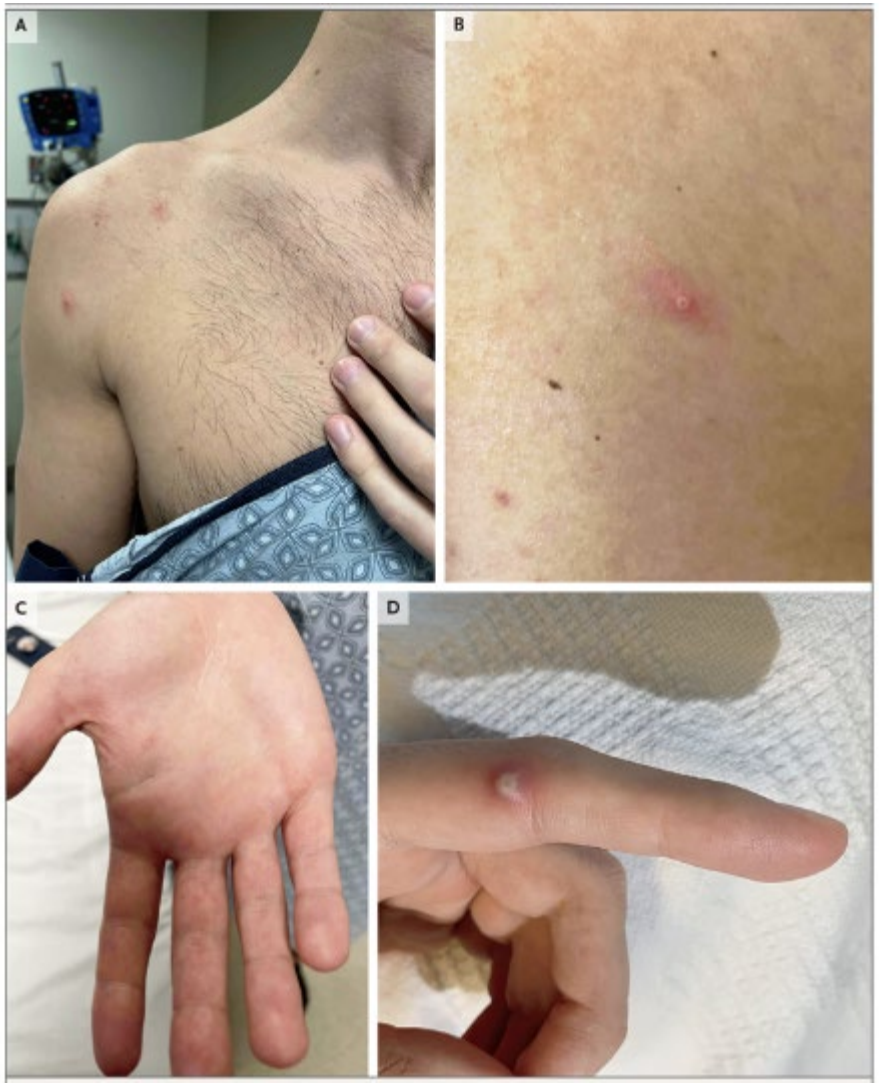


Figure 3. Photograph from Anoscopic Examination.

DDX:

- Viral: HSV, VZV, HIV, molluscum contagiosum
- Bacterial:
  - Gonorrhoea
  - Syphilis
  - LGV
  - Chancroid



Severe Proctocolitis leading to GIB

(Hb dropped from 15 to 7g/dL)

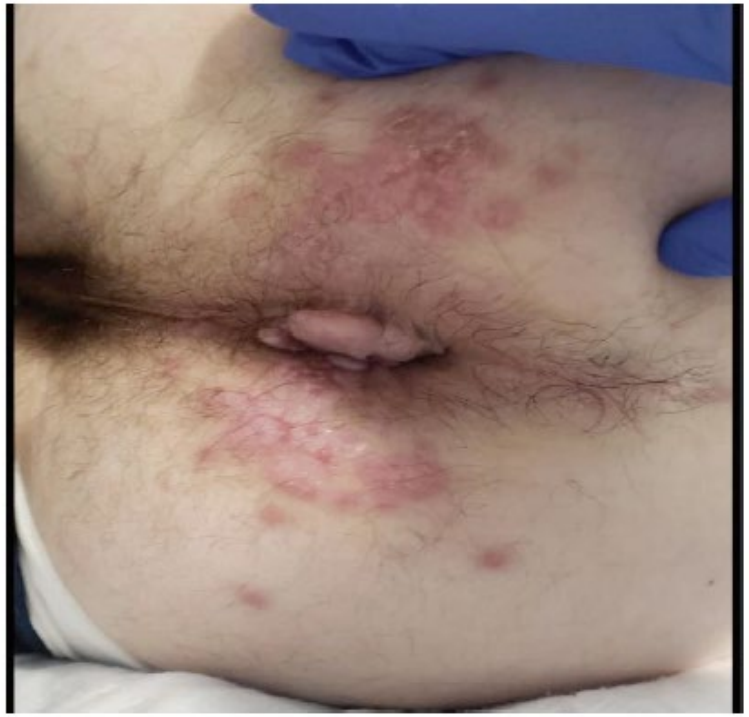


FIGURE 1: Monkeypox-induced perianal lesions. These painful perianal lesions were the initial manifestation of the monkeypox virus infection.

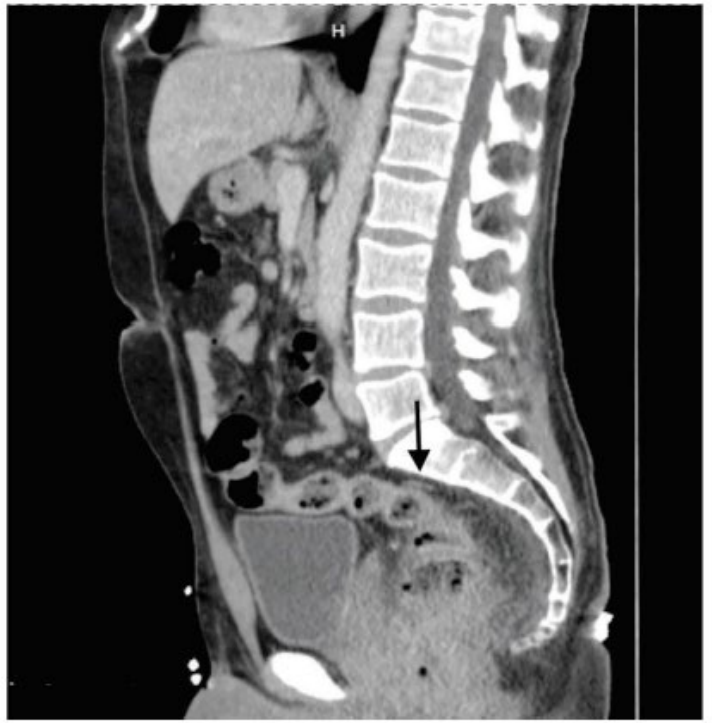
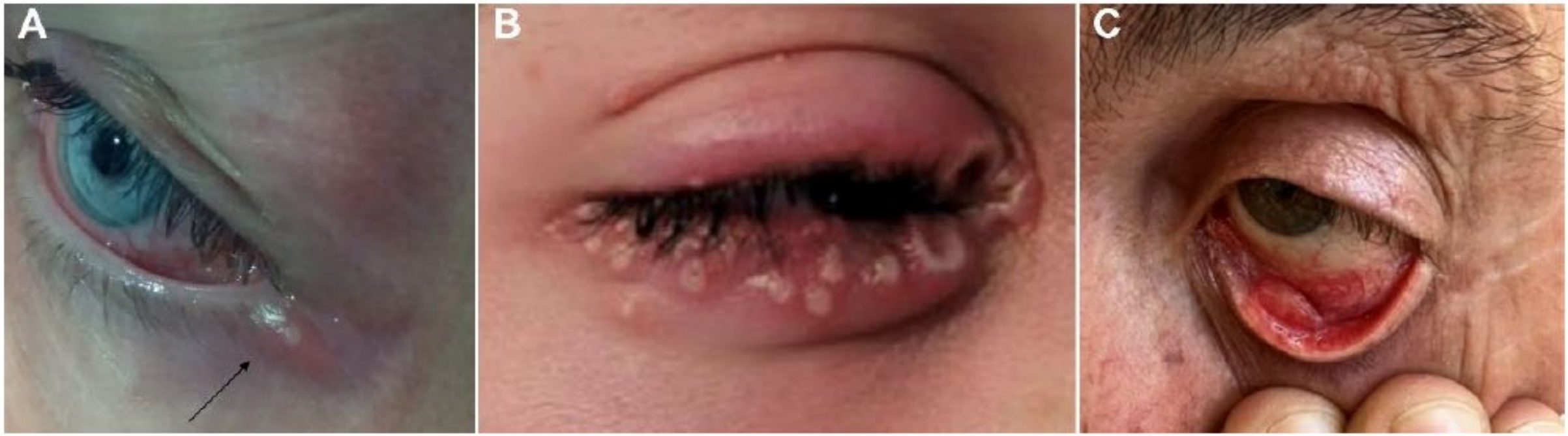


FIGURE 2: CT angiography (CTA) of the abdomen and pelvis. CT angiography revealed circumferential wall thickening with significant inflammatory changes at the level of the distal rectum and anus, indicating proctocolitis (black arrow). Small rounded hypodensities, adjacent to the distal rectum measuring 11 and 14 mm, were suspicious for rectal abscesses.

