MPOX update

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The Peter Doherty Institute of Infection and Immunity

VIDS, The Royal Melbourne Hospital

Immunisation Coalition ASM Monday 6th February, 2023

Session 5, 3:45pm

A joint venture between The University of Melbourne and The Royal Melbourne Hospital

Nomenclature, offense and stigma

Consensus–
"Congo basin" ("Central African") → **Clade one (I)**
- (higher mortality/severity)

"West African" → **Clade two (II)**
- Subclades IIa, IIb (circulating in 2022 global outbreak)

Renaming 28 Nov 2022, WHO recommended using the name "mpox" as a new name for monkeypox

Pre-exposure prophylaxis / PEP vs 'primary preventative measure'

Stigma - at-risk groups

World Health Organization

Risk Communication and Community Engagement

Risk communications and community engagement public health advice on understanding, preventing and addressing stigma and discrimination related to monkeypox

1 September 2022

This public health advice from WHO provides information on the potential impact of stigma, recommended language and actions to counter stigmatizing attitudes and discriminatory behaviours and policies related to the monkeypox outbreak. It will be updated as more is known about effective strategies against stigma and discrimination in the context of this outbreak.

Overview

An outbreak of monkeypox, a viral infectious disease, is currently being reported in countries where the disease had not been found before. The risk of monkeypox is not limited to any one community or any one place. Anyone who has close contact with someone who is infectious is at risk.

The impact of stigma and discrimination on the monkeypox outbreak must be mitigated through active strategies to prevent people being unable or unwilling to access health services and support and to create an enabling environment where people feel able to report their symptoms.

https://www.who.int/publications/m/item/communications-and-community-engagement-interim-guidance-on-using-inclusive-language-in-understanding--preventing-and-addressing-stigma-and-discrimination-related-to-monkeypox
https://www.who.int/news/item/12-08-2022-monkeypox--experts-give-virus-variants-new-names

Understanding the past

1958 – First *identified* in non-human primate

1968- Smallpox eliminated in DRC

1970- human case *report*: 9mo boy DRC, Liberia, Sierra Leone

Retrospective/Rétrospective

(The following article first appeared in: *Bulletin of the World Health Organization*, 1975, **52**: 209–222)

Smallpox eradication in West and Central Africa*

WILLIAM H. FOEGE,[1] J. D. MILLAR,[2] & D. A. HENDERSON[3]

In 1966, a programme to eradicate smallpox and control measles began in West and Central Africa. With WHO and US bilateral technical and financial assistance, the 20 countries mounted a coordinated campaign of mass vaccination, assessment, surveillance, and maintenance activities. The last cases of smallpox occurred in May 1970. The introduction of epidemiologically directed surveillance-containment activities and their rapid success resulted in interruption of smallpox transmission much sooner than anticipated. The area has remained free of smallpox. From 1966 to 1972, over 28 000 000 children 1–6 years of age also received measles vaccination. The campaign established or strengthened structures for preventive health care services in all the countries.

Monkeypox

In the past 3 years, 17 cases of human monkeypox have been reported from West and Central Africa (21). Clinically, the disease is indistinguishable from smallpox and it can be diagnosed only by laboratory examination. It appears to be a disease of very low incidence, probably mistaken for smallpox in the past, most likely the result of chance spread from smallpox eradication.

In addition to its scientific interest (the disease is a zoonotic curiosity), the discovery of monkeypox has broader ramifications in the setting of smallpox-free Africa. That monkeypox cases have been repeatedly identified and investigated as suspected smallpox is strong evidence of the existence of a surveillance system adequate to identify smallpox resulting from importation.

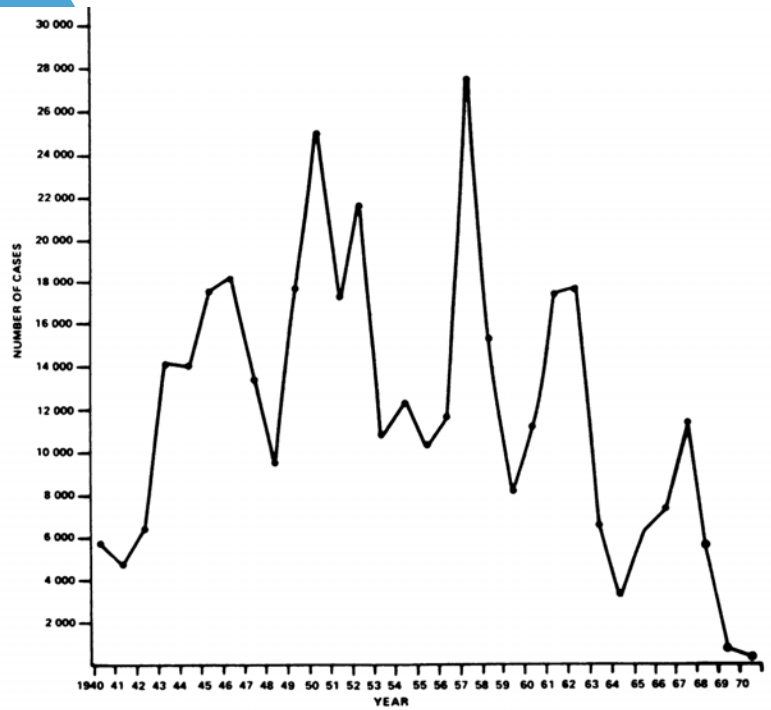


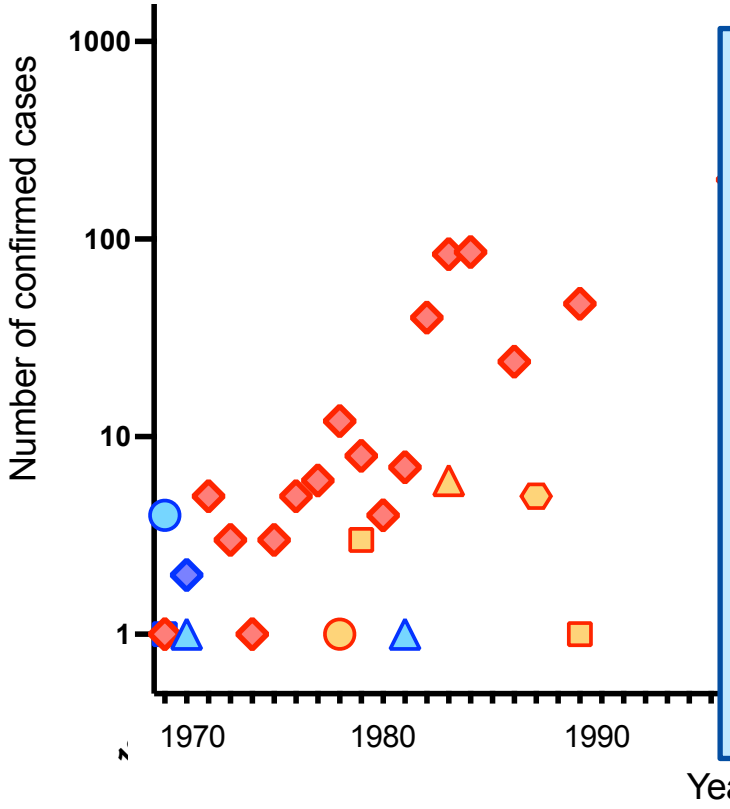
Fig. 2. Reported smallpox cases in West and Central Africa, 1940-67. Source: World Health Organization.

The key factors appeared to be a surveillance system that quickly identified the infected areas and control activities that focused on rapid vaccination of family and village contacts of cases

von Magnus P, et al, A pox-like disease in cynomolgus monkeys. Acta Pathol Microbiol Scand 1959; 46: 156–76

Foege, Millar, Henderson, Smallpox eradication in West and Central Africa, Bull WHO 1975, re-print 1998

1970-



1980-84, Zaire (DRC) 214 cases; 2510 contacts (74% vaccinated) ('co-primary' if illness within 1 week)

Table 3. Attack rates for contacts of patients with monkeypox.

Type of contact	Total no. of contacts	Vaccination scar present: No. of contacts	Vaccination scar present: No. of new cases	Vaccination scar present: Attack rate (%)	Vaccination scar absent: No. of contacts	Vaccination scar absent: No. of new cases	Vaccination scar absent: Attack rate (%)
Household	1,187	910	14	1.5	277	34	12.3
Other	1,323	959	2	0.2	364	12	3.3
Total	2,510	1,869	16	0.9	641	46	7.2

Illness / infection less common in vaccinated **1.5% vs 12.3%**

household contacts

CLADE 1 - Central African/Congo basin

- Democratic Republic of the Congo (Zaire)
- Gabon
- Benin
- Cameroon
- Central African Republic
- Republic of the Congo

CLADE 2 - West African

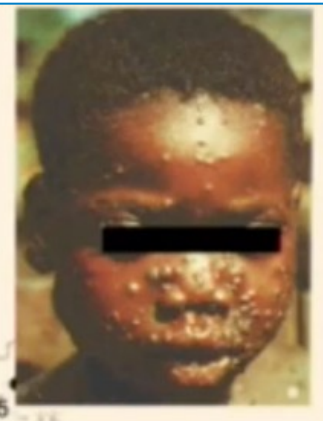
- Nigeria
- Liberia
- Sierra Leone
- Cote D'Ivoire

- USA
- Sudan
- UK
- Singapore
- Israel

Smallpox vaccination (3-19 years prior) 85% effective at preventing monkeypox in household setting (contacts)

(Clade I) *Jezek et al, Human monkeypox: a study of 2,510 contacts of 214 patients J. Infect. Dis. 1986*

The first cases of human monkeypox in West Africa (1970-89)

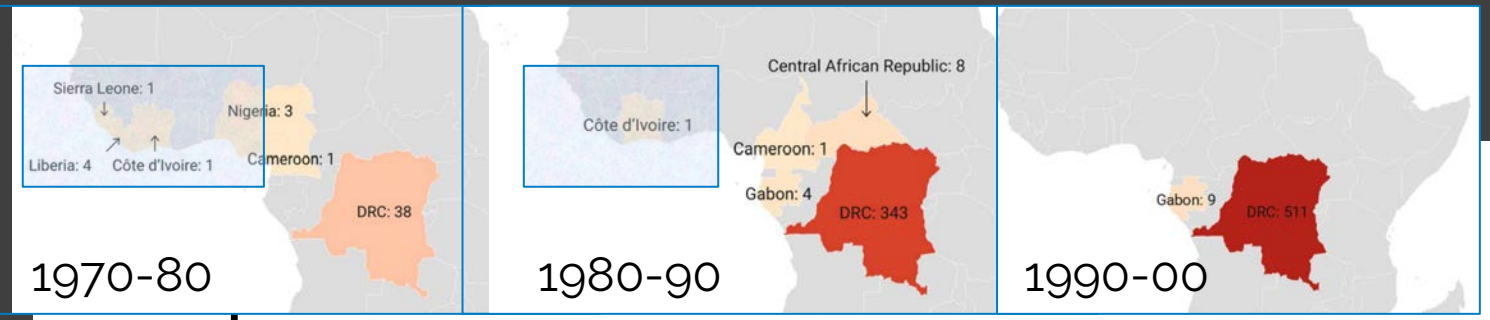


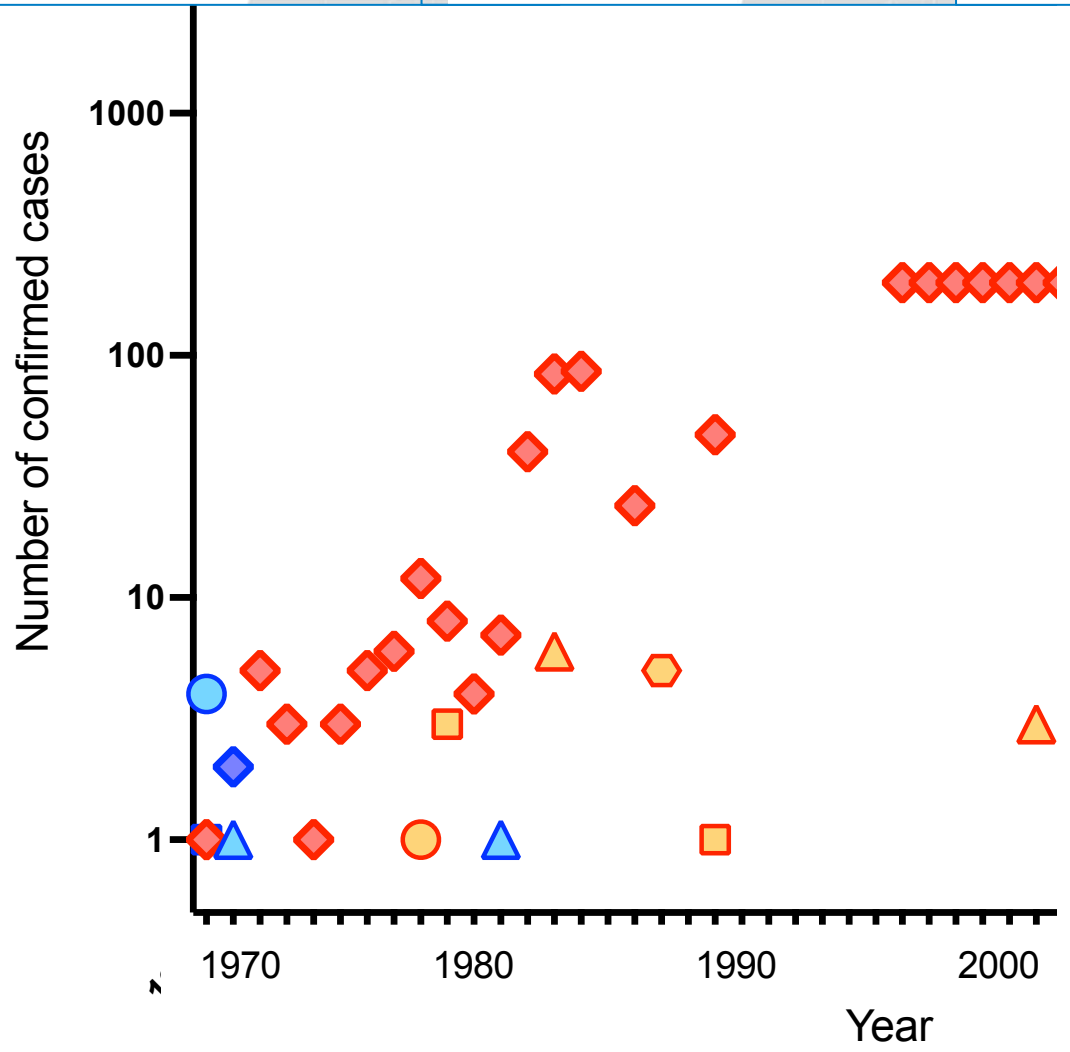
Year	Cameroon	Cote dvoire	Liberia	Nigeria	Sierra Leone	Gabon	CAR	Zaire	Total
1970	0	0	4	0	1	0	0	1	6
1971	0	1	0	2	0	0	0	0	3
1972	0	0	0	0	0	0	0	5	5
1973	0	0	0	0	0	0	0	3	3
1974	0	0	0	0	0	0	0	1	1
1975	0	0	0	0	0	0	0	3	3
1976	0	0	0	0	0	0	0	5	5
1977	0	0	0	0	0	0	0	6	6
1978	0	0	0	1	0	0	0	12	13
1979	2	0	0	0	0	0	0	8	10
1980	0	0	0	0	0	0	0	4	4
1981	0	1	0	0	0	0	0	7	8
1982	0	0	0	0	0	0	0	40	40
1983	0	0	0	0	0	0	0	84	84
1984	0	0	0	0	0	0	6	86	91
1987	0	0	0	0	0	5	0	24	29
1989	1	0	0	0	0	0	0	47	48
Total	3	2	4	3	1	5	6	316	354

- All in rainforest area
- >80% = children, M = F

- Source of infection: Wild animals 70% (rest person to person, esp adults)
- 80% small villages (<1000pp)

Bunge EM et al. The changing epidemiology of human monkeypox-A potential threat? A systematic review. PLoS Negl Trop Dis. 2022;16(2):e0010141





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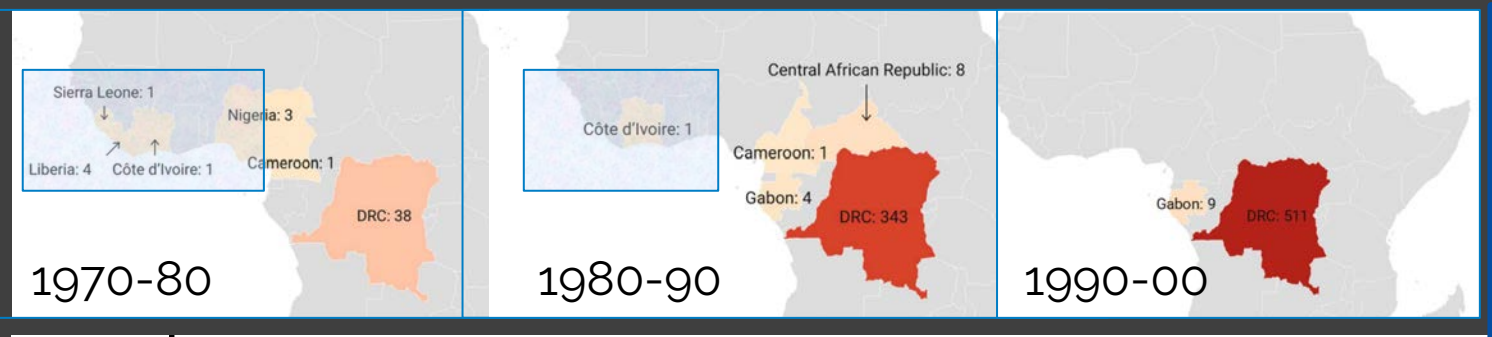
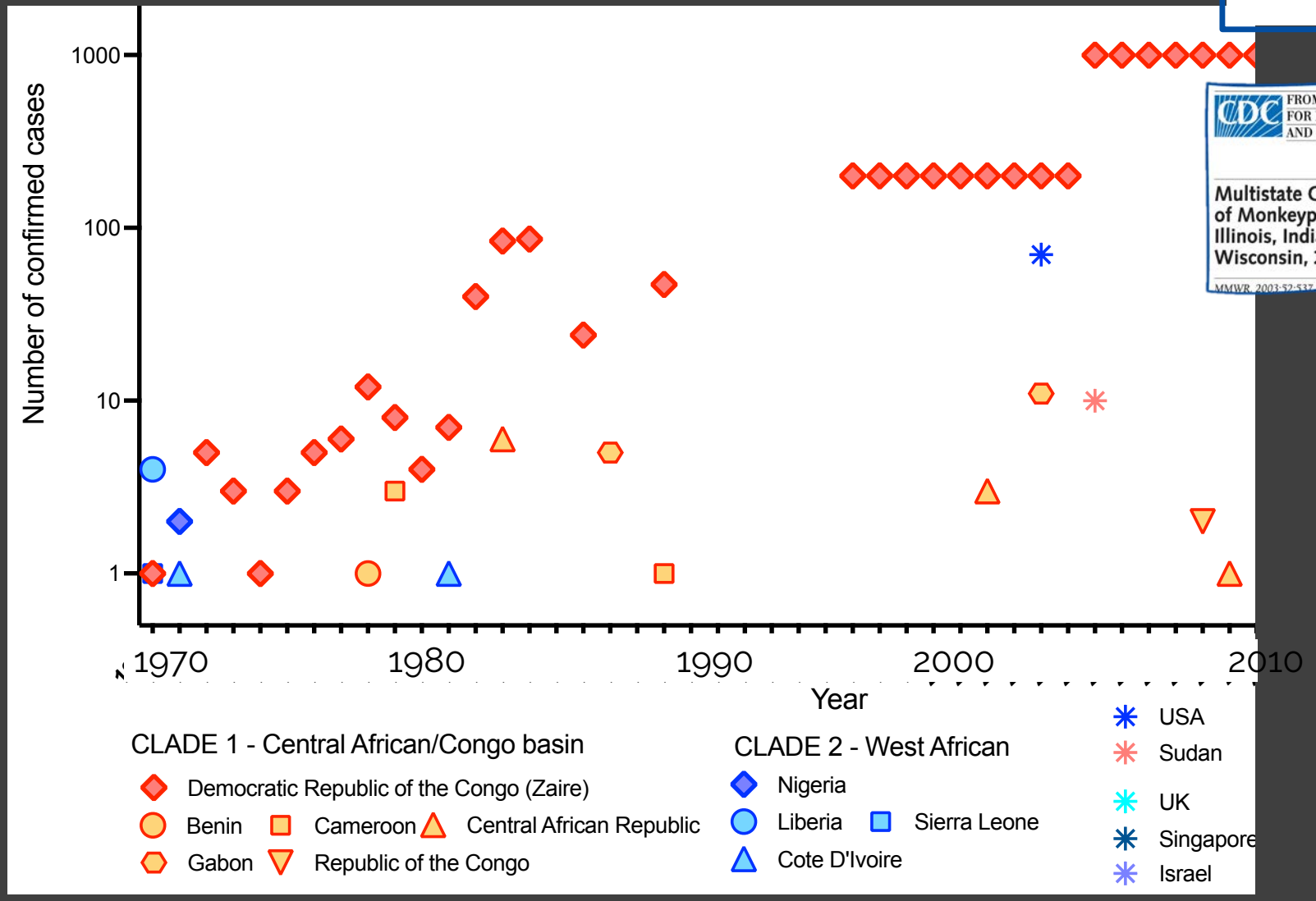
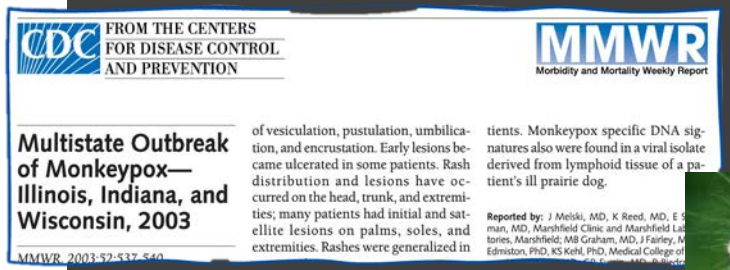
Bunge EM et al, PloS Neglected Trop Diseases, 2022



2003 shipment of African rodents to USA – 33 animals PCR positive; 22 culture positive





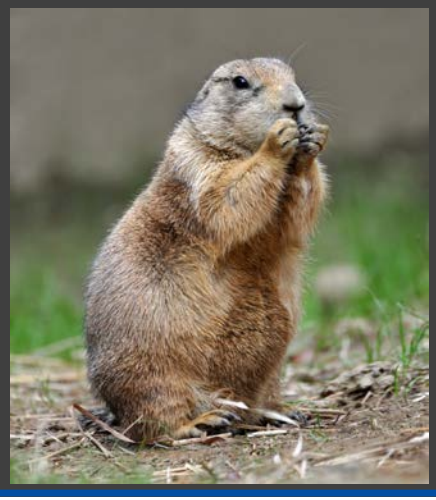
FROM THE CENTERS FOR DISEASE CONTROL AND PREVENTION

MMWR Morbidity and Mortality Weekly Report

Multistate Outbreak of Monkeypox—Illinois, Indiana, and Wisconsin, 2003

of vesiculation, pustulation, umbilication, and encrustation. Early lesions became ulcerated in some patients. Rash distribution and lesions have occurred on the head, trunk, and extremities; many patients had initial and satellite lesions on palms, soles, and extremities. Rashes were generalized in

tients. Monkeypox specific DNA signatures also were found in a viral isolate derived from lymphoid tissue of a patient's ill prairie dog.



Clinical Manifestations of Human Monkeypox Influenced by Route of Infection

Mary G. Reynolds, Krista L. Yorita, Mathew J. Kuehnert, Whitni B. Davidson, Gregory D. Huhn,* Robert C. Holman, and Inger K. Damon

Centers for Disease Control and Prevention, Division of Viral and Rickettsial Diseases, Atlanta, Georgia

Natural reservoir?

Published in final edited form as:
Future Virol. 2013 February 1; 8(2): 129–157. doi:10.2217/fvl.12.130.