Taj S, et al. ***Case Rep Gastrointest Med*** *2023, 9981631.*

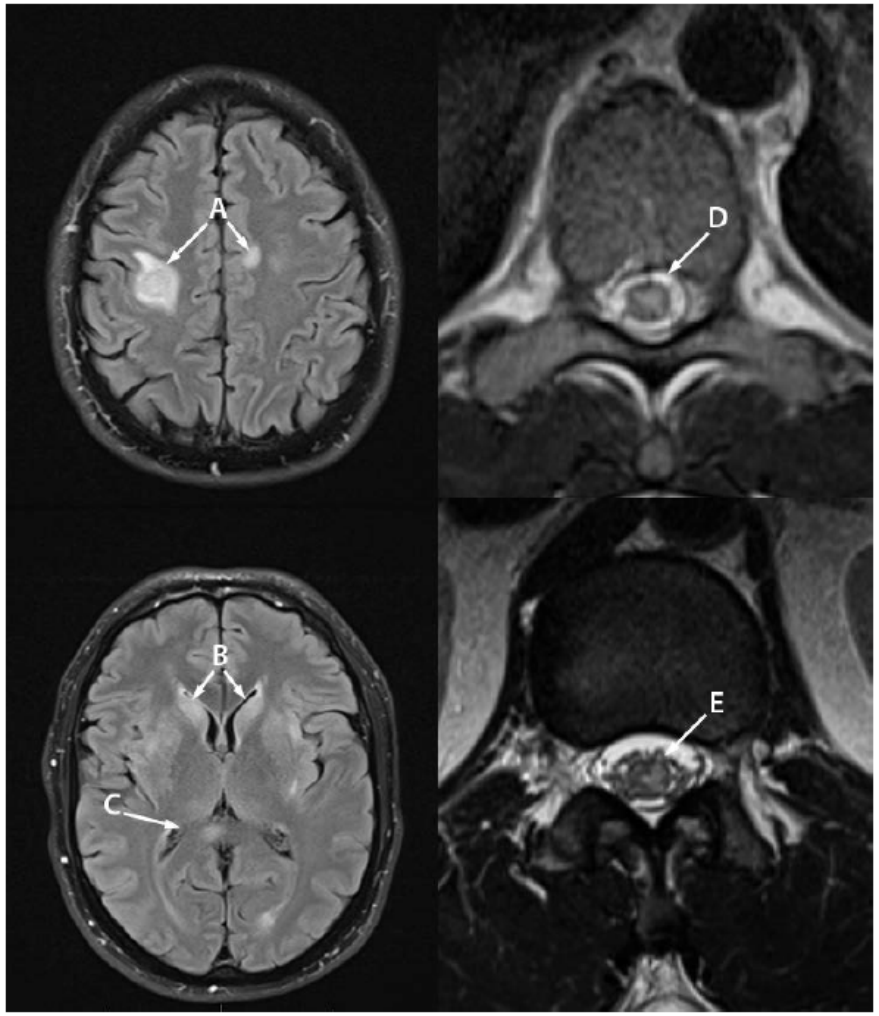
Eye lesions



(A) Vesicles on the left lower eyelid (black arrow).
(B) Multiple papular lesions on the right eyelid.
(C) Ulceration of the palpebral conjunctiva

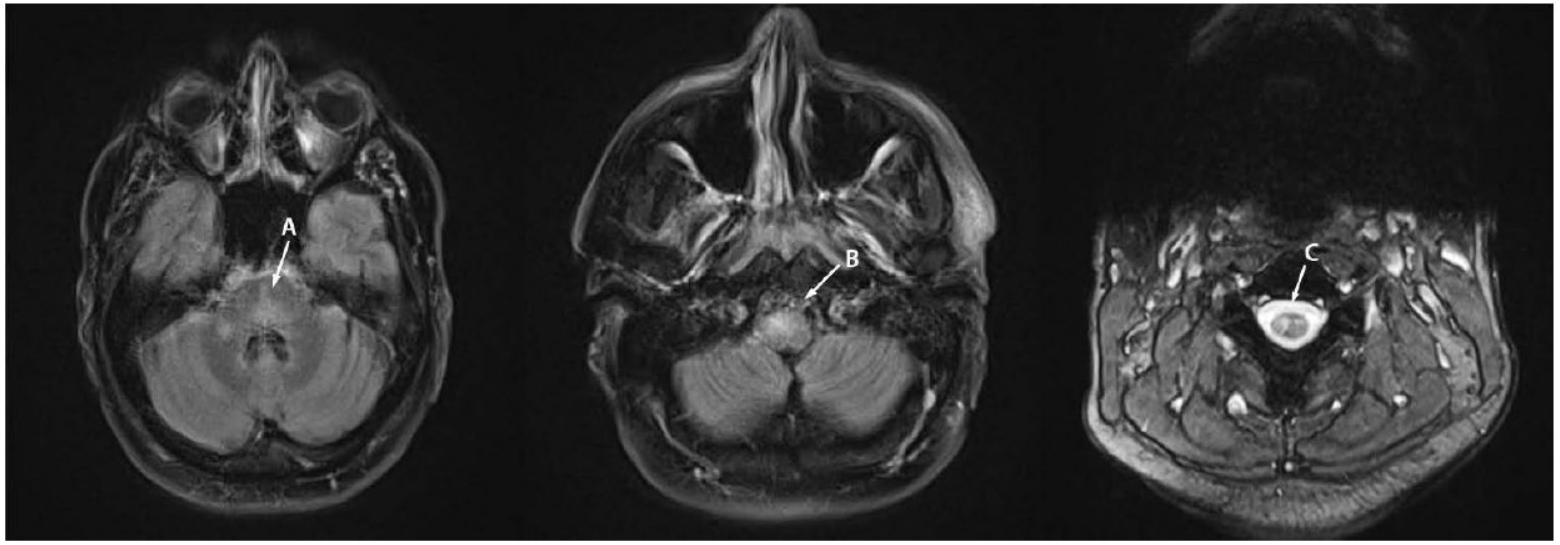
Zong Y, et al. ***Viruses*** *2023, 15, 616.*

CNS encephalomyelitis



Abnormal T2/fluid attenuated signal in:

(A) right frontal and left frontal lobes
(B) bilateral basal ganglia
(C) bilateral medial thalami and right splenium
(D) central thoracic spinal cord
(E) gray matter of the conus medullaris



Abnormal T2/fluid attenuated signal in:

(A) pons and cerebellum
(B) Medulla
(C) gray matter of the cervical spinal cord

Pastula DM, et al. ***MMWR Morb Mortal Wkly Rep.*** *2022 Sep 23;71(38):1212-1215.*

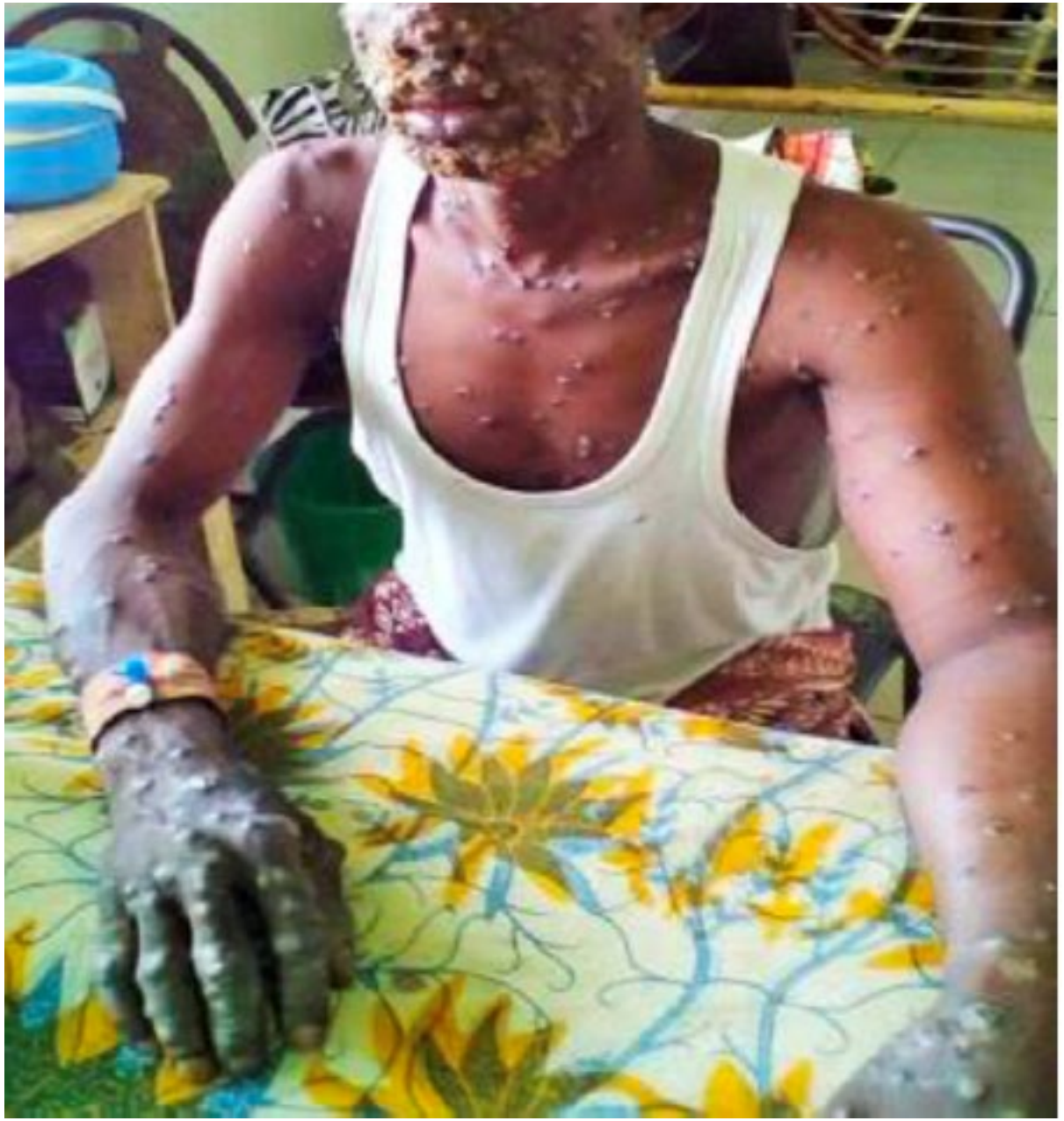
Differential diagnosis

- Chickenpox
- HSV
- Primary or secondary syphilis
- Disseminated gonococcal infection
- Hand, foot and mouth disease
- Chancroid
- Lymphogranuloma venereum
- Granuloma inguinale
- Molluscum contagiosum, measles, scabies, Rickettsia pox
- Chikungunya, zika virus, dengue fever
- Vasculitis and other bacterial skin and soft tissue infections