A review of experimental and natural infections of animals with monkeypox virus between 1958 and 2012

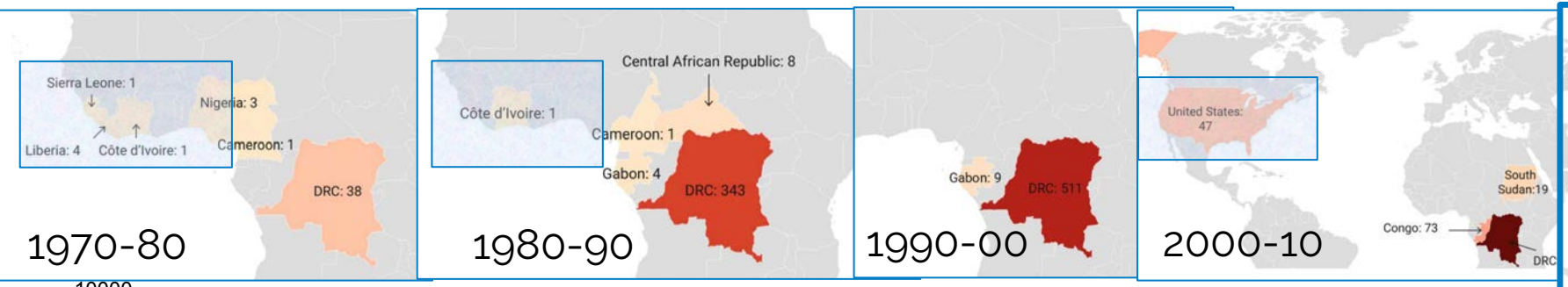
Scott Parker[1] and **R Mark Buller**[*,1]
[1]Department of Molecular Microbiology & Immunology, Saint Louis University School of Medicine, 1100 S. Grand Blvd, Saint Louis, MO 63104, USA

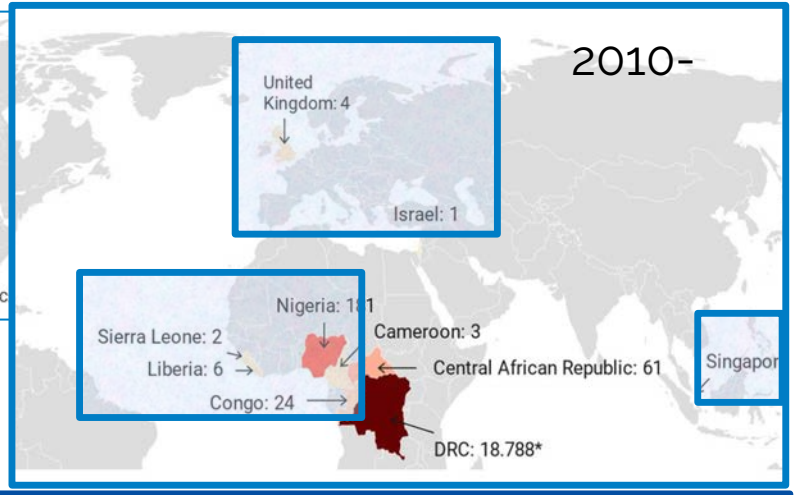
- **2003 shipment of African rodents to USA**
  - **33 animals PCR positive; 22 culture positive**
  - **71 human cases –related to prairie dogs (not imported rodents), many unwell ? Amplifying hosts**

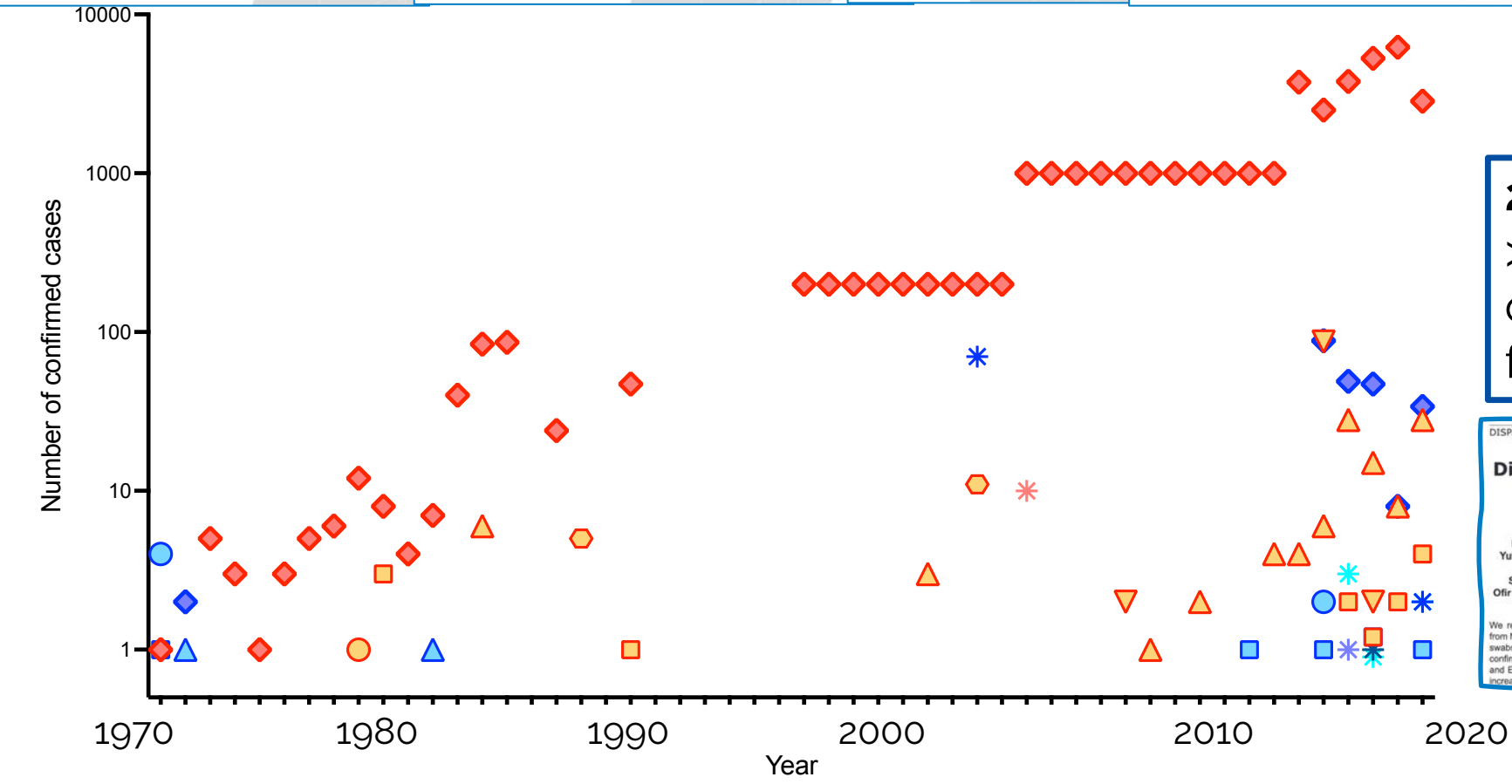
- 1964 Outbreak at **Rotterdam Zoo** – (anteaters, orangutan, Gorilla, chimpanzees, Asian gibbon, Sth American squirrel monkeys, African owl-faced monkeys, Sth American common marmoset).

- MPOX antibodies and virus detection in so many distinct species suggest that **the natural lifecycle is a complex interaction of reservoir hosts and incidental species**

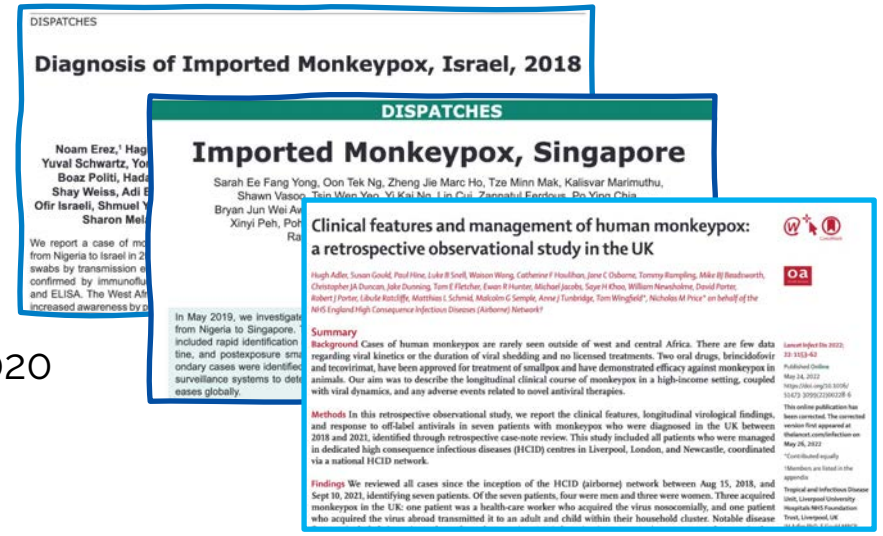
- The role of insects in the natural lifecycle of MPXV ? worth evaluating.







2017- outbreak in Nigeria has >500 suspected cases and >200 confirmed cases and a case fatality ratio of around 3%.



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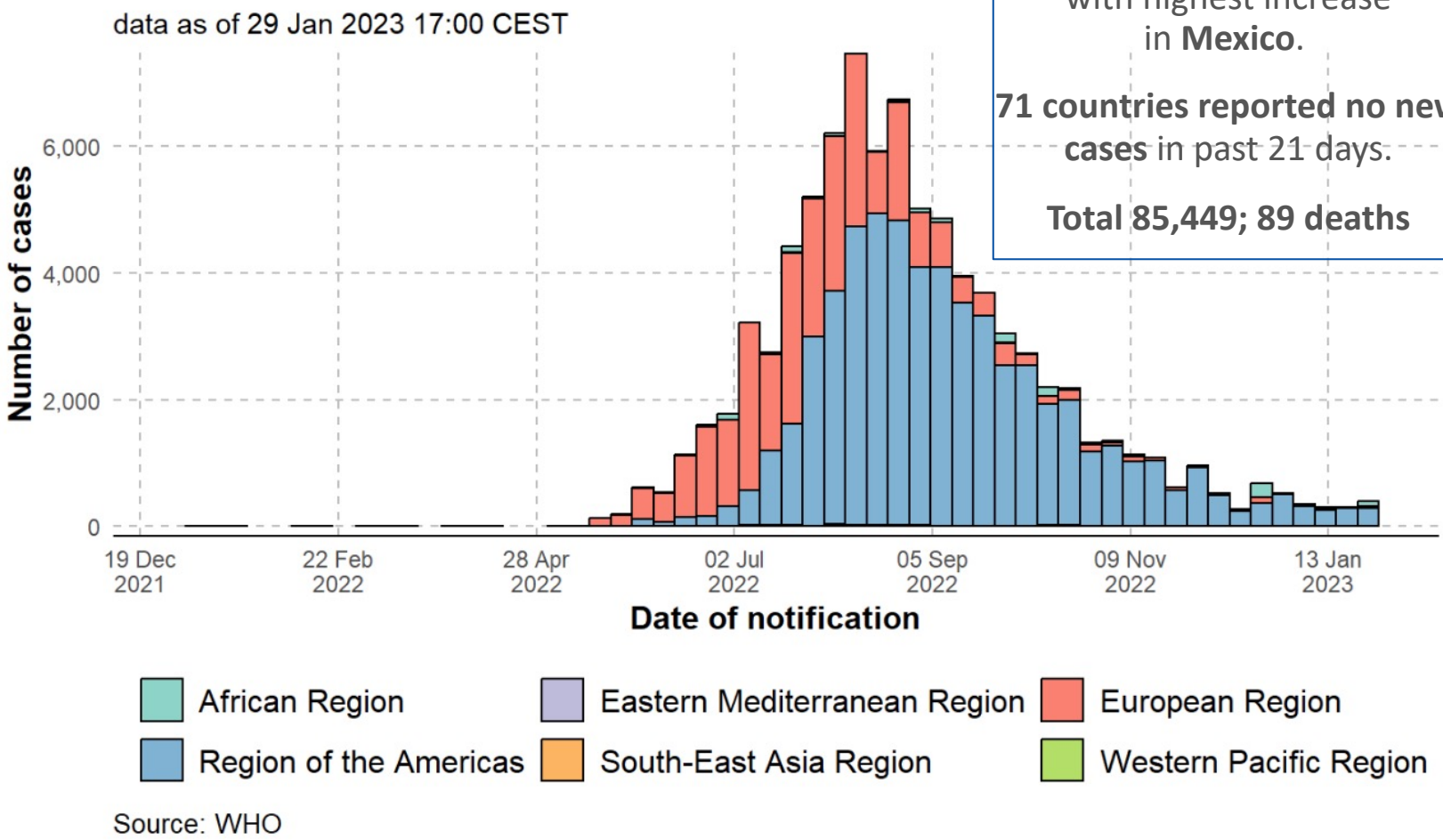
Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 27, No. 4, April 2021

Vivancos R, community transmission of monkeypox in the UK, April to May 2022 Eurosurveillance. 2022;27(22)

2022 - Multi-country outbreak of monkeypox

Global risk: '**moderate**'



In the past 7 days, **13 countries reported an increase** in weekly cases, with highest increase in **Mexico**.

71 countries reported no new cases in past 21 days.

Total 85,449; 89 deaths

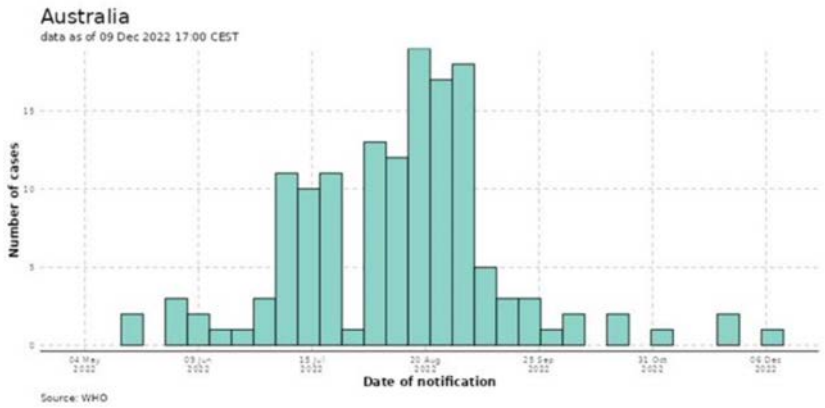
'IHR' = international health regulation;
''PHEIC = public health emergency of international concern

https://worldhealthorg.shinyapps.io/mpx_global/#33_Case_profile_(overall)

Local epidemiology –

AUSTRALIA- 144 cases

70 Victoria, 52 NSW, 5 WA, 3 QLD, 3 ACT, 2 SA



VICTORIA- 70 cases

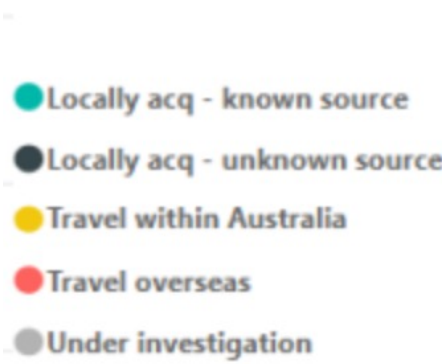
All local transmission in metro Melbourne

100% male; Median age 37 (22-61)

23/11/22 most recent (overseas acquired)

8 hospitalised, 5 tecovirimat

No deaths



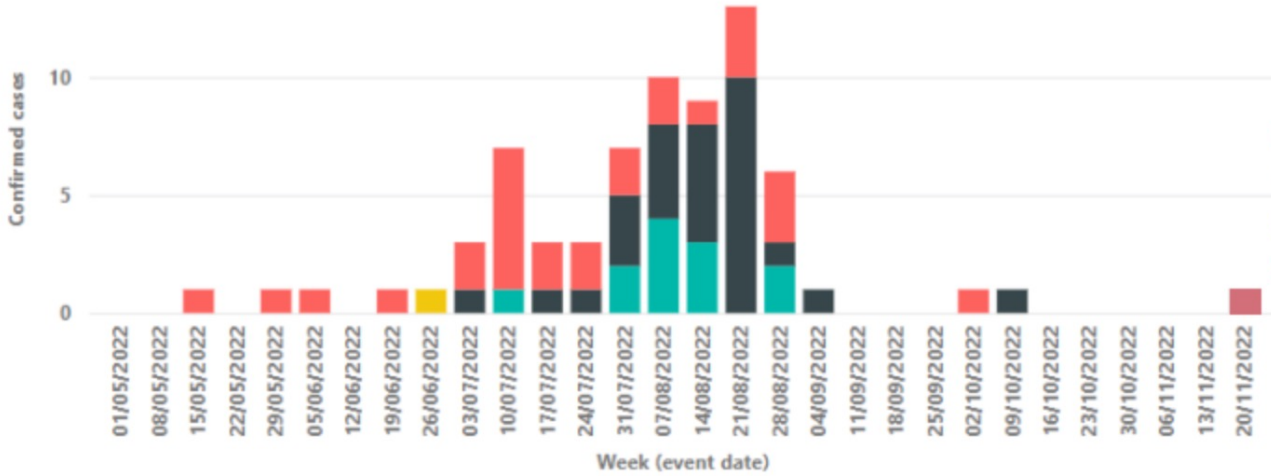


Fig 2. Weekly notifications of monkeypox by primary risk factor, 1 May 2022 – 23 November 202

Population risk - 2022

MSM

high-risk sexual behaviour as a potential risk factor.

Some reported having **multiple or anonymous sexual partners in the previous 2 weeks**, attending **sex-on-premises** venues (eg, saunas or bathhouses) or group-sex sessions, and using **recreational** drugs during sex.

Concomitant sexually transmitted infections reported in 16–29% tested in the published cohorts, with gonorrhoea, chlamydia, and syphilis being the most common infections.

33–42% with MPOX are on pre-exposure prophylaxis to prevent acquiring HIV (ie, sexually active HIV-negative adults),

36-42% are people living with HIV (36–42%)

Australia - Surveillance data – case definition

<u>Confirmed</u> = lab definitive evidence only

detection (or isolation) of MPOX virus/sequences from clinical specimens by nucleic acid amplification testing (NAAT) OR next generation sequencing (NGS) OR culture

<u>Probable</u> = laboratory *suggestive* evidence (clinical specimens) detection-

- 1. Orthopoxvirus by NAAT OR 2. Orthopoxvirus by electron microscopy in absence of exposure to other orthopoxvirus

AND clinical evidence = compatible rash /lesion(s)[1,2,3,4] on any part of body with or without one or more: • lymphadenopathy • fever (>38˚C) or history of fever • headache • myalgia • arthralgia • back pain • fatigue

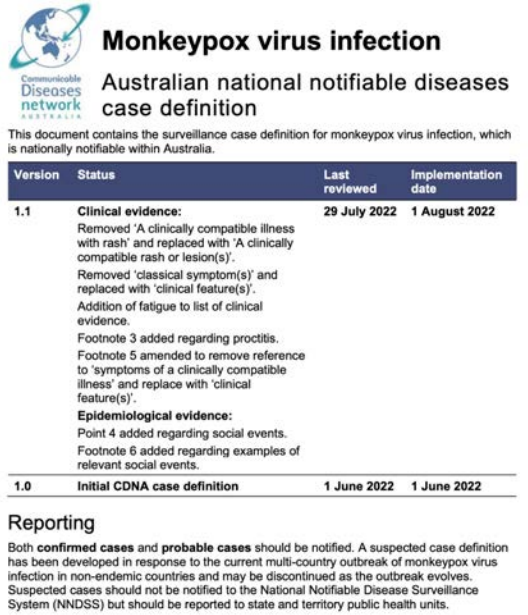
<u>Suspected</u> case[4] requires clinical evidence[5] (as per probable) AND epidemiological evidence

1. An **epidemiological link to a confirmed or probable case of monkeypox virus** infection 21 days before symptom onset

OR 2. **Overseas travel** in the 21 days before symptom onset

OR 3. **Sexual contact and/or other physical intimate contact with a gay, bisexual or other MSM** in 21 days before symptom onset

OR 4. Sexual contact and/or other physical intimate contact with individuals **at social events associated with monkeypox activity[6]** in the 21 days before symptom onset



Monkeypox virus infection

Australian national notifiable diseases case definition

This document contains the surveillance case definition for monkeypox virus infection, which is nationally notifiable within Australia.

Version	Status	Last reviewed	Implementation date
1.1	**Clinical evidence:** Removed 'A clinically compatible illness with rash' and replaced with 'A clinically compatible rash or lesion(s)'. Removed 'classical symptom(s)' and replaced with 'clinical feature(s)'. Addition of fatigue to list of clinical evidence. Footnote 3 added regarding proctitis. Footnote 5 amended to remove reference to 'symptoms of a clinically compatible illness' and replace with 'clinical feature(s)'. **Epidemiological evidence:** Point 4 added regarding social events. Footnote 6 added regarding examples of relevant social events.	29 July 2022	1 August 2022
1.0	**Initial CDNA case definition**	1 June 2022	1 June 2022

Reporting

Both **confirmed cases** and **probable cases** should be notified. A suspected case definition has been developed in response to the current multi-country outbreak of monkeypox virus infection in non-endemic countries and may be discontinued as the outbreak evolves. Suspected cases should not be notified to the National Notifiable Disease Surveillance System (NNDSS) but should be reported to state and territory public health units.

Notes 1. Lesions typically begin to develop simultaneously and evolve together on any given part of body, and may be generalised or localised, discrete or confluent. Evolution of lesions progress through 4 stages macular, papular, vesicular, to pustular then scabbing over.

2. For which the following causes of acute rash do not explain the clinical features: <u>chickenpox, shingles, measles, herpes simplex, or bacterial skin infections.</u>

3. Some cases may present with proctitis (painful inflammation of the rectum) in the absence of an externally visible rash or lesion(s)

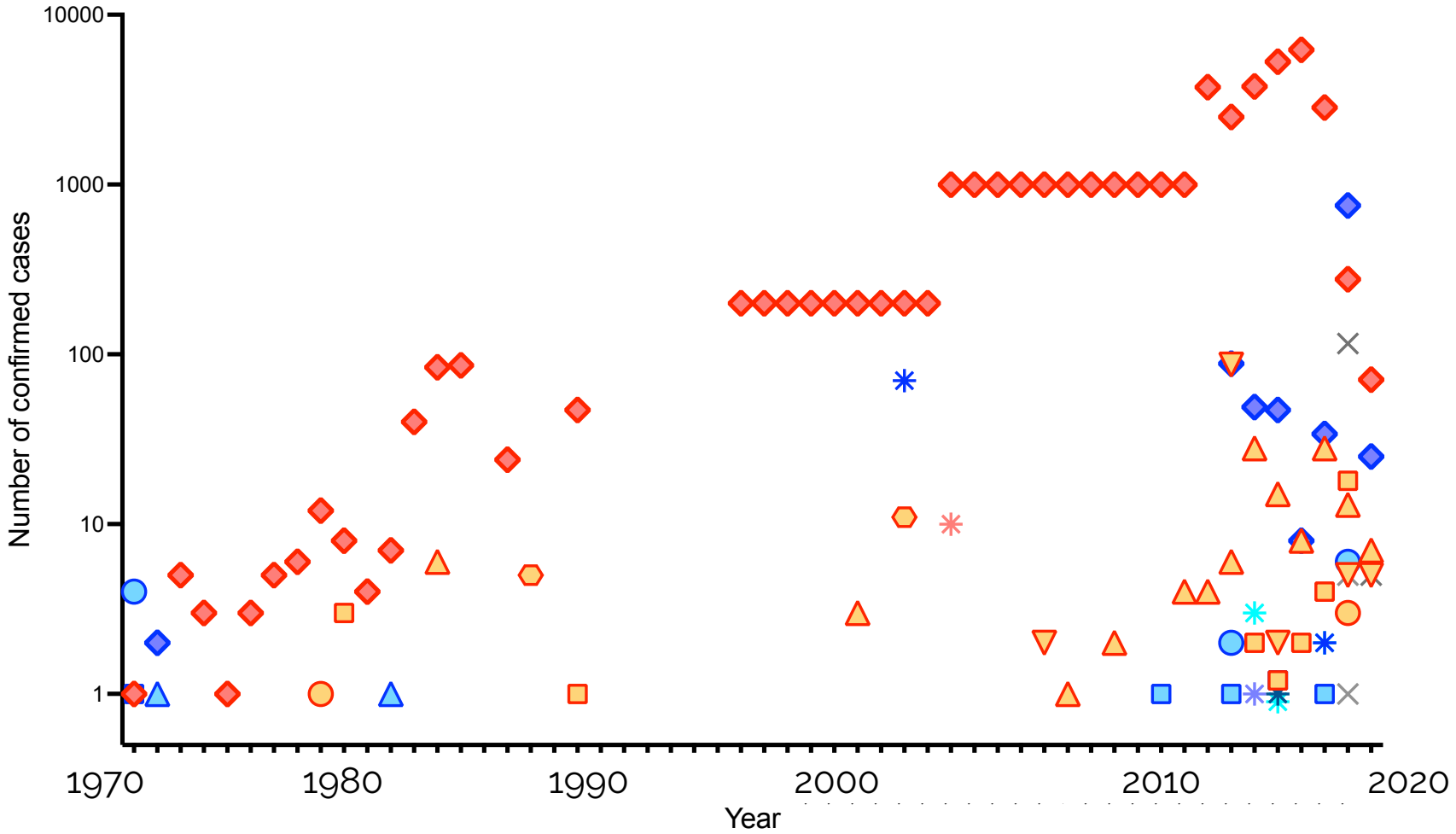
4. Seek advice from the responsible authorising pathologist and the clinician regarding testing for monkeypox virus and other alternative causes.

5. A high or medium risk contact of a confirmed or probable case only requires one or more clinical feature(s) (i.e. does not require rash or lesion(s), if another symptom present) to be a suspected case.

6. This includes events previously associated with monkeypox activity internationally such as sex-on-premises venues, raves, festivals and other mass gatherings where there is likely to be prolonged close contact, or meeting new sexual partners through a dating or hook-up "app".

https://www.health.gov.au/sites/default/files/documents/2022/08/monkeypox-virus-infection-surveillance-case-definition.pdf

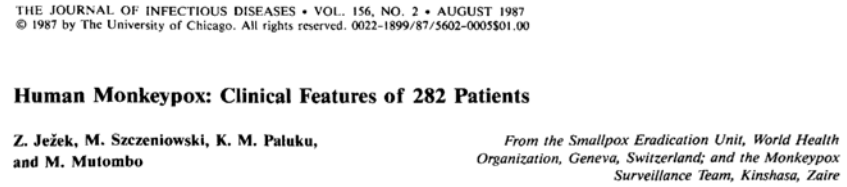
Epidemiology in Africa during 2022-23



What do we know about the clinical presentation of MPXV?