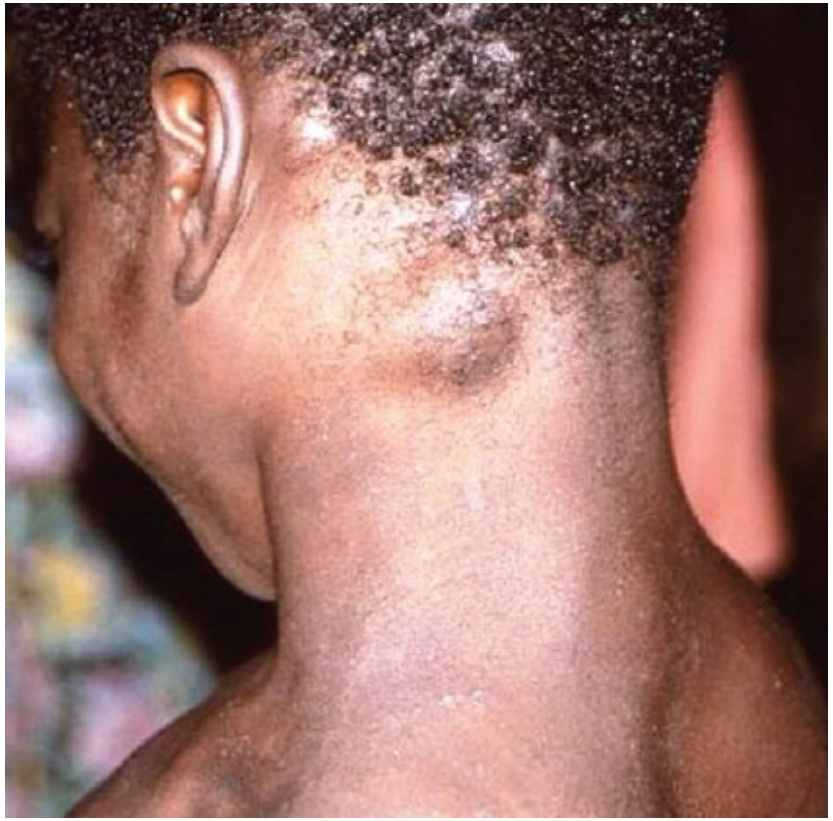
Variable	Monkeypox	Smallpox	Chickenpox
Time period (days)			
Incubation stage	7–17	7–17	10–21
Prodromal stage	1–4	1–4	0–2
Illness stage (from the appearance of rashes to desquamation)	14–28	14–28	10–21
Severity of symptoms			
Prodromal fever	Moderate	Severe	None or mild
Fever	Moderate	Severe	Mild
Malaise	Moderate	Moderate	Mild
Headache	Moderate	Severe	Mild
Lymphadenopathy	Moderate	None	None
Lesions			
Distribution	Centrifugal	Centrifugal	Centripetal
Frequency of lesions on the palms or soles	Common	Common	Rare
Appearance	Hard, well-circumscribed, umbilicated	Hard, well-circumscribed, umbilicated	Superficial, irregular borders, "dew drop on a rose petal"
Depth (diameter in mm)	Deep (4–6)	Deep (4–6)	Superficial (2–4)
Evaluation	Homogenous	Homogenous	Heterogeneous
Progression	Slow progression with each stage lasting 1–2 days	Slow progression with each stage lasting 1–2 days	Fast progression
Extracutaneous manifestations			
Secondary skin/soft-tissue infection	19%	Possible	Possible
Pneumonitis	12%	Possible	3–16%
Ocular complications	4–5%	5–9%	No
Encephalitis	<1%	<1%	<1%

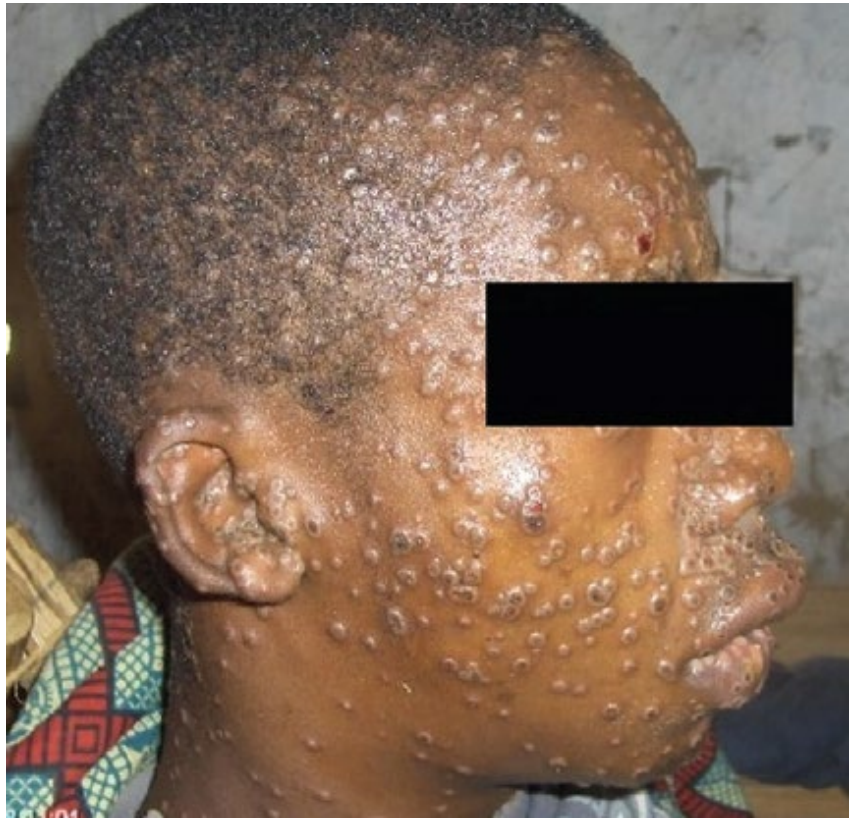
Zahmatyar M, et al. ***Front Med*** *2023;10:1157670*

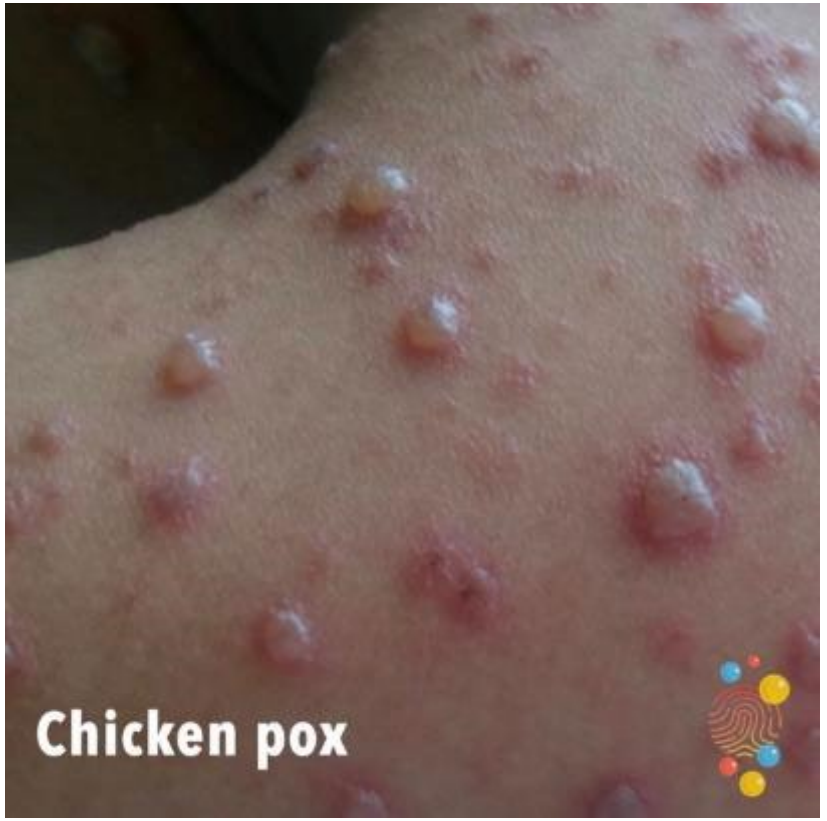
Centrifugal distribution



Petersen E, et la. ***Infect Dis Clin North Am.*** *2019 Dec;33(4):1027-1043*

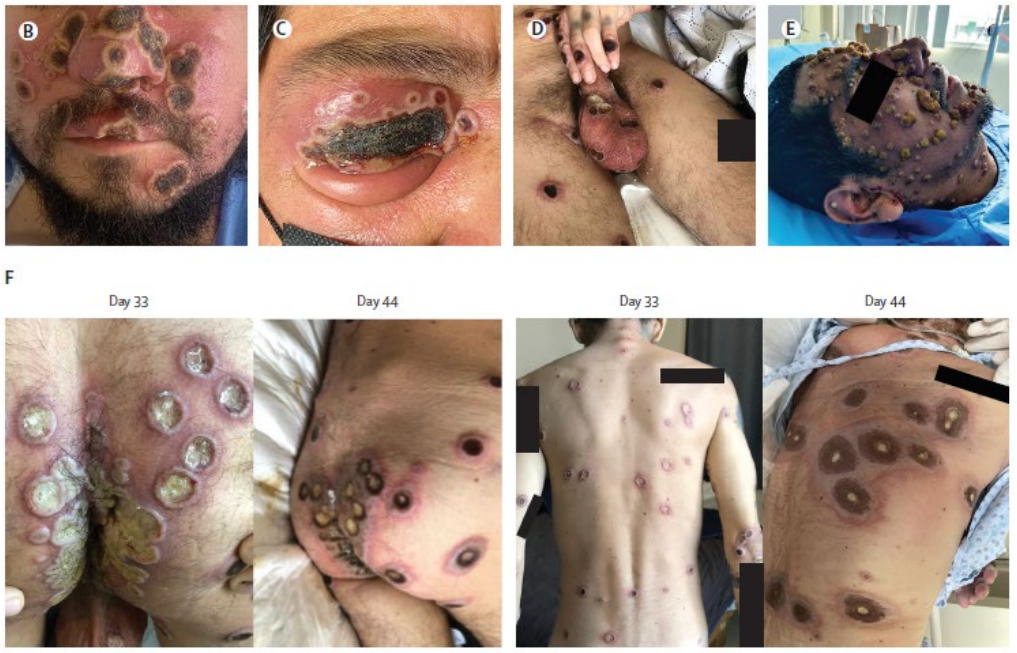






McCollum AM, et al. ***Clin Infect Dis*** *2014;58(2):260–7*

MPOX in HIV



HIV with CD4 < 200 cells/mL has more:

- Longer course of diseases
- Fulminant disseminated necrotizing cutaneous lesions
- Systemic diseases
- Higher mortality