Previous reports Clade I –

*Jezek et al, Zaire (DRC), JID 1987, n=**282***


THE JOURNAL OF INFECTIOUS DISEASES • VOL. 156, NO. 2 • AUGUST 1987
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Human Monkeypox: Clinical Features of 282 Patients

Z. Ježek, M. Szczeniowski, K. M. Paluku, and M. Mutombo

From the Smallpox Eradication Unit, World Health Organization, Geneva, Switzerland; and the Monkeypox Surveillance Team, Kinshasa, Zaire

Previous reports Clade II –

*Yinka-Obunleye, Nigeria, Lancet ID 2019, n=**122***


Outbreak of human monkeypox in Nigeria in 2017–18: a clinical and epidemiological report

Summary

Background In September, 2017, human monkeypox re-emerged in Nigeria, 39 years after the last reported case. We aimed to describe the clinical and epidemiological features of the 2017–18 human monkeypox outbreak in Nigeria.

Recent reports –*Since May 2022*

sexual health clinics, n=100-650


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Monkeypox Virus Infection in Humans across 16 Countries — April–June 2022

Demographic and clinical characteristics of confirmed human monkeypox virus cas… sexual health centre in Londo…

Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: a prospective observational cohort study

Summary

Background Historically, human monkeypox virus cas… west Africa. Currently, the UK and several other count… individuals attending sexual health clinics, with no a… demographic and clinical characteristics of patients … health centre.

WHO – 'detailed case data' (confirmed cases),
n=81,319, representing **95.2%** of all aggregated cases reported https://worldhealthorg.shinyapps.io/mpx_global/#1_Overview

Mpox reporting completeness

As of 30 Jan 2023[1]

	Total Confirmed Cases	Total Detailed Confirmed Cases[2]	% Detailed Cases reported
Region of the Americas	57,922	55,229	95.4%
European Region	25,804	25,691	99.6%
African Region	1,302	174	13.4%
Western Pacific Region	235	131	55.7%
Eastern Mediterranean Region	82	57	69.5%
South-East Asia Region	37	37	100.0%

[1] Total confirmed cases shown as of date of last detailed case report for the WHO Region of the Americas and WHO European Region.
[2] Note that in rare cases total detailed cases may exceed total confirmed cases due to ongoing data cleaning issues

WHO data - demographics 'of all cases w available data'

- **M 96.6% (73000/75600)**, median **34y** (IQR 29-41)
  - M between **18-44 yo 79.2%** of cases.
  - 84.1% (26532/31545) MSM. 6.7% bisexual M.

- **3.4% (2600/75600)** F:
  - Region of the Americas (2081/2600; 80%),
  - European Region (434/2600; 17%)
  - Heterosexual (909/1024; 89%)
  - Exposure setting household (49/108; 45%), form of transmission sexual encounters (230/580; 40%)
- 57 F pregnant or recently pregnant.

- **802/79072** (1.0%) 0-17yo, 221 (0.3%) aged 0-4:
  - 0-17 from Region of the Americas (648 /802; 81%); 0-17, 1 have reported exposure in a school setting.

- **48.1% (16,940/35,252) HIV+;** (skewed to those w positive HIV results).

- **1219** cases reported to be **health workers**.

most infected in community and further investigation is ongoing to determine whether remaining infection was due to occupational exposure.

- **Sexual encounter** was most common reported transmission, **14,934 of 21,741 (68.7%)** of all reported transmission events.

- Settings - most common **party setting with sexual contacts**, with **3,434 of 5,191 (66.2%)** of all likely exposure categories.

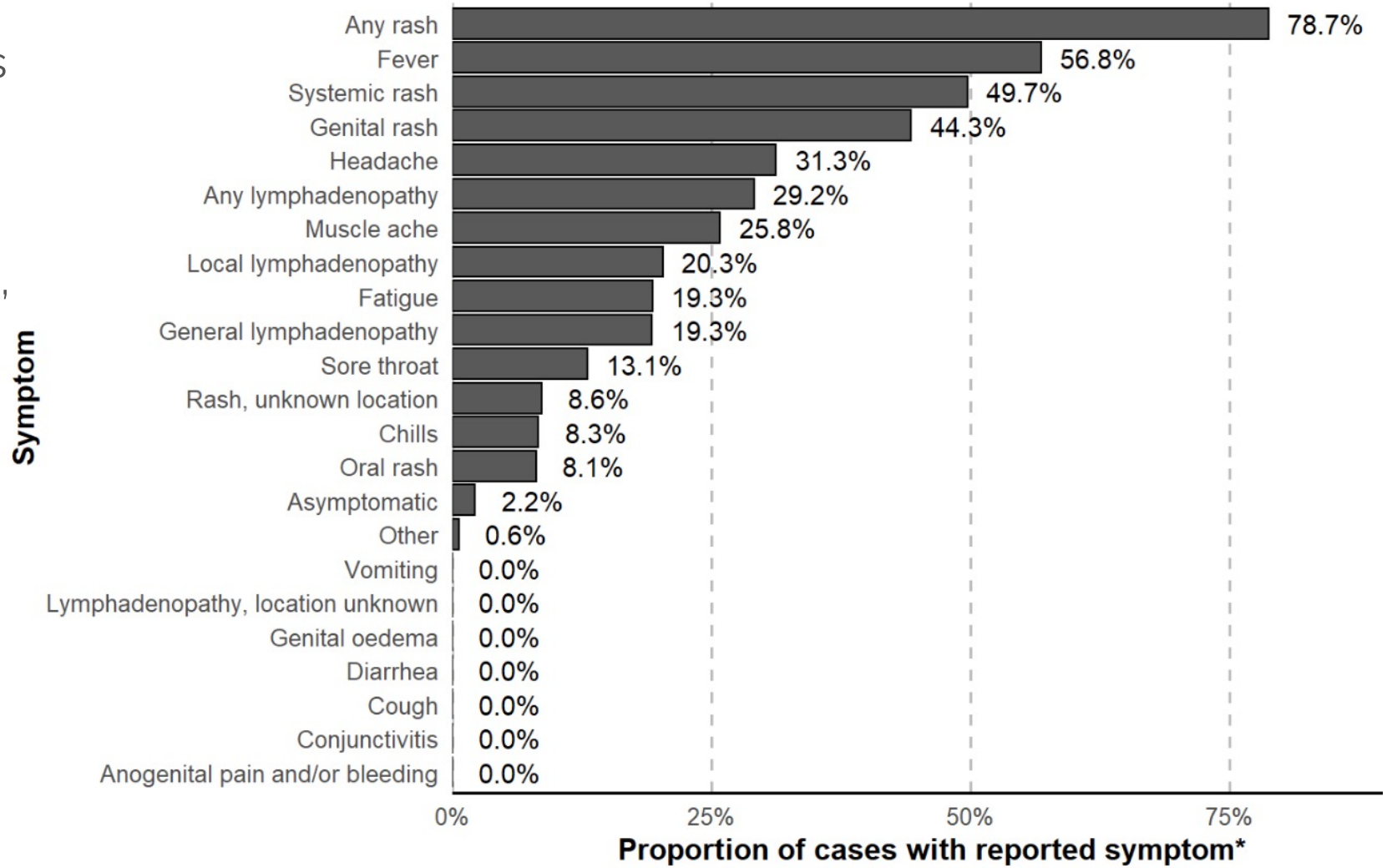
WHO data - Among cases reporting at least one symptom, most common symptom is **any rash** in **79%**.

Identifying true denominators is difficult

- **lack of negative reporting.**
- symptom definitions that may vary between countries' reporting systems.

Here *any rash* refers to **one or more rash symptoms (systemic, oral, genital, or unknown location)**,

and *any lymphadenopathy* refers to either **general or local lymphadenopathy.**



Source: WHO
*38399 cases with at least one reported symptom from a country where at least two unique symptoms reported used as denominator

Clinical presentation - What do we know?

Previously reported characteristics

	MONKEYPOX	CHICKENPOX	SMALLPOX (ERADICATED)
Virus	Monkeypox virus, orthopoxvirus family	Varicella-zoster virus	Variola virus, orthopoxvirus family
Fever	1–5 days before rash	1–2 days before rash	2–4 days before rash
Rash appearance	Often starts on the face then spreads to other parts of the body, including palms and soles. The rash eventually forms a scab that falls off.	Itchy, blister-like rash — first on the chest, back, and face, and then spreads over the entire body. Absent on palms and soles.	Starts as small red spots on the tongue and mouth. Rash then appears on the skin, starting on the face and spreads to arms and legs, and then palms and soles. The rash eventually forms a scab that falls off.
Swollen lymph nodes	Yes	No	No
Time between catching it and symptoms	5–21 days	10–21 days	7–19 days
How long illness lasts	2–4 weeks	4–7 days	Up to 5 weeks
Death	1–10% of cases, depends on strain	Rare	Up to 30% of cases, depends on type

Characteristics of recent cases

Transmission related to intimate contact, MSM

Prodrome less prominent/may be absent

Rash may predate systemic symptoms and may be 'atypical'

Genital lesions common

- Multiple stage at same time, Non-pustular

Complications related to pain - rectal/penile lesions

- Pain – proctitis, urinary retention, urethritis
- Secondary infections
- Encephalitis

Asymptomatic infection, ? Importance

Clinical presentations and differentials

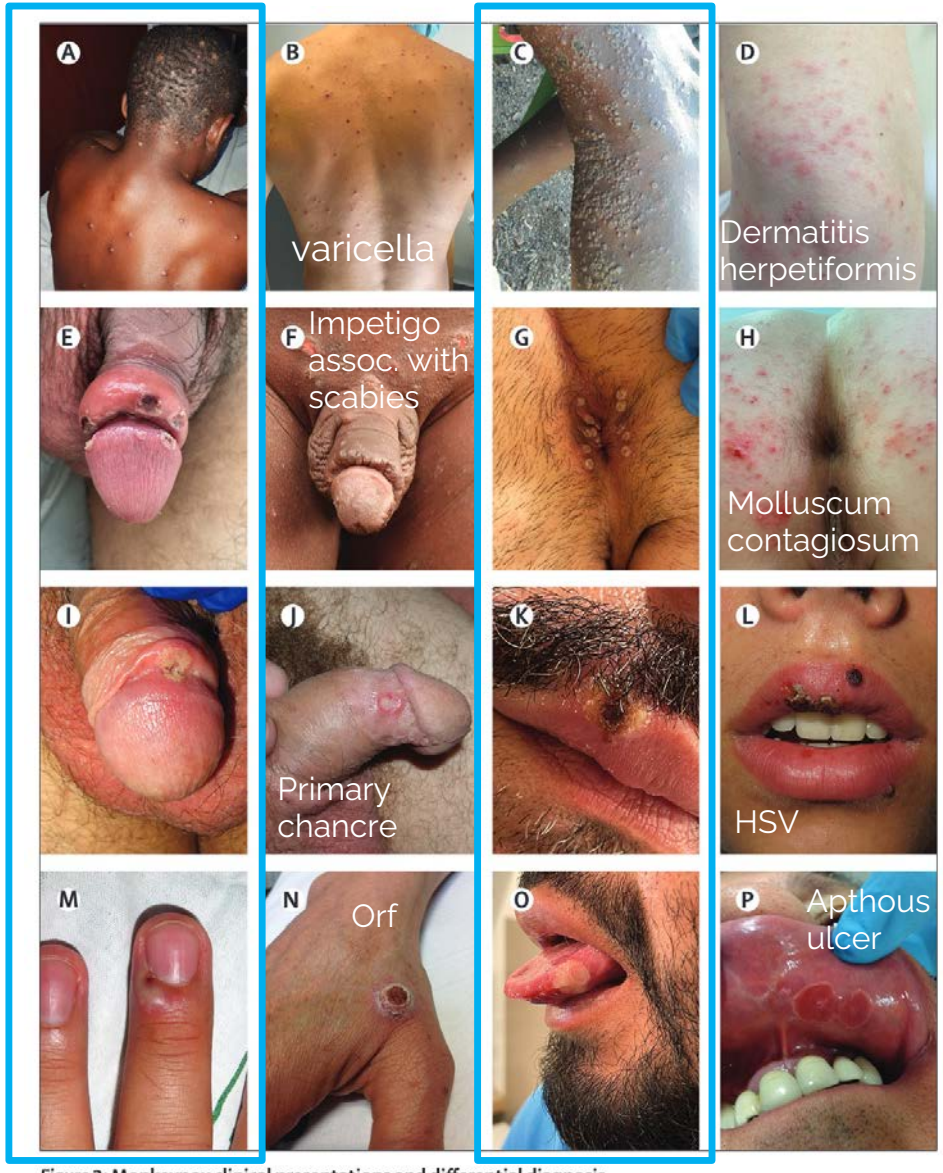


Figure 2: Monkeypox clinical presentations and differential diagnosis

Discrete rash on the thorax caused by monkeypox (Nigeria; A) and varicella (Spain; B);

a generalised monkeypox rash (Democratic Republic of the Congo; C) and a blistering rash caused by dermatitis herpetiformis (Spain; D);

localised monkeypox lesions causing penile oedema (Spain; E) and impetigo associated with scabies (Malawi; F);

localised perianal rash caused by monkeypox (Spain; G) and molluscum contagiosum (Spain, H);

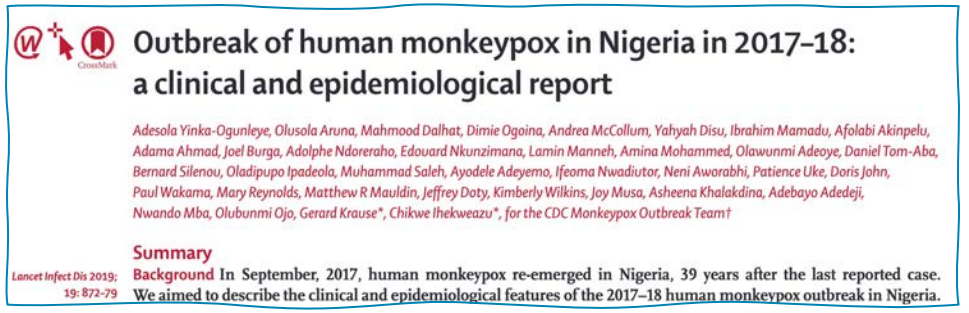
a solitary monkeypox genital ulcer (Spain; I) and a primary syphilis chancre (Spain; J);

lip lesion caused by monkeypox (Spain; K) and herpes simplex (Spain; L); hand lesions caused by monkeypox (Spain; M) and Orf virus infection (Spain; N);

monkeypox lesions on the tongue (Spain; O) and aphthous ulcer on the labial mucosa (Spain; P).