	Total (n=382)	CD4 <100 cells per mm³* (n=85)	CD4 100–200 cells per mm³ (n=94)	CD4 201–300 cells per mm³ (n=128)	CD4 >300 cells per mm³ (n=75)
Mpox rash presentation					
Peak number of skin lesions	15 (8–35)	30 (15–100)	20 (12–35)	12 (6–20)	10 (4–15)
Rash duration in days	23 (18–33)	31 (21–45)	26 (19–40)	21 (16–28)	21 (15–30)
Mpox organ complications†					
Dermatological skin lesions distant from the point of entry					
Overall	94 (25%)	49 (58%)	20 (21%)	18 (14%)	7 (9%)
Large necrotising lesions	84 (22%)	46 (54%)	19 (20%)	14 (11%)	5 (7%)
Ecchymosis haemorrhage	10 (3%)	3 (4%)	1 (1%)	4 (3%)	2 (3%)
Respiratory					
Overall	35 (9%)	25 (29%)	5 (5%)	5 (4%)	0
CNS					
Overall	12 (3%)	9 (11%)	1 (1%)	0	1 (1%)
Ultimate Outcome					
Death§	27 (7%)	23 (27%)	4 (4%)	0	0
Organ support					
Need for ventilation	21 (5%)	16 (19%)	4 (4%)	1 (1%)	0
Need for inotropes	16 (4%)	13 (15%)	3 (3%)	0	0
Indication for ventilation					
Respiratory failure	17 (4%)	14 (16%)	2 (2%)	1 (1%)	0
Sedation	1 (0%)	0	1 (1%)	0	0
Low Glasgow Coma Score or coma	3 (1%)	2 (2%)	1 (1%)	0	0

Mitja O, et al. ***Lancet*** *2023; 401: 939–49*

Updated on 27 Jul 2023

Case reporting criteria for Mpox (Last updated on 27 Jul 2023)

Clinical criteria		Epidemiological criteria

Presented with
• Unexplained acute rash or acute skin lesions
AND
one of the following signs / symptoms:
  • Acute onset of fever (>38 °C)
  • Chills, headache, myalgia, back pain, joint pain or profound weakness (asthenia)
  • New lymphadenopathy
• A case may be excluded if an alternative diagnosis can fully explain the illness [1]
	AND	**Fulfilling (a), (b), (c) or (d) within 21 days of illness onset:**
		(a) History of travel to country/area previously known as mpox endemic in Africa[2, 3]
		(b) Had contact with a person or people who have a similar appearing rash or received a diagnosis of confirmed or probable mpox;
		(c) Man who regularly has close or intimate in-person contact with other men;
		(d) Contact with a dead or live wild animal or exotic pet that is an African endemic species or used a product derived such animals (e.g., game meat, creams, lotions, powders, etc.)

Timeline of PCR results, monkeypox cases, Italy, May 2022 (n = 4)

	Patient 1		Patient 2			Patient 3				Patient 4
Day after symptom onset	Day 5	Day 9	Day 3	Day 5	Day 9	Day 5	Day 6	Day 8	Day 11	Day 4
Serum	Pos (29.7)	NA	AO	AO	NA	AO	AO	NA	NA	AO
Plasma	Pos (30.2)	NA	AO	AO	NA	NA	AO	NA	NA	AO
Genital or rectal lesions	Pos (15.6)	NA	Pos (17.5)	AO	NA	Pos (15.3)	NA	NA	NA	Pos (14.7)
Nasopharyngeal swab	Pos (27.6)	AO	Pos (30.2)	NA	NA	NA	AO	NA	NA	Pos (30.4)
Skin lesions	NA	NA	Pos (30.4)	AO	NA	Pos (18.2)	Pos (19.4)	NA	NA	Pos (17.6)
Seminal fluid	NA	Pos (30.1)	NA	Pos (29.4)	Pos (43.2)	NA	Pos (29.3)	Pos (27.7)	Neg	NA
Scab	Pos (13.1)	NA	NA	NA	NA	Pos (20.0)	NA	NA	NA	NA
Faeces	NA	NA	Pos (22.6)	NA	NA	NA	Pos (26.1)	NA	NA	NA
Saliva	NA	NA	Pos (27.1)	NA	NA	NA	AO	NA	NA	NA

AO: analysis ongoing; Cq: quantification cycle; NA: not available; neg: no detection of monkeypox DNA; pos: detection of monkeypox DNA.
Cq values are indicated in brackets after positive results.

Antinori A, et al. ***Euro Surveill.*** *2022;27(22): online 2 June 2022*

Infection control

Method:

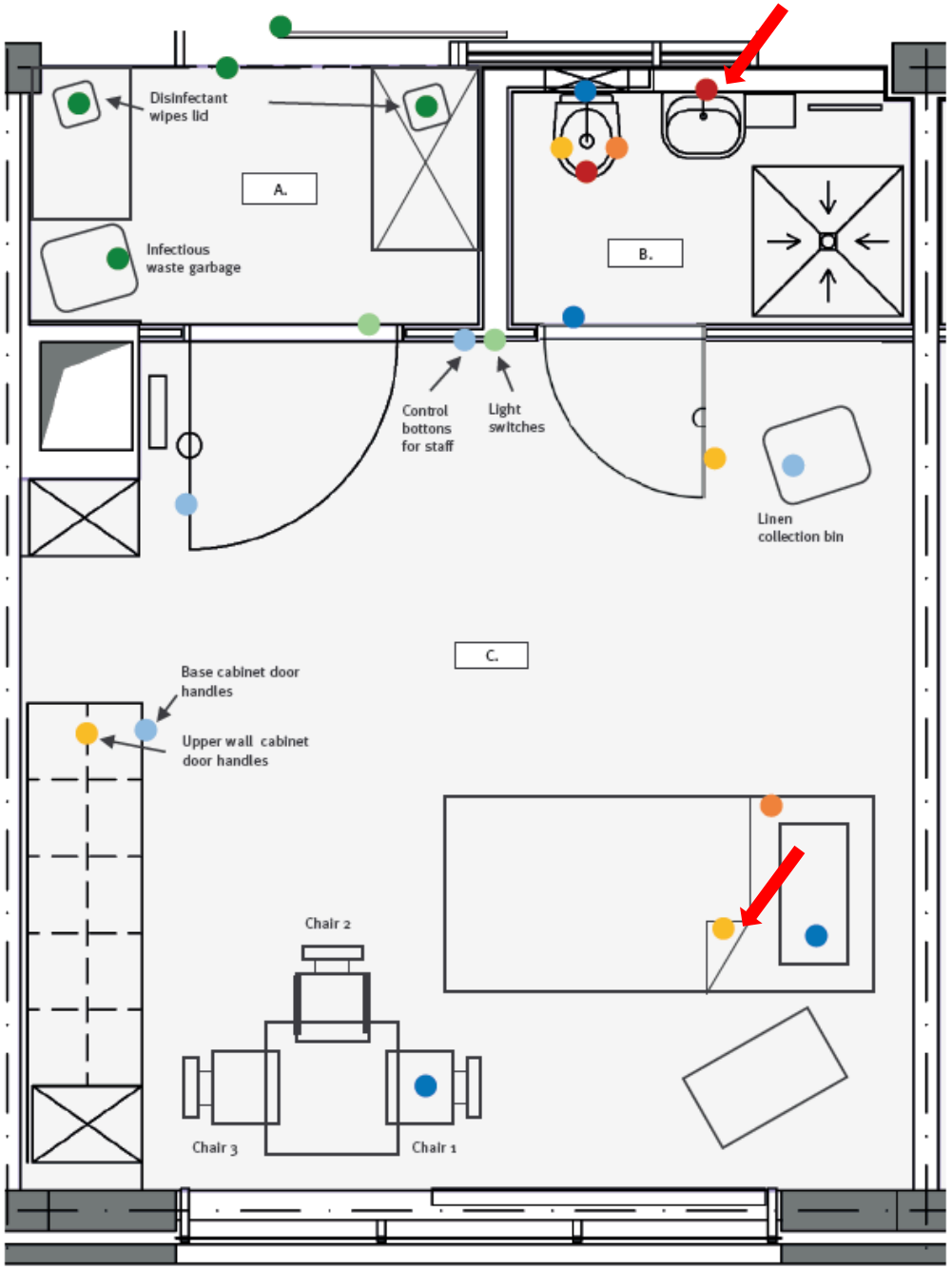
- Examined surfaces in rooms occupied by monkeypox patient on their 4th hospitalisation day.
- Contamination with up to 10^5 viral copies/cm2 on inanimate surfaces was estimated by PCR and the virus was successfully isolated from surfaces with > 10^6 copies

Cultivatable virus with VL > 6 log in:

- Soap dispenser operating lever
- Towel in bed to protect the bed sheet
- Glove of the examiner after contact with fabrics

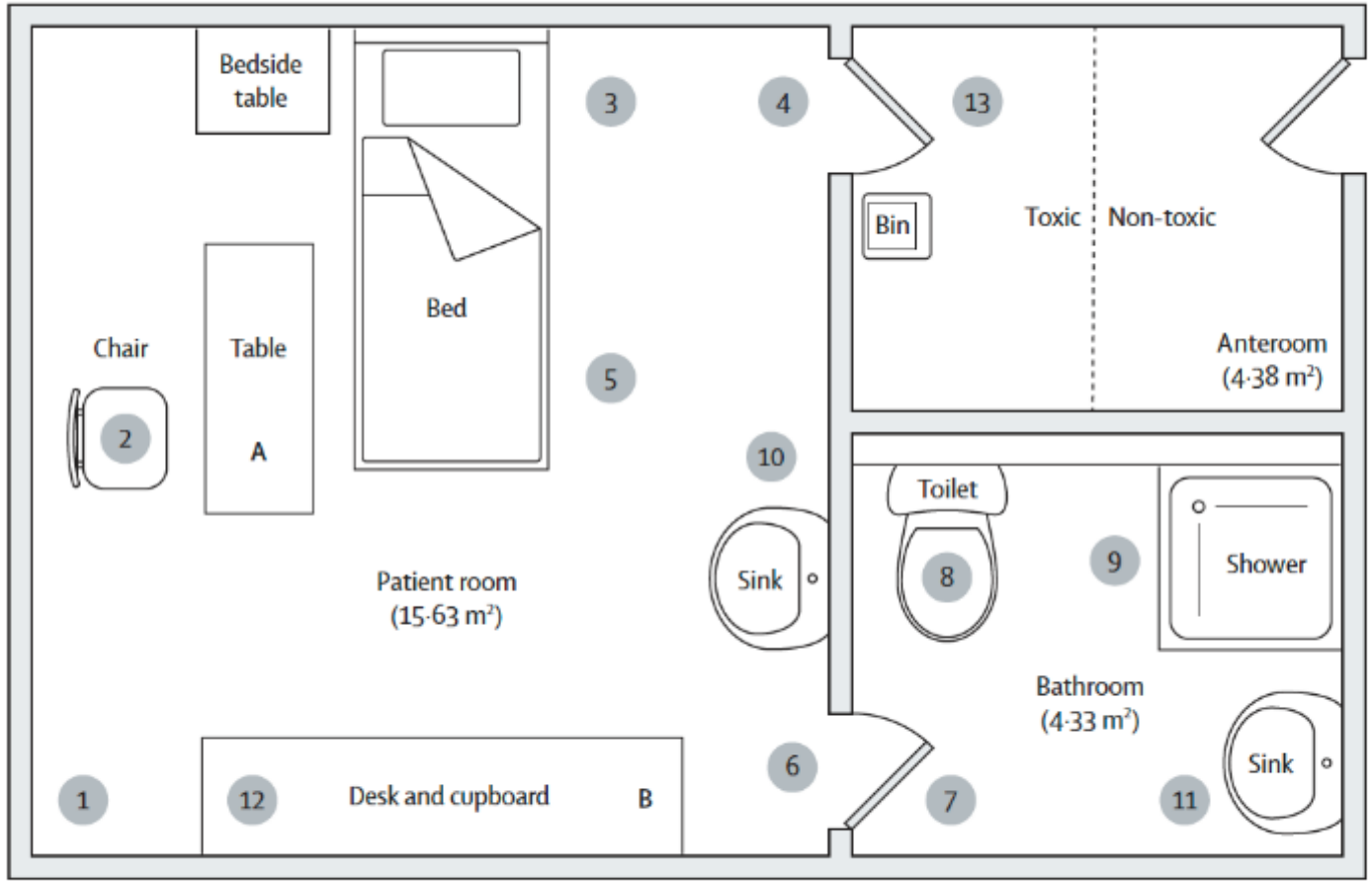
Conclusion:

these data underscore the importance to remind hospital personnel of the need to follow recommended protection measures for monkeypox



N.rz Dominik, et al. ***Euro Surveill****. 2022;27(26):pii=2200477. https://doi.org/10.2807/1560-7917.ES.2022.27.26.2200477*

Droplet transmission?



	Area sampled	Ct values
1	Deposition area (window ledge)	28·8
2	Chair (arm rest)	29·9
3	Call button	27·5
4	Light switch	24·7
5	Observation machine	26·4
6	Air vent	26·4
7	Door handle	26·7
8	Toilet flush	28·7
9	Shower handle	28·8
10	Tap handle 1 (patient room)	32·4
11	Tap handle 2 (bathroom)	29·2
12	Television remote control	25·0
13	Anteroom floor	26·3
A1*	Air sample (<1 m), before bedding change	ND
A2*	Air sample (<1 m), during bedding change	32·7
B1*	Air sample (>1·5 m), before bedding change	36·2
B2*	Air sample (>1·5 m), during bedding change	35·8

Figure: **Plan of room A representing the sites of samples and Ct values**

*Air samples were collected over a period of 10 min at a rate of 50 L/min (500 L total). Ct=quantitative PCR crossing threshold value of monkeypox DNA detected.

Gould S, et al. ***Lancet Microbe*** *2022; 3: e904–11*

Morbidity and Mortality Weekly Report

Monkeypox Virus Infection Resulting from an Occupational Needlestick — Florida, 2022

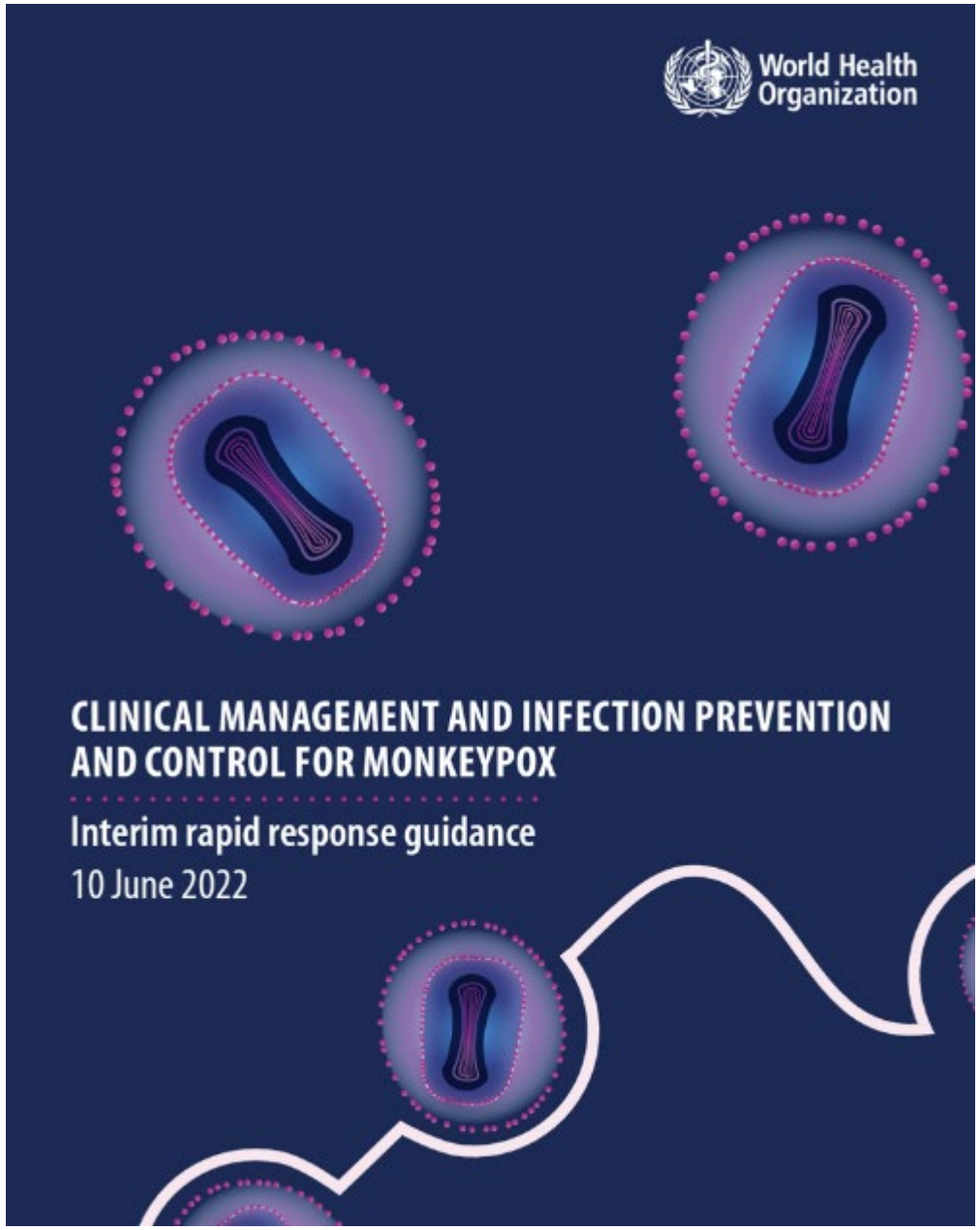
- A nurse used a needle to puncture the vesicle to facilitate swabbing
- NSI occurred when recapping with small amount of bleeding.
- Immediately washed with soap and water and drenched with Betadine antiseptic solution (10% povidone-iodine).
- Received 1st dose of JYNNEOS vaccine 15 hours after the incident as PEP
- 10 days after the exposure, a single skin lesion formed at the site of the needlestick.
- Swabbed +ve for MPOX
- ↑ in size but < 1cm. Then crusted & fallen off 19 days later.
- No additional lesions
- No Rx given

Conclusion:

- NSI can transmitted MPOX
- PEP is effective

Mendoza R, et al. ***MMWR Morb Mortal Wkly Rep****. 2022 Oct 21;71(42):1348-1349. doi: 10.15585/mmwr.mm7142e2.*

Management of Monkeypox



Management

- Aim: prevent complication, relieve discomfort, speed healing
- Support care
- Prevent secondary bacterial infection
- Pain relief
- Nutritional support
- Adequate hydration
- Symptomatic treatment
- Monitoring
- Antivirals for severe diseases

WHO. ***CLINICAL MANAGEMENT AND INFECTION PREVENTION AND CONTROL FOR MONKEYPOX*** *Interim rapid response guidance* ***10 June 2022***

Table 3.1. Risk factors and clinical findings described as being associated with severe disease and poor outcomes (based on small, uncontrolled, observational studies)

Patient groups at higher risk of severe disease or complications	• Children, pregnant women, persons who are immunosuppressed such as persons living with HIV having poorly controlled disease *(5,6,10,11,13,26)*. • Though data are lacking, patients with chronic skin conditions (e.g. atopic dermatitis), acute skin conditions (i.e. burns) may also be at higher risk for complications, such as bacterial infection *(33)*.
Clinical signs and symptoms of complications	• Nausea and vomiting *(11,16)*, painful cervical lymphadenopathy causing dysphagia, poor oral intake, eye pain, vision abnormalities, hepatomegaly, sepsis, dehydration, respiratory distress/pneumonia, and/or confusion.
Laboratory abnormalities	• Elevated hepatic transaminases (AST and/or ALT), low blood urea nitrogen (BUN), low albumin, elevated white blood count (WBC), or low platelet count *(16)*.
Skin lesion severity score	• From smallpox experience *(28,94)*: – Mild (< 25 skin lesions) – Moderate (25–99 skin lesions) – Severe (100–250 skin lesions) – Very severe (> 250 skin lesions).

Antivirals and vaccines

- **Treatment**
  - Tecovirimat
  - Brincidofovir
  - Cidofovir
  - Vaccinia Immune Globulin Intravenous (VIGIV)

- **Vaccines**
  - JYNNEOS (Imvamune, Imvanex or MVA-BN)
  - ACAM2000

Antivirals vs MPOX

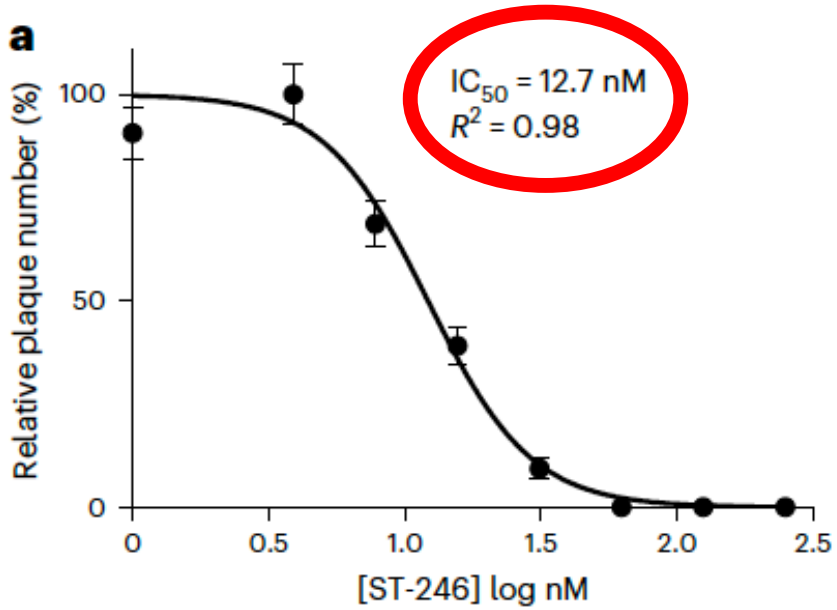
Table 1 - General characteristics of tecovirimat, cidofovir and brincidofovir.