Mitja et al, Monkeypox, Lancet 2023:401:60

2017 – Nigerian outbreak



Outbreak of human monkeypox in Nigeria in 2017–18: a clinical and epidemiological report

Adesola Yinka-Ogunleye, Olusola Aruna, Mahmood Dalhat, Dimie Ogoina, Andrea McCollum, Yahyah Disu, Ibrahim Mamadu, Afolabi Akinpelu, Adama Ahmad, Joel Burga, Adolphe Ndoreraho, Edouard Nkunzimana, Lamin Manneh, Amina Mohammed, Olawunmi Adeoye, Daniel Tom-Aba, Bernard Silenou, Oladipupo Ipadeola, Muhammad Saleh, Ayodele Adeyemo, Ifeoma Nwadiutor, Neni Aworabhi, Patience Uke, Doris John, Paul Wakama, Mary Reynolds, Matthew R Mauldin, Jeffrey Doty, Kimberly Wilkins, Joy Musa, Asheena Khalakdina, Adebayo Adedeji, Nwando Mba, Olubunmi Ojo, Gerard Krause*, Chikwe Ihekweazu*, for the CDC Monkeypox Outbreak Team†

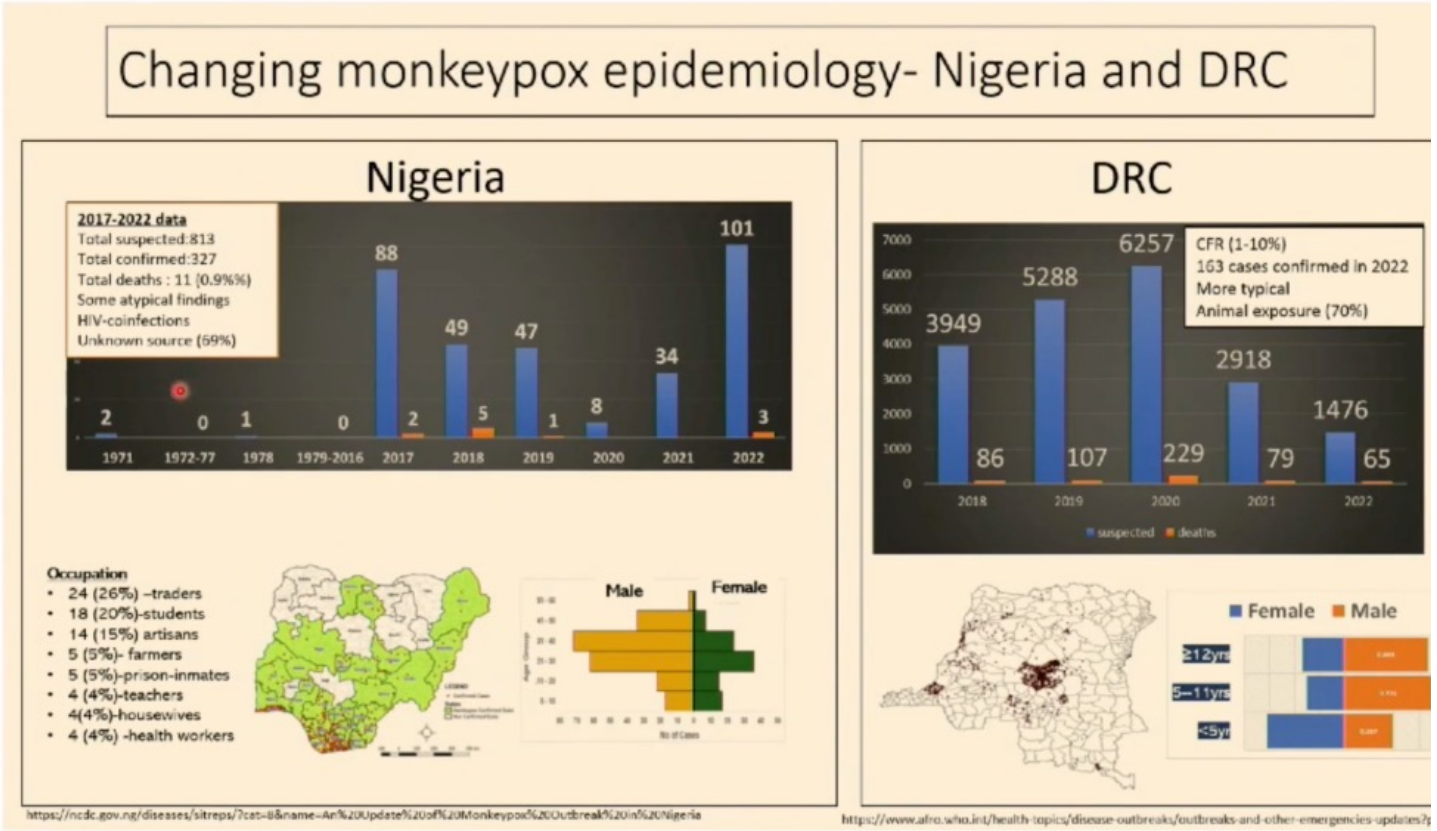
Lancet Infect Dis 2019; 19: 872-79

Summary

Background In September, 2017, human monkeypox re-emerged in Nigeria, 39 years after the last reported case. We aimed to describe the clinical and epidemiological features of the 2017–18 human monkeypox outbreak in Nigeria.

- **Genital rash and rash without fever**
- **Spread beyond rainforest to urban areas**
- **Men>F**
- **Older (no longer children)**
- **Many cases unconfirmed**
- **? 4-6 generations of transmission**

In light of the outbreak/increasing cases in the region, the potential for epidemic and more widespread transmission was also hypothesized



https://ncdc.gov.ng/diseases/sitreps/?cat=8&name=An%20Update%20of%20Monkeypox%20Outbreak%20in%20Nigeria

https://www.afro.who.int/health-topics/disease-outbreaks/outbreaks-and-other-emergencies-updates?y

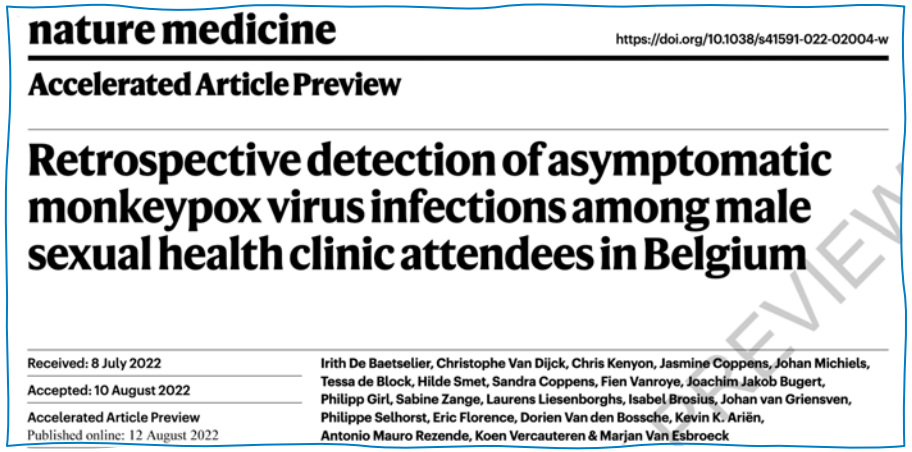
Published cohorts	*Jezek et al, Zaire (DRC), JID 1987, n=**282** **Clade 1***	*Yinka-Obunleye, Nigeria, Lancet ID 2019, n=122 Clade 2*	*2022 Thornhill, multi- country, (NEJM); n=528, Girometti, UK (AIDS), n=101 Tarin-Vicente, Spain, (Lancet), n=181; Patel A, UK, (BMJ) n=196*	*WHO CRF (19 Sept 2022) n=32,125*
AGE	**0-4yo 50.3%** 5-9yo 35.5%	**Age 29**	**Age 37-39**	**Age 35**
M/F	**M 50.7%**	**M 69%**	**M 97-100%** MSM 92-100%	**M 97%** MSM 91%
TRANS-MISSION	ND	30% epi link **7 (58%) h/hld or sexual contact**; 1 HCW 10 animal contact	**Sexual transmission 25-95%** (if exposure known)	**Sexual transmission 88%**
HIV	ND	[4/7 dec. in PLWH not on ART]	**30-41%** >90% ART, ND	**48%** (16,932/46,059)
Other STI	ND	NR	17-35% (gono, chlamydia, syphilis)	NR

Published cohorts	*Jezek et al, Zaire (DRC), JID 1987, n=**282***	*Yinka-Obunleye, Nigeria, Lancet ID, 2019, n=122*	*2022: Thornhill, multi- country, (NEJM); n=528; Girometti, UK (AIDS), n=101; Tarin-Vicente, Spain, (Lancet), n=181; Patel A, UK, (BMJ) n=196*	*WHO CRF (19 Sept 2022) n=32,125*
PRODROME 'pre-eruptive'	80% fever 1-3d before rash 5% same day 15% >3d after	57%	36-62% 2-4d	NR
Systemic features	**Fever 100%** Headache (maybe before fever)	**Fever 88%** H/ache 79% Myalgia 63%	**Fever 62-66%** Headache 27-32% Myalgia 31-36%	**Fever 57%** H/ache 31% Myalgia 26%
Rash	100% Usually first on face **Genitalia 27%** Pharyngitis 52%	100% Face 96% **Genitalia 68%** Pharyngeal 58% Palm/sole 65%	Face 25% **Anogenital 73-93%** Oropharyngeal 6-43% Palm/sole 10%	**79%** **Genital 44%** Pharyngitis 13% Oral 9%
Lymphadenopathy	50-84%	69%	56-85%	29%
Deaths	11% (27/250), all children 8m-8yo (none if smallpox scar)	7/122 (6%) 4/7 dec. in PLWH not on ART	0	91

Asymptomatic viral shedding that can lead to transmission?