	Tecovirimat	*Cidofovir*	*Brincidofovir*
Mechanism of action	Inhibitor of the Orthopoxvirus VP37 envelope wrapping protein	DNA polymerase inhibitor	DNA polymerase inhibitor
EMA approval	Poxviridae Infections, Smallpox Cowpox, Vaccinia Monkeypox	No	No - Orphan drug designation
FDA approval	Smallpox	CMV retinitis	Smallpox
Dosing	PO: 13 kg-24 kg: 200 mg bid; 25 kg-40 kg: 400 mg bid; >40 kg: 600 mg bid; IV: 3kg-35 kg: 6 mg/kg bid over 6 hours; 35 kg-120kg: 200 mg bid over 6 hours; >120 kg: 300 mg bid over 6 hours	PO: Not available IV: 5 mg/kg once weekly	PO: <10 kg: 6 mg/kg/dose once weekly in 2 doses (on days 1 and 8); 10 kg - 48 kg: 4 mg/kg once weekly for 2 doses (on days 1 and 8); >48 kg: 200 mg once weekly for 2 doses (on days 1 and 8) IV: Not available
Course duration	14 days	2 consecutive weeks	2 consecutive weeks
Renal toxicity	IV Tecovirimat is contraindicated if CrCl < 30 mL/min	Possible. Adjust dose accordingly	No
Hepatic toxicity	No	No	Possible. Adjust dose accordingly

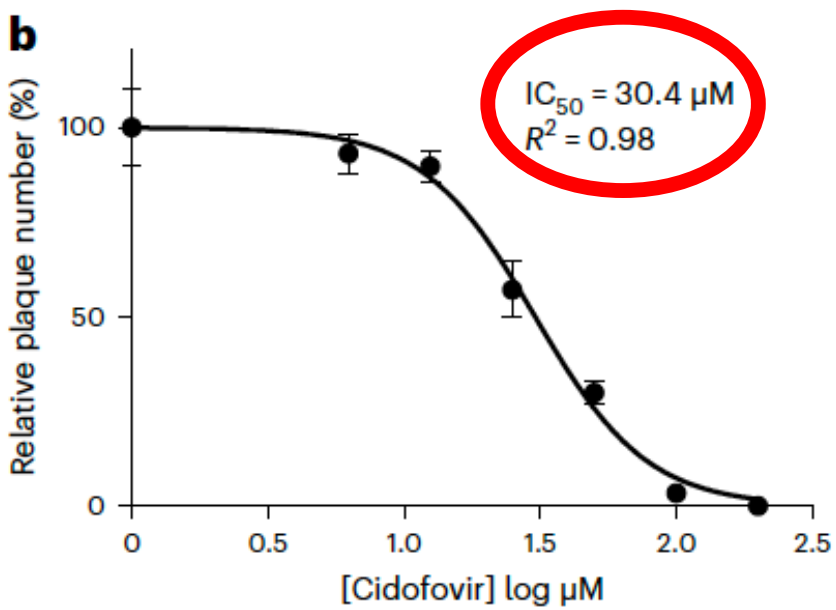
Abbreviations: PO, per os (by mouth); bid, bis in die (twice daily); IV, intravenous; CrCl, creatinine clearance.

Ivanov DT, et al. ***Infez Med****. 2023 Jun 1;31(2):186-194.*

In in vitro of antivirals for mpox



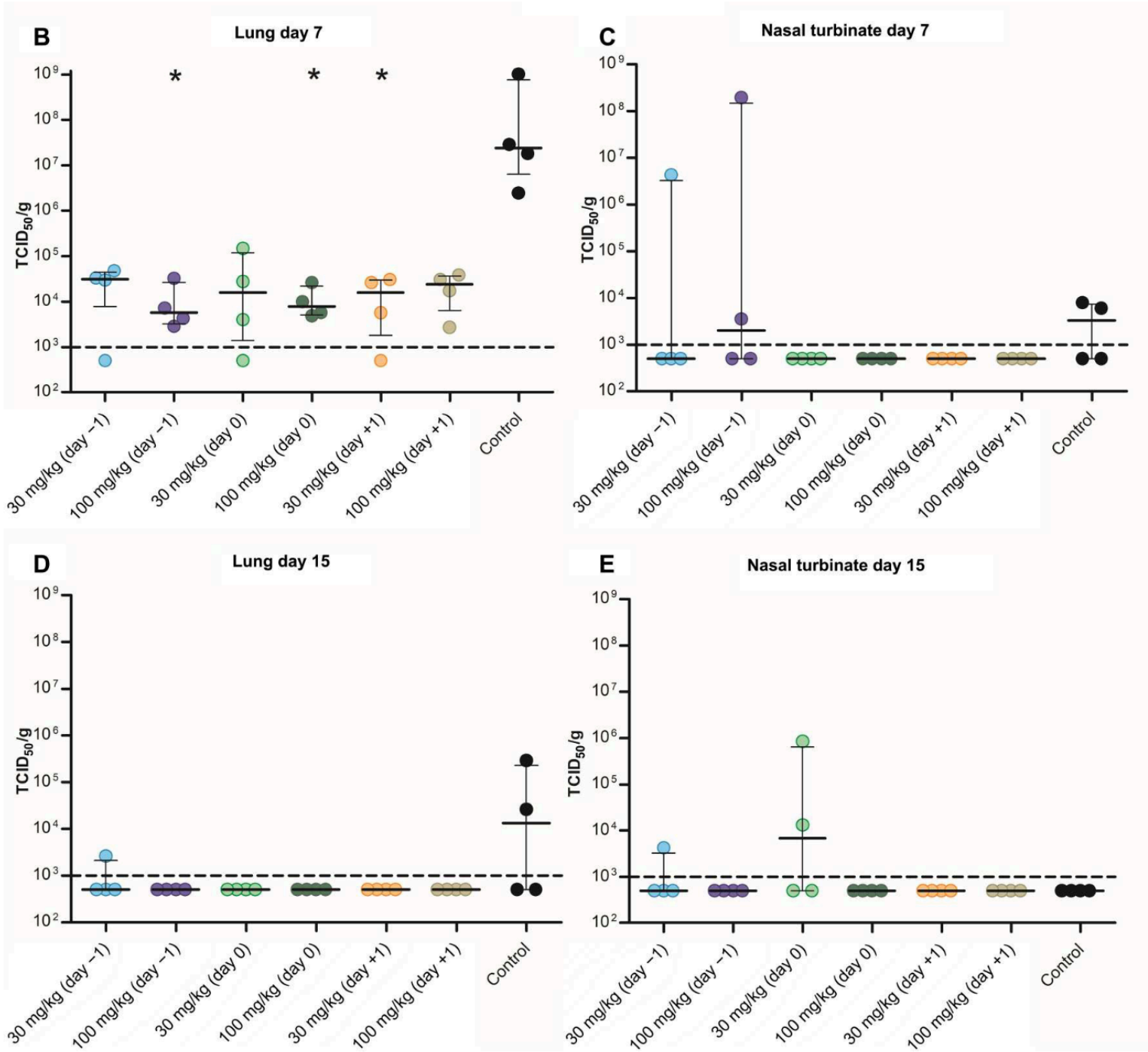
Tecovirimat



Frenois-Veyrat G, et al. ***Nat Microbiol****. 2022 Dec;7(12):1951-1955.*

Tecovirimat: mice study

- Mice were given 2 doses of Tecovirimat:
  - 30mg/kg or
  - 100mg/kg
- Rx given at D-1, D0 or D+1 of viral inoculation x 5d
- Measure viral loads at D7 or D15 after Rx
- Vs control



Warner, BM, et al. ***Sci Transl Med.*** *2022 Nov 30;14(673):eade7646.*

Efficacy of Tecovirimat

- Case series in Germany[1]:
  - All 12 cases showed clinical improvement
- Case series in US[2]:
  - 2 cases showed resolution of lesions after prolonged Rx
  - 6 cases showed resolution of lesions after 14d Rx

- Cases control study[3]:
  - 19 Rx vs 22 Un-Rx
  - No significant changes in clinical recovery and viral loads after 14d Rx

1. *Hermanussen L, et al.* ***Infection****. 2023 Oct;51(5):1563-1568.*
2. *Seifu L, et al.* ***MMWR Morb Mortal Wkly Rep****. 2023 Apr 28;72(17):471-472.*
3. *Mazzotta V, et al****. J Med Virol.*** *2023;95:e28868.*

Tecovirimat for mpox

- 369 outpatients given Tecovirimat
- 99.8% oral tecovirimat
- 46.3% HIV +ve
- Median time from initiation of tecovirimat to improvement: **3 days**
- Adverse events **3.5%:** headache (3), nausea (2), visual disturbance (2), weakness (2), vomiting (1), ↑ALT (1), psychiatric admission (1), rash (1), hives (1), numbness (1), fatigue (1), and dizziness (1).