Belgium May 2022, n=224 samples collected for gono/chlamydia testing

- **PCR + 4**; 3 asymptomatic D21-37 FU,
- Serology positive



nature medicine

https://doi.org/10.1038/s41591-022-02004-w

Accelerated Article Preview

Retrospective detection of asymptomatic monkeypox virus infections among male sexual health clinic attendees in Belgium

Received: 8 July 2022

Accepted: 10 August 2022

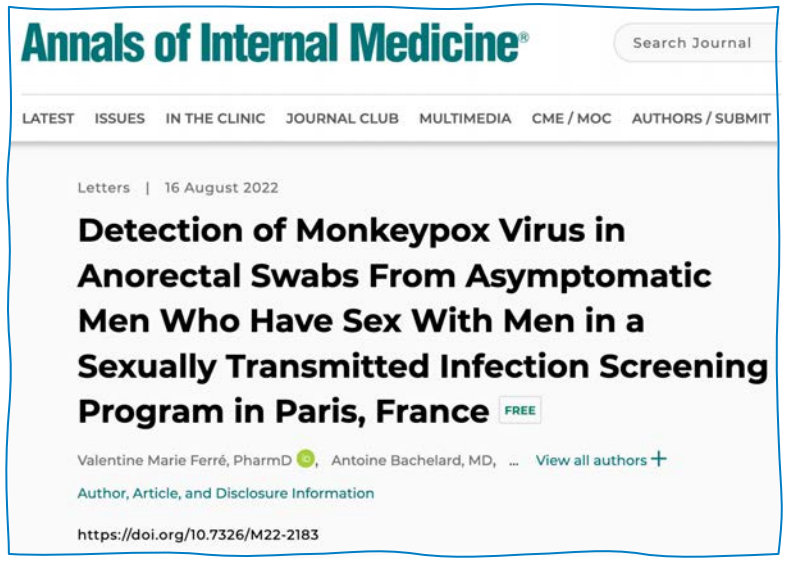
Accelerated Article Preview

Published online: 12 August 2022

Irith De Baetselier, Christophe Van Dijck, Chris Kenyon, Jasmine Coppens, Johan Michiels, Tessa de Block, Hilde Smet, Sandra Coppens, Fien Vanroye, Joachim Jakob Bugert, Philipp Girl, Sabine Zange, Laurens Liesenborghs, Isabel Brosius, Johan van Griensven, Philippe Selhorst, Eric Florence, Dorien Van den Bossche, Kevin K. Ariën, Antonio Mauro Rezende, Koen Vercauteren & Marjan Van Esbroeck

Paris 5 Jun-11 Jul, MSM testing neg. gono/C.trach, n=200

- **PCR + 13 (6.5%),** 11/13 asymptomatic D21 FU



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Letters | 16 August 2022

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, ... View all authors +

Author, Article, and Disclosure Information

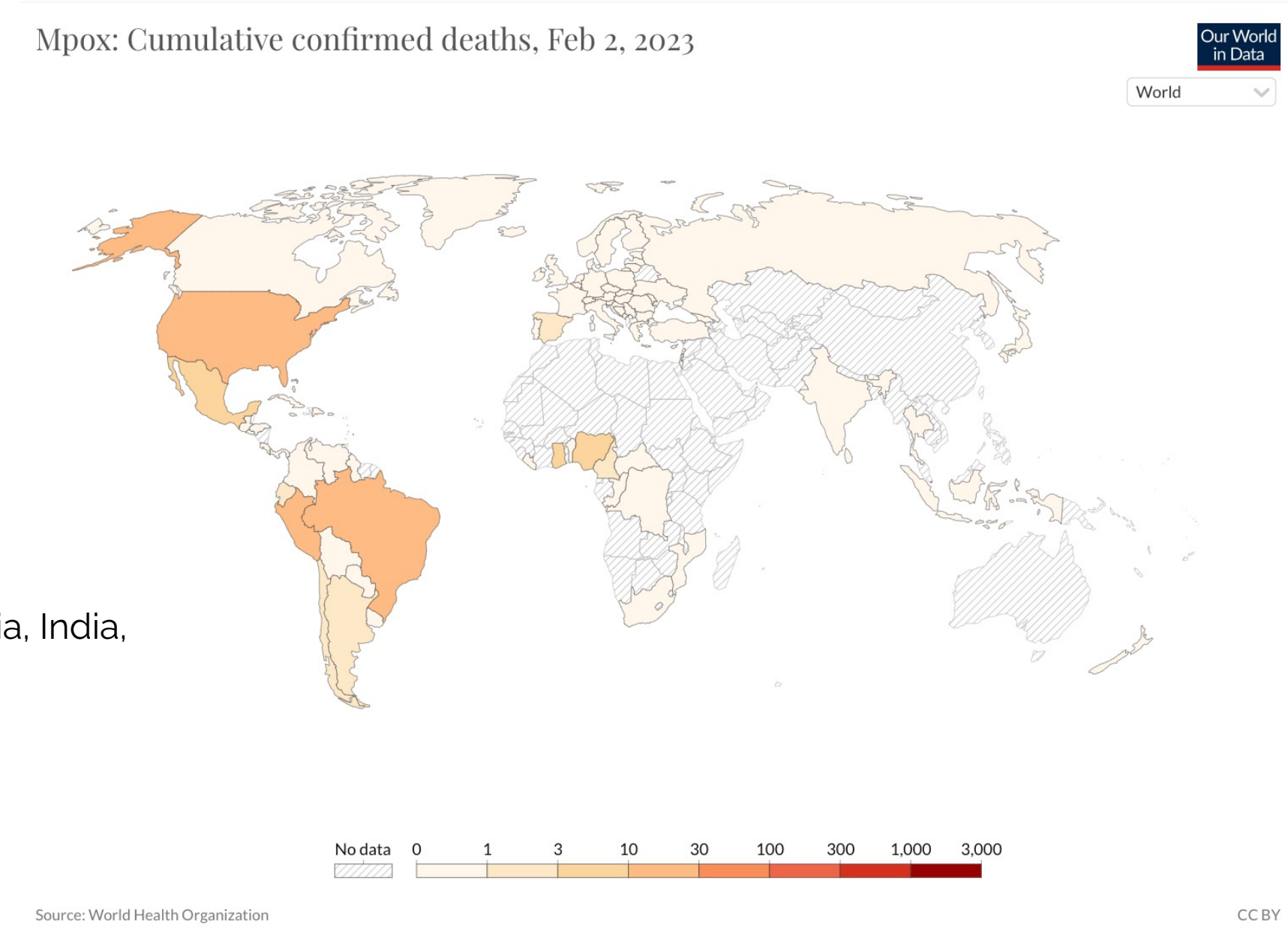
https://doi.org/10.7326/M22-2183

Deaths, n=91

USA 26
Brazil, Peru 15

Nigeria 7
Ghana , Mexico 4
Cameroon, Spain 3
Argentina, Chile, Ecuador 2

Belgium, Cuba, Czechoslovakia, India, Mozambique, Sudan 1



Deaths, n=91
Details lacking

- **USA**: 2 deaths – both severely immunocompromised, 1 Texas, 1 LA county

- **Peru**: 41yo M HIV/TB (no ART – resp failure, renal failure, septic shock, confirmed MPX
- **Brazil** July: 41yo M lymphoma, septic shock
- **Ecuador**

- **Spain** (2) Jul 22:
  - 44yoM encephalitis
  - 31yoM encephalitis, (both prev well)
- **Belgium** (1) Aug 22

- **India** 31 Jul 22: 22yo M recently returned from UAE, adm 27/7 fever, encephalitis, lymph node swelling; no rash; prior diagnosis MPX UAE 19/7

https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-n

Transmission and pathogenesis

- **Respiratory or dermal route**
- **Animal-human or human-human transmission**
- **Direct contact with infectious sores or lesions on mm has been the primary mode of transmission during the 202 outbreak**
- **Might be facilitated by breach in recipient skin/mucosa incl microscopic abrasions during sex**

? Role for fomites/environmental contamination

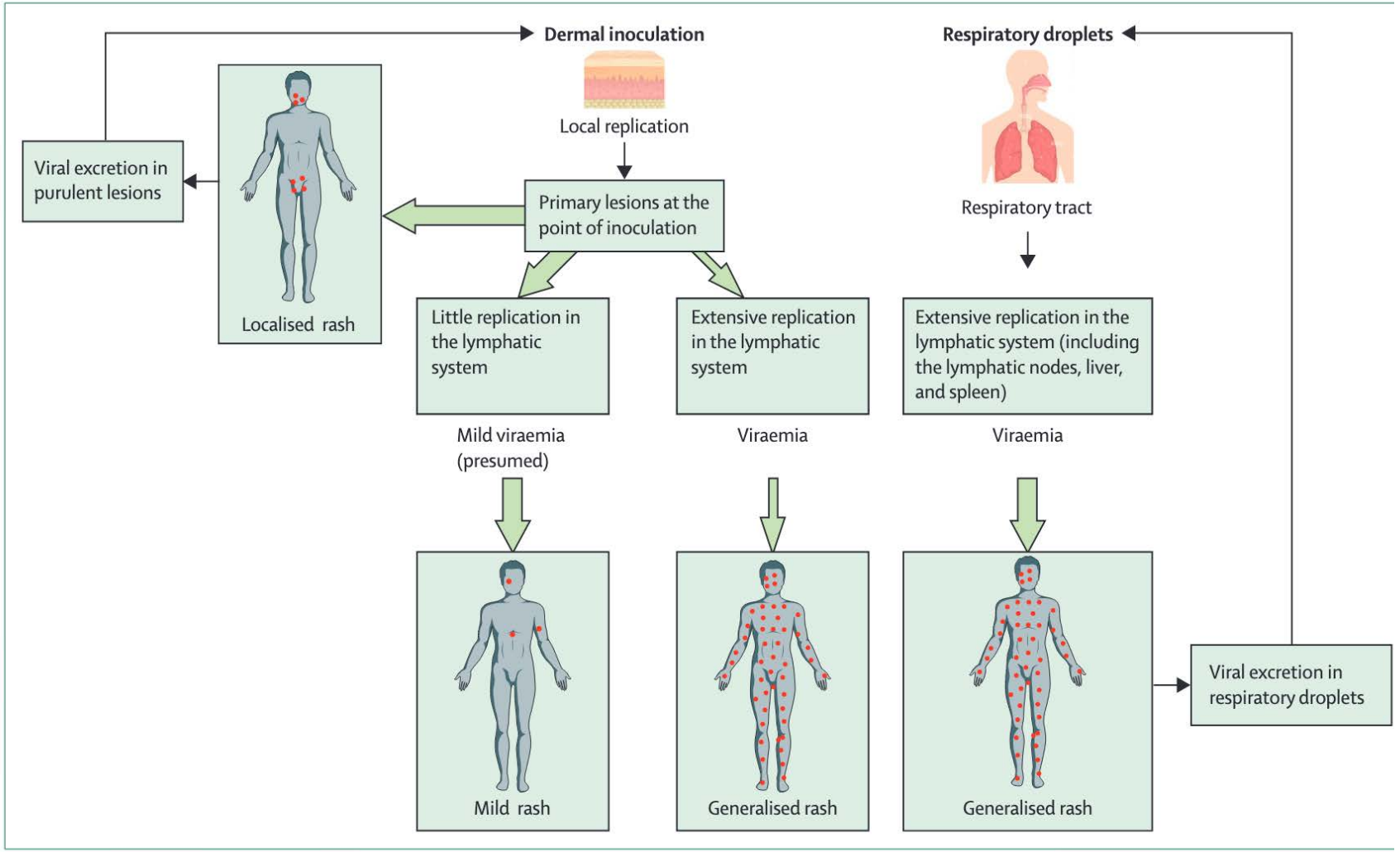


Figure 1: **Proposed mechanism for the spread of the monkeypox virus throughout the body and its relation to the transmission route**

Mitja et al, Monkeypox, Lancet 2023:401:60

Treatment and vaccination

Tecovirimat inhibits an orthopoxvirus protein essential for di
within an infected hos

No Human RCT on ef

In non-human primate
monkeypox disease, t
survival and case studies in humans show anecdotal improvement of symptoms and viral clearance

Resistance

VACCINATION – Following exposure, those at high risk

3rd generation JYNNEOS®

(MVA-BN: modified vaccinia Ankara vaccine-Bavarian Nordic) –

Highly-attenuated – replication deficient

Subcutaneous

OR Intradermal – for prevention only 1/5 dose; not immunocompromised

ent only for

opic dermatitis

Live-attenuated, replication-competent

Percutaneous scarification w bifurcated needle

Single dose, post-vaccination wound care (prevent self-inoculation/vulnerable contacts)

Contraindications- atopic dermatitis, children, pregnancy

Rare, serious AEs

Summary

Monkeypox epidemiology is changing, may have been changing for some time.