Outcome (no. unknown or missing)	No. (%)
Hospitalized (38)	
Yes*	23 (6.9)
Intensive care unit*	2 (0.6)
No	308 (93.1)
Outcome† (52)	
Recovered without sequelae	189 (59.6)
Recovered with sequelae	41 (12.9)
Not yet recovered	87 (27.4)
Days to subjective improvement§ (114)	
Median, days (IQR)	3.0 (2–4)
Adverse event¶ (29)	
Yes	12 (3.5)
No	328 (96.5)

Median no. of days to follow up after treatment initiation (IQR)**	
During treatment: assessment A (day 1–7)	6 (4–7)
During treatment: assessment B (day 8–14)	10 (8–13)
Posttreatment: assessment C	21 (20–23)
Assessment A (day 1–7) (156)	213 (57.7)
New lesions (22)	
Yes	25 (13.1)
No	166 (86.9)
All lesions crusted and healed with new layer of skin (59)	
Yes	49 (31.8)
No	105 (68.2)
Assessment B (day 8–14) (187)	182 (49.3)
New lesions (19)	
Yes	22 (13.5)
No	141 (86.5)
All lesions crusted and healed with new layer of skin (25)	
Yes	78 (49.7)
No	79 (50.3)
Assessment C (posttreatment) (225)	144 (39.0)
New lesions (7)	
Yes	3 (2.2)
No	134 (97.8)
All lesions crusted and healed with new layer of skin (11)	
Yes	119 (89.5)
No	14 (10.5)

O'Laughlin K , et al. ***MMWR Morb Mortal Wkly Rep****. 2022 Sep 16;71(37):1190-1195.*

Monkeypox vaccines

	ACAM2000 (2nd generation)	JYNNEOS (3rd generation)
License for Monkeypox	US for PEP (2007)	US (2019), Canada, EU (Smallpox only in 2013)
Vaccine virus	Replication-**competent** vaccinia virus	Replication-**deficient** modified vaccinia Ankara virus
Inadvertent inoculation & Autoinoculation	**Risk exists**	No risk
Serious adverse event	**Risk exists**	Fewer expected
Cardiac adverse events	**Myopericarditis 5.7/1000** primary vaccinees	Lower than ACAM2000
Effectiveness	Comparing immunologic response & "Take" rates to "**Dryvax**" (1st generation vaccine), **~ 85% in preventing MKP**	Comparing to ACAM2000 & animal studies: ● **100% protective in animal vs MKP** ● **Seroconversion >90% in human**
Administration	**Percutaneous 15 punctures by bifurcated needle**	Subcutaneously in 2 doses, 28d apart

CDC

Adverse effects associated with JYNNEOS (Imvamune, Imvanex or MVA-BN)

Very common (> 1/10)	Common (up to 1/10)	Uncommon (up to 1/100)	Rare (up to 1/1000)
• headache • aching muscles • feeling sick • tiredness • pain, redness, swelling, hardness or itching at the injection site	• chills • fever • joint pain, pain in extremities • loss of appetite • discolouration, lump or bruising at the injection site	• nose and throat infection, URTI • swollen lymph nodes • abnormal sleep • dizziness, abnormal skin sensations • muscle stiffness, back pain, neck pain • sore throat, runny nose, cough • diarrhoea, vomiting, abdominal pain, dry mouth • rash, itch, skin inflammation, skin discolouration • warmth, bleeding, irritation, scaling, inflammation, abnormal skin sensation, reaction • underarm swelling, flushing, chest pain, pain in the armpit • bruising	• sinus infection • pink eye • hives (nettle rash) • skin bruising • sweating • night sweats • lump in skin • muscle cramps, pain, weakness • swelling of the ankles, feet or fingers • swelling of the face, mouth and throat • faster heart beat • spinning sensation (vertigo) • migraine • nerve disorder causing weakness, tingling or numbness, drowsiness • rash, numbness, dryness, movement impairment, blisters at injection site • weakness • feeling unwell • influenza-like illness

UKHSA. *Recommendations for the use of pre and post exposure vaccination during a monkeypox incident. Updated* ***17 June 2022 v9***

CHP recommendations

(23 August 2023)

- **Mass vaccination is not recommended**.
- First-or second- generation smallpox vaccines are **not recommended**.
- PEP is recommended in the order of exposure risk from high to low, with appropriate **3rd generations** vaccine, ideally **within 4d** of 1st exposure (up to 14d in the absence of symptoms)
- **PrEP for high risk groups :**
  - **HCW** caring for confirmed MKP cases
  - **Lab** workers handling zoonotic pox viruses
  - **Animal** workers with potential exposure
  - Individuals with high risk sexual practices: men having sex with men, multiple sexual partners, sex workers, sexual transmitted infection within the last 12m
- In principle, **one dose would be sufficient in persons with past history of smallpox vaccination**.

How effective is JYNNEOS Vaccine Against Diagnosed Mpox

	Mpox case-patients (n = 252)	All STI controls (n = 255)	
Vaccination status	No. (%)	No. (%)	VE (95% CI)
Unvaccinated	230 (91.3)	204 (80.0)	Ref
0–13 days after first dose	10 (4.0)	9 (3.5)	−36.2 (<−100 to 56.3)
≥14 days after first dose	10 (4.0)	23 (9.0)	68.1 (24.9 to 86.5)
≥0 days after second dose	2 (0.8)	19 (7.5)	88.5 (44.1 to 97.6)
≥14 days after first dose or ≥0 days after second dose	12 (4.8)	42 (16.5)	75.7 (48.5 to 88.5)

Abbreviations: Mpox = monkeypox; Ref = referent group; STI = sexually transmitted infection; VE = vaccine effectiveness.
* Outside of New York City.

Rosenberg ES, et al. ***MMWR Morb Mortal Wkly Rep.*** *2023 May 19;72(20):559-563.*

Vaccine efficacy

- Case–control study based on nationwide electronic health record database
- Aim: assess the effectiveness of **JYNNEOS** vaccination
- **Case**: an mpox Dx code or +ve mpox laboratory result
  - ➢ 2193 cases with 25 cases fully vaccinated
- **Control**: Dx of HIV or those on PrEP vs HIV
  - ➢ 8319 control with 335 control fully vaccinated

Table 2. Estimated Vaccine Effectiveness against Diagnosed Mpox among Persons Seeking Health Care, August 15 through November 19, 2022.*

Persons Seeking Health Care	Case Patients	Control Patients	Vaccine Effectiveness (95% CI)	
			Unadjusted	Adjusted†
	number		*percent*	
Unvaccinated, reference population	2022	6984		
Partially vaccinated, 1 dose	146	1000	52.0 (42.3–60.1)	35.8 (22.1–47.1)
Fully vaccinated, 2 doses	25	335	77.2 (65.0–85.1)	66.0 (47.4–78.1)

Table 3. Estimated Vaccine Effectiveness against Diagnosed Mpox among Persons Seeking Health Care, According to Subpopulations of Interest, August 15 through November 19, 2022.

Subpopulation	Case Patients	Control Patients	Vaccine Effectiveness (95% CI)	
			Unadjusted	Adjusted*
	number		*percent*	
Men only†				
Unvaccinated, reference group	1792	6075		
Partially vaccinated	136	983	54.5 (45.0–62.5)	35.9 (21.6–47.6)
Fully vaccinated	25	335	77.3 (65.3–85.2)	64.8 (45.2–77.3)
Men only, 18–49 yr of age and without ACAM2000 vaccination†				
Unvaccinated, reference group	1561	4632		
Partially vaccinated	119	787	56.9 (46.7–65.2)	35.5 (19.1–48.6)
Fully vaccinated	23	247	73.4 (58.3–83.0)	58.7 (33.9–74.3)
Not immunocompromised				
Unvaccinated, reference group	1151	5368		
Partially vaccinated	102	932	47.0 (33.2–58.0)	40.8 (24.8–53.4)
Fully vaccinated	14	312	80.6 (65.5–89.1)	76.3 (57.7–86.8)

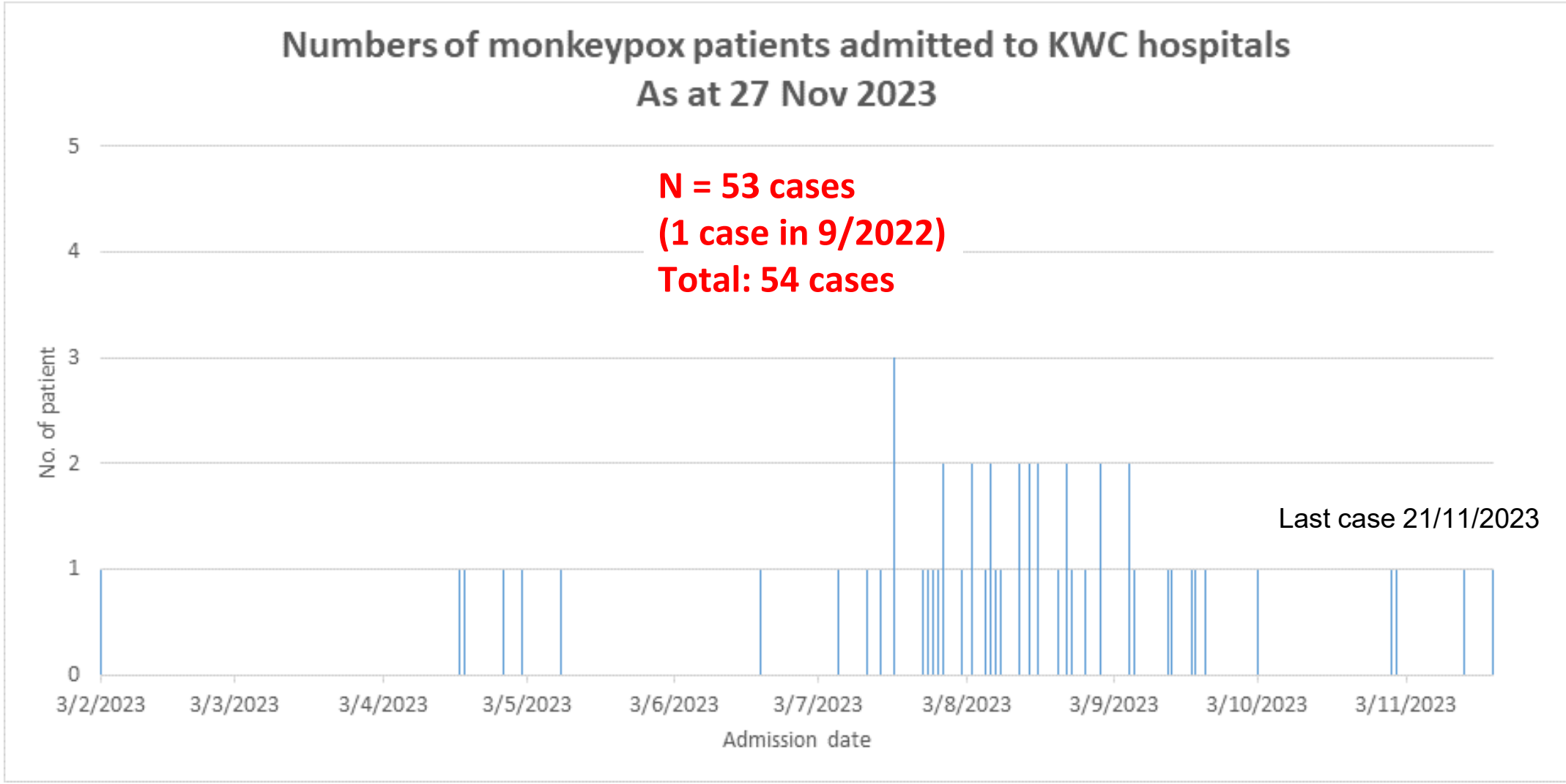
Deputy NP, et al. ***N Engl J Med*** *2023;388:2434-43.*