Significant knowledge gaps

Symptomatic Infections

generally self-limited, supportive mx,
rx of complications antiviral therapy – in consultation with ID/sexual health physician.
Immunocompromised may be at particular risk

Pre-symptomatic infection ? implications for control strategies ? Role for screening

Tecovirimat vaccinia immunoglobulin may have a role in severe disease / early therapy in those at risk and are held in the national medical stockpile

Vaccination may modify disease course

Research gaps-

- Natural history, endemic vs opportunistic species and why
- Vulnerability ? Immunosuppression
- Transmission (direct inoculation, other)

Diagnostic testing

droplet, GOWN
contact, GLOVES
splash
GOGGLES/face shield

+/-N95 (resp syx, differential, aerosol generating proc)

Sampling – PPE

Sterile dry swab from at least 2 open/active lesions

- Vigorously rub bottom of lesion (cellular material @ base)

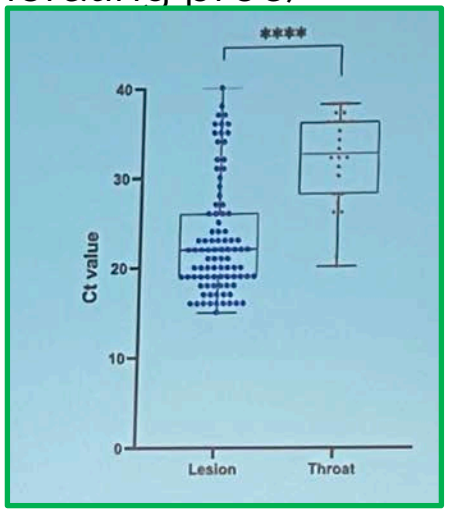
Throat swab (pharyngeal lesion, atypical/no rash)

Anorectal mucosa (pain), urine

Notify laboratory

Double bag for transport/refrigerate (4°C up to 7d)

CONSIDER- measles, VZV, syphilis, HSV, chancroid, molluscum, LGV +/- other STIs if appropriate



Deb Williamson, VIDRL,ASHM 2022

Testing PCR for viral DNA → results 24-48h

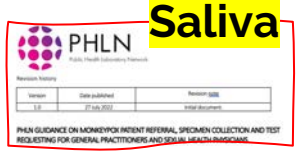
Public health labs

Commercial assays in development, not TGA approved

Targets – DNA polymerase, env protein

Blood for serology – role in detecting asyx/past infection, cross reactivity (orthopoxviruses, vaccination)

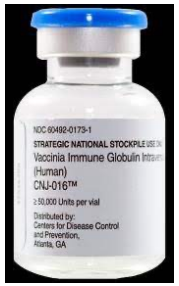
Saliva



https://www.health.gov.au/resources/publications/phln-guidance-on-monkeypox-patient-referral-specimen-collection-and-test-requesting-for-general-practitioners-and-sexual-health-physicians

Treatment– Tecovirimat, Vaccinia Ig

Vaccinia Ig



Tecovirimat

High risk of severe disease – early treatment

Immunocompromised

- HIV (CD4<200/not on rx), leukaemia; lymphoma; malignancy; solid organ transplant; HSCT<24m OR >24m GVHDx/disease relapse; autoimmune disease with immunodeficiency
- Alkylating agents, antimetabolites, radiation, TNF inhibitors, high-dose steroids,

Children, esp. <8yo

Pregnant or breastfeeding ***

Severe disease **Haemorrhagic, confluent lesions, sepsis, encephalitis**

Other

Eyes/mouth (areas where risk of complicated skin and soft tissue infections is high).

gastroenteritis with severe nausea/vomiting, diarrhea, dehydration;

pneumonia

Management of complications associated with replication-competent vaccinia vaccination (e.g ACAM 2000)**

2.3. TPOXX Oral Dosage for Pediatric Patients Weighing at Least 13 kg and Adults

The recommended dosage of TPOXX capsules in pediatric patients weighing at least 13 kg and adults is displayed in Table 1 below.

Table 1: Recommended Dosage and Preparation Instructions for TPOXX Capsules in Pediatric Patients Weighing at Least 13 kg and Adults

Body Weight	Oral Dosage for 14 Days*	
	Dosage (Number of Capsules)	Drug Food Preparation for Patients Who Cannot Swallow Capsules
13 kg to less than 25 kg	200 mg (1 capsule) every 12 hours	Carefully open the required number of capsules and mix contents of capsule(s) of TPOXX with 30 mL of liquid (e.g., milk, chocolate milk) or soft food (e.g., apple sauce, yogurt). The entire mixture should be administered within 30 minutes of its preparation.
25 kg to less than 40 kg	400 mg (2 capsules) every 12 hours	
40 kg to less than 120 kg	600 mg (3 capsules) every 12 hours	
120 kg and above	600 mg (3 capsules) every 8 hours	

*TPOXX capsules should be taken within 30 minutes after a full meal containing moderate or high fat *[see Clinical Pharmacology (12.3)]*

preferred treatment = **Vaccinia Immunoglobulin (VIG)**

Australian Human Monkeypox Treatment Guidelines <Health.gov.au/resources/publications/monkeypox-treatment-guidelines>

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/214518s000lbl.pdf

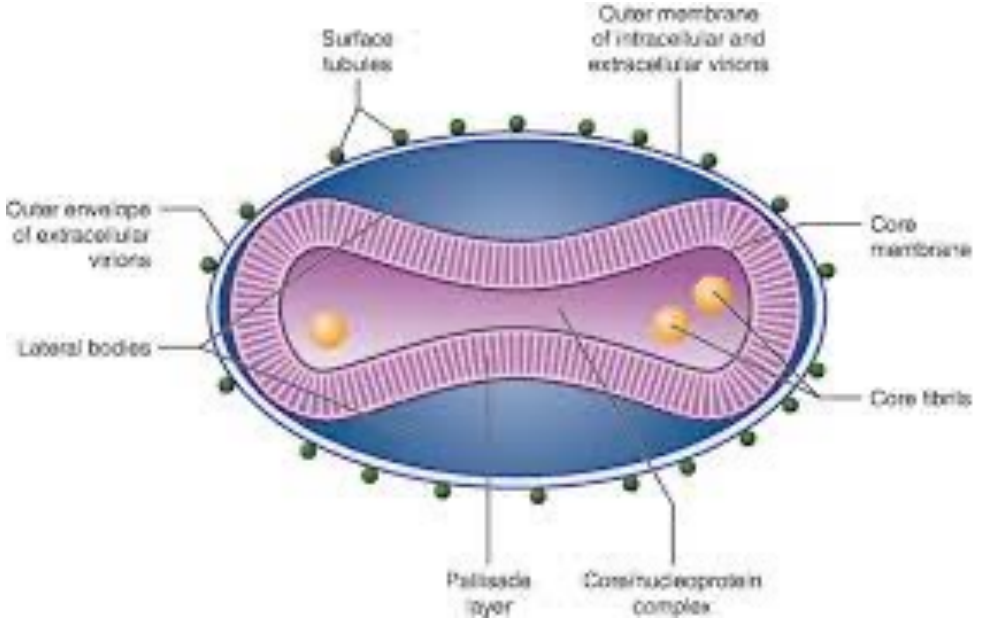
Virology

Orthopoxvirus (ds DNA virus)

same genus as variola, vaccinia, cowpox virus.

Brick-like virion from 200nm-250nm (indistinguishable from virions of variola/vaccinia viruses)

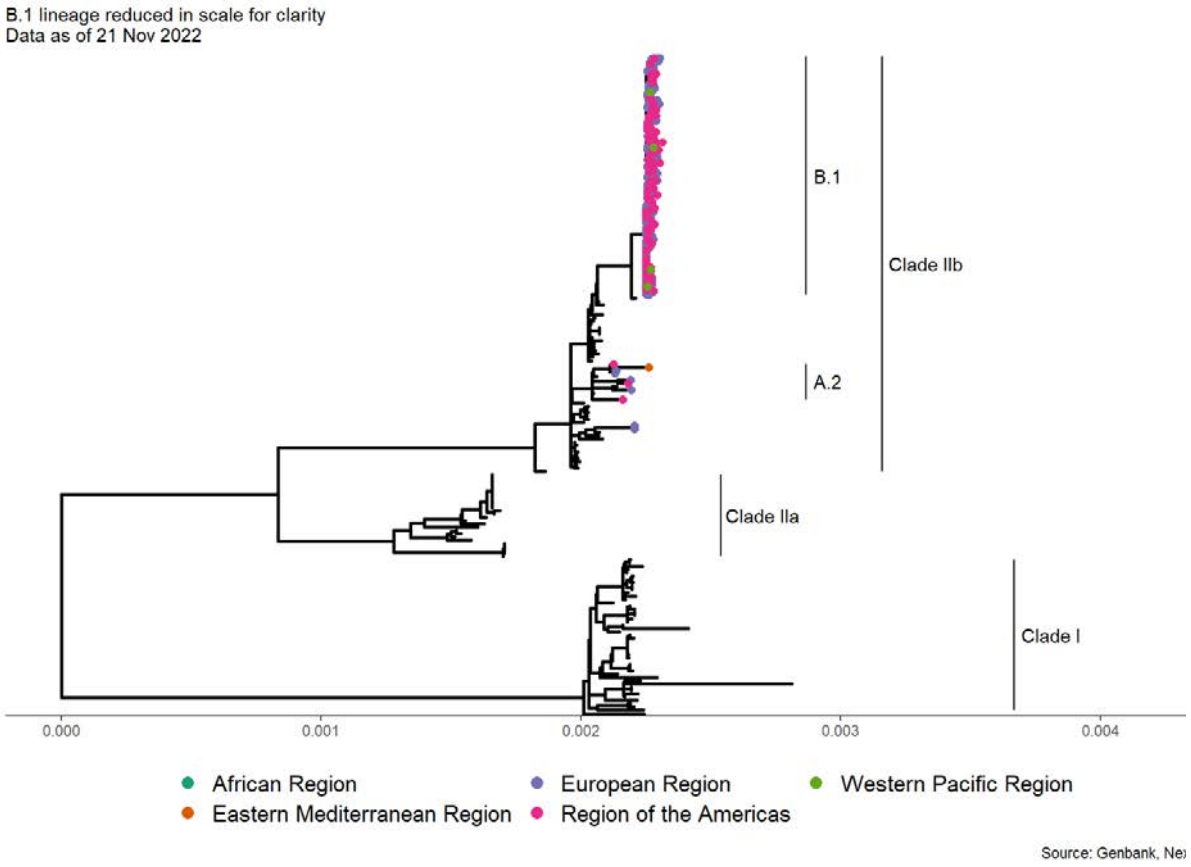
Genome large w about 200kb pairs



Genomics – WHO website

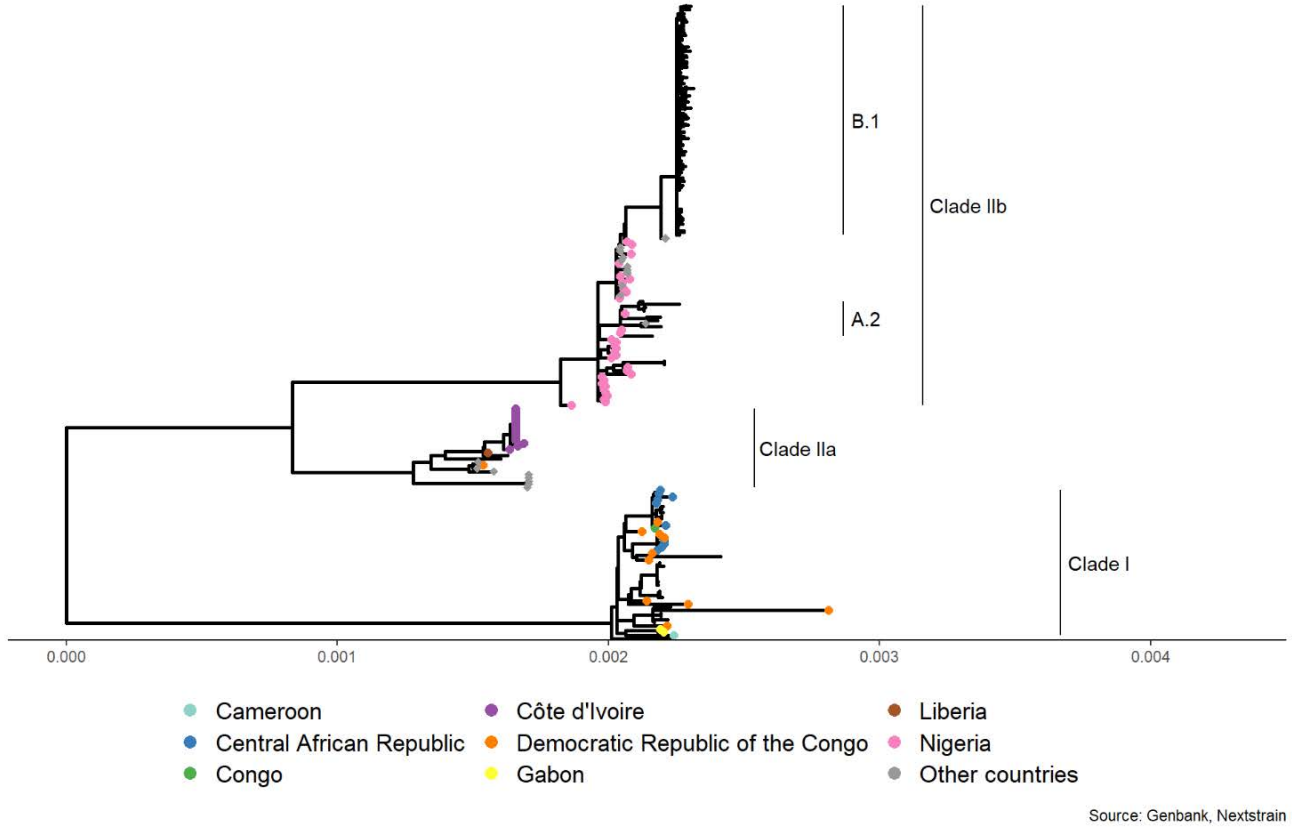
5.1. Phylogeny focused on 2022 outbreak | 5.2. Phylogeny prior to 2022 outbreak

Click on image to expand



5.1. Phylogeny focused on 2022 outbreak | 5.2. Phylogeny prior to 2022 outbreak

Click on image to expand



https://worldhealthorg.shinyapps.io/mpx_global/#5_Genomic_epidemiology