Effectiveness of PEP

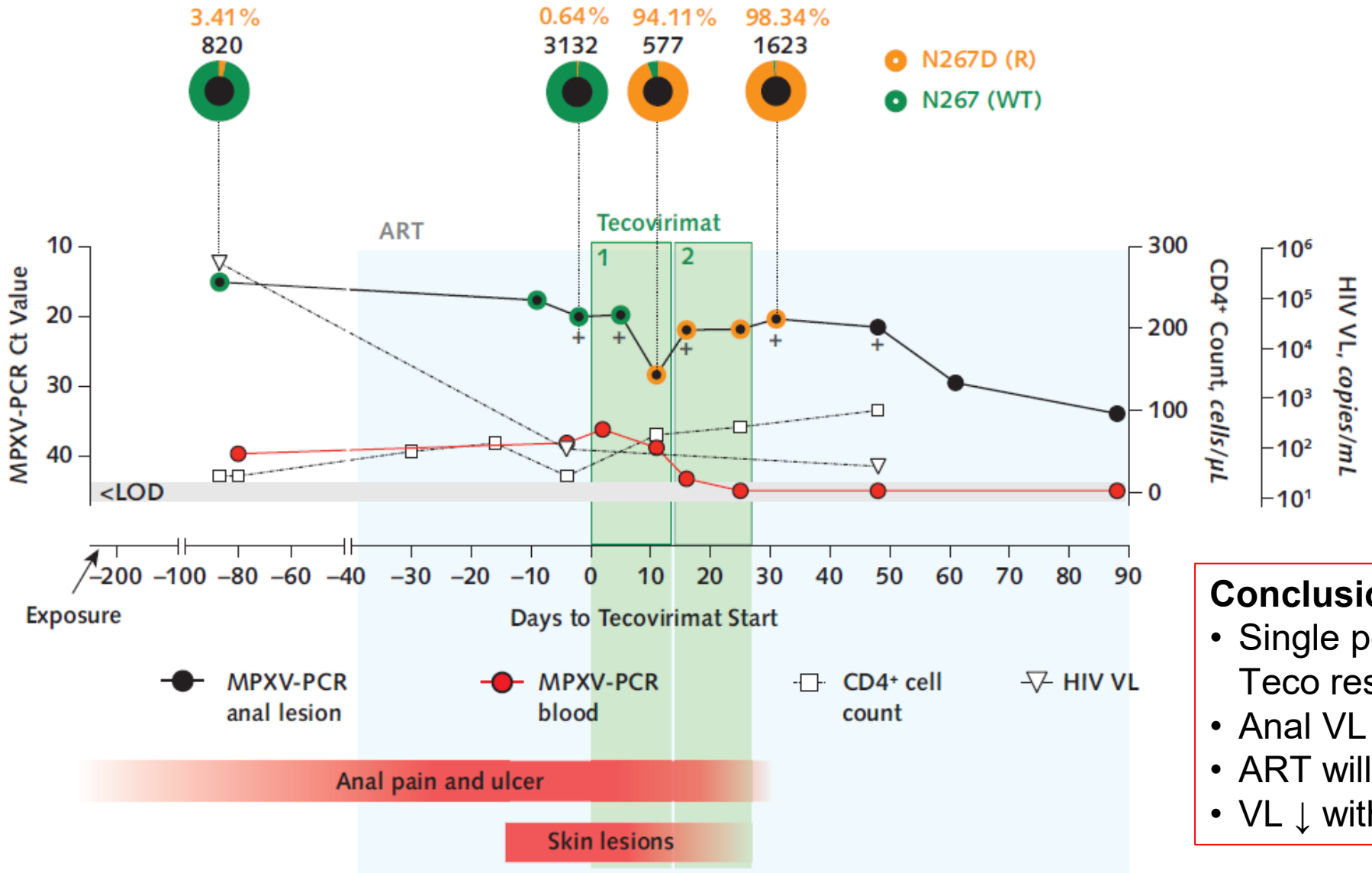
Variable	Vaccine effectiveness (n = 484)					
	Person-days	Events	Crude %[a]	95% CI[a]	Adjusted %	95% CI
Overall vaccine effectiveness						
Unvaccinated	5,774	49	Reference		Reference	
Vaccinated	6,099	8	84.4	66.4 to 92.8	88.8	76.0 to 94.7
Time from exposure to vaccination						
Unvaccinated	5,774	49	Reference		Reference	
0–6 days	1,152	2	81.1	20.6 to 95.5	85.5	39.3 to 96.6
7–13 days	3,233	4	85.7	59.6 to 95.0	90.2	72.5 to 96.5
14–20 days	1,595	2	82.0	24.6 to 95.7	86.7	44.0 to 96.9
21–25 days	119	0	100	NA[b]	100	NA[c]
Vaccination effectiveness by clinical symptoms						
General symptoms						
Unvaccinated	390	38	Reference		Reference	
Vaccinated	110	5	68.8	-1.5 to 90.4	71.6	18.1 to 90.2
Polysymptomatic disease						
Unvaccinated	390	29	Reference		Reference	
Vaccinated	110	2	87.5	6.2 to 98.3	85.5	26.7 to 97.1

Morales LM, et al. ***Euro Surveill****. 2023;28(24):pii=2200883*

Hong Kong Mpox data



Tecovirimat resistance: N267D



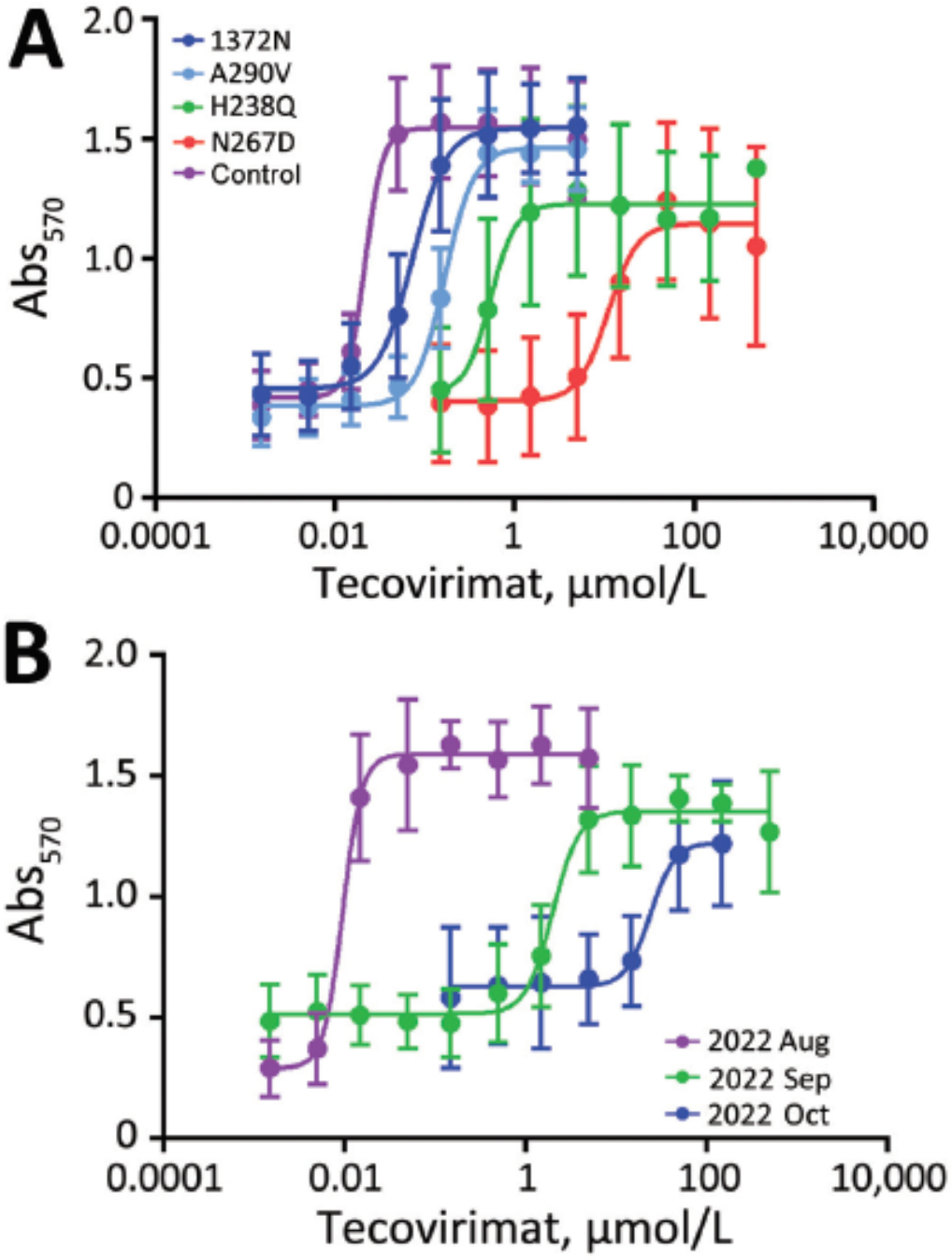
Conclusion:

- Single point mutation N267D confers Teco resistance
- Anal VL > Blood VL
- ART will ↑ CD4
- VL ↓ with ↑ CD4

Mertes H, et al. ***Ann Intern Med.*** *2023 Aug;176(8):1141-1143.*

Tecovirimat resistance

- Envelop protein VP37 mutations associated with Tecovirimat resistance:
  - prior studies: H238Q, P243S, **N267D**, A288P, A290V, D294V, A295E & I372N
  - 5 more new mutations T220A/I, T245I, A265D, and T289A
- Tecovirimat resistance ↑ **over time**
- **Single amino acid mutation** can confer resistance



Garrigues JM, et al. ***Antimicrob Agents Chemother.*** *2023 Jul 18;67(7):e0056823.*
Smith TG, et al. ***Emerg Infect Dis.*** *2023 Dec;29(12):2426-2432.*

Summary

- Mpox has been circulating since 1970
- 2022 outbreak is likely related to the transmission within a defined group
- Current strain belongs to Western Africa clade with less virulence
- Sexual transmission is possible besides other common routes
- Atypical presentation includes genital lesions & proctitis with mild or no prodrome
- But severe complications may involve the eyes and the brain
- Antivirals include Tecovirimat, Brincidofovir & cidofovir can be used.
- Antiviral resistance may be an issue
- Smallpox vaccines can help to protect Mpox

Thanks

~~Monkey~~pox