

Monkeypox pandemic update:

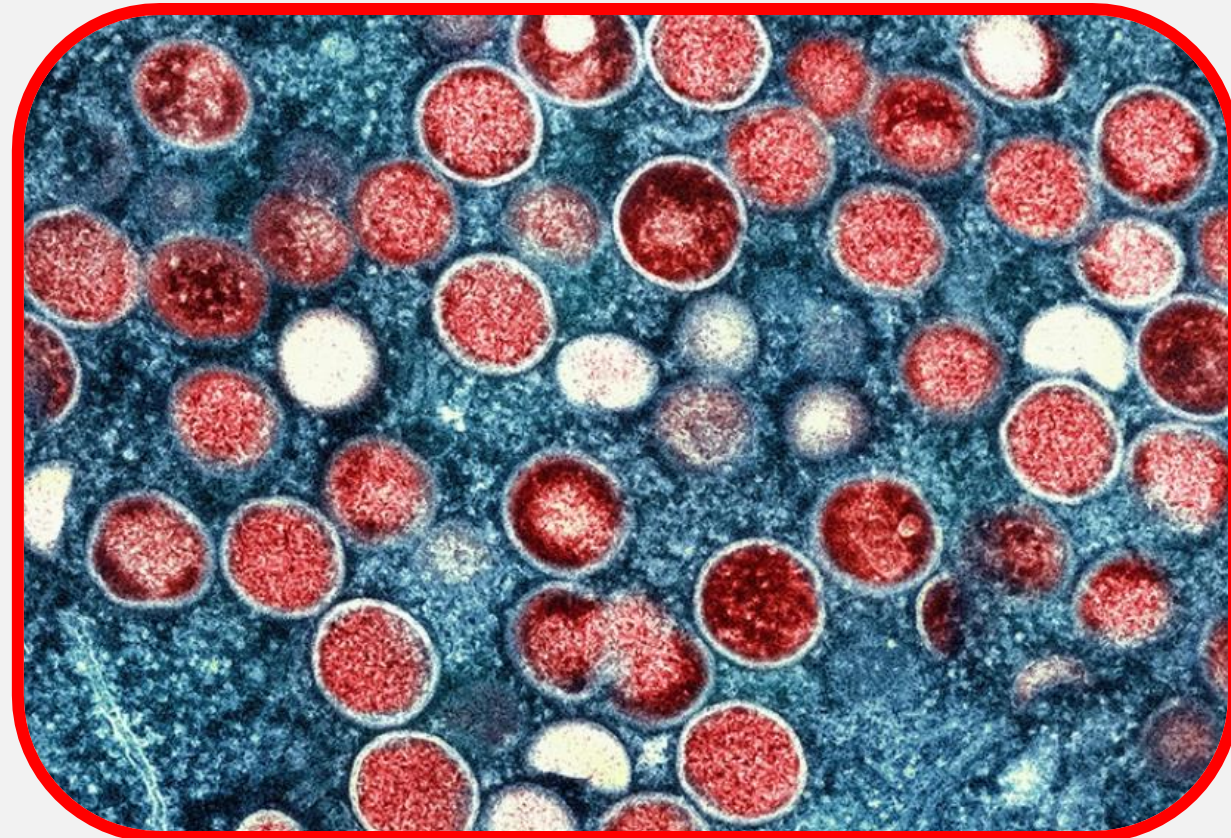
IPFA/PEI 28th International Workshop on Surveillance & Screening of Blood-borne Pathogens

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Louis M. Katz MD

**CMO (emeritus) ImpactLife Blood Services
Davenport, IA**

**Adj. Clin. Prof: Carver College of Medicine
Dept. of Medicine/Infectious Diseases
Iowa City, IA**



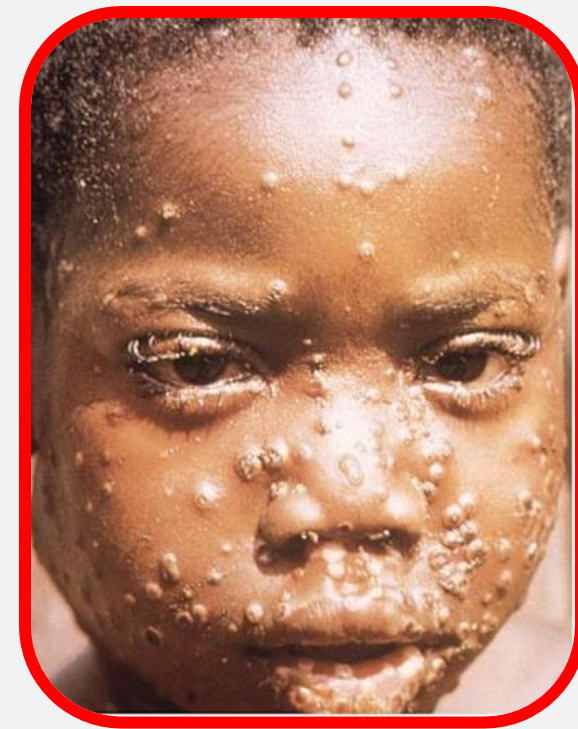
Disclosures

- **Honoraria &/or consulting agreements 2020-2022**
 - **TerumoBCT**
 - **Ortho Clinical Diagnostics**
 - **Cellphire Therapeutics**
- **None are relevant to today's topic**

“Classic” human monkeypox

An orthopoxvirus with a 197 kB DNA genome

- 1958 in non-human primates (lab outbreaks in Denmark)
- 1970 human infection in the Democratic Republic of Congo
- Now 1-2,000 cases/year in expanding endemic areas
- 2 clades: Central & West African (now I & IIa + b).
 - In animal reservoirs, so eradication unlikely *cf.* smallpox
- Animal-to-human: bites & scratches, body fluid contact & indirect from contaminated environment, bushmeat consumption
 - U.S.: 2003 (34 cases): imported rodents → prairie dogs → humans
 - Also 2 travel-associated cases in 2021.
- Human-to-human: direct contact (incl. sexual), indirect from fomites, droplets
- **High** clinical penetrance (conventional wisdom), asymptomatic not well studied



Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo

*Smallpox vaccination
was discontinued in DRC
in 1980.*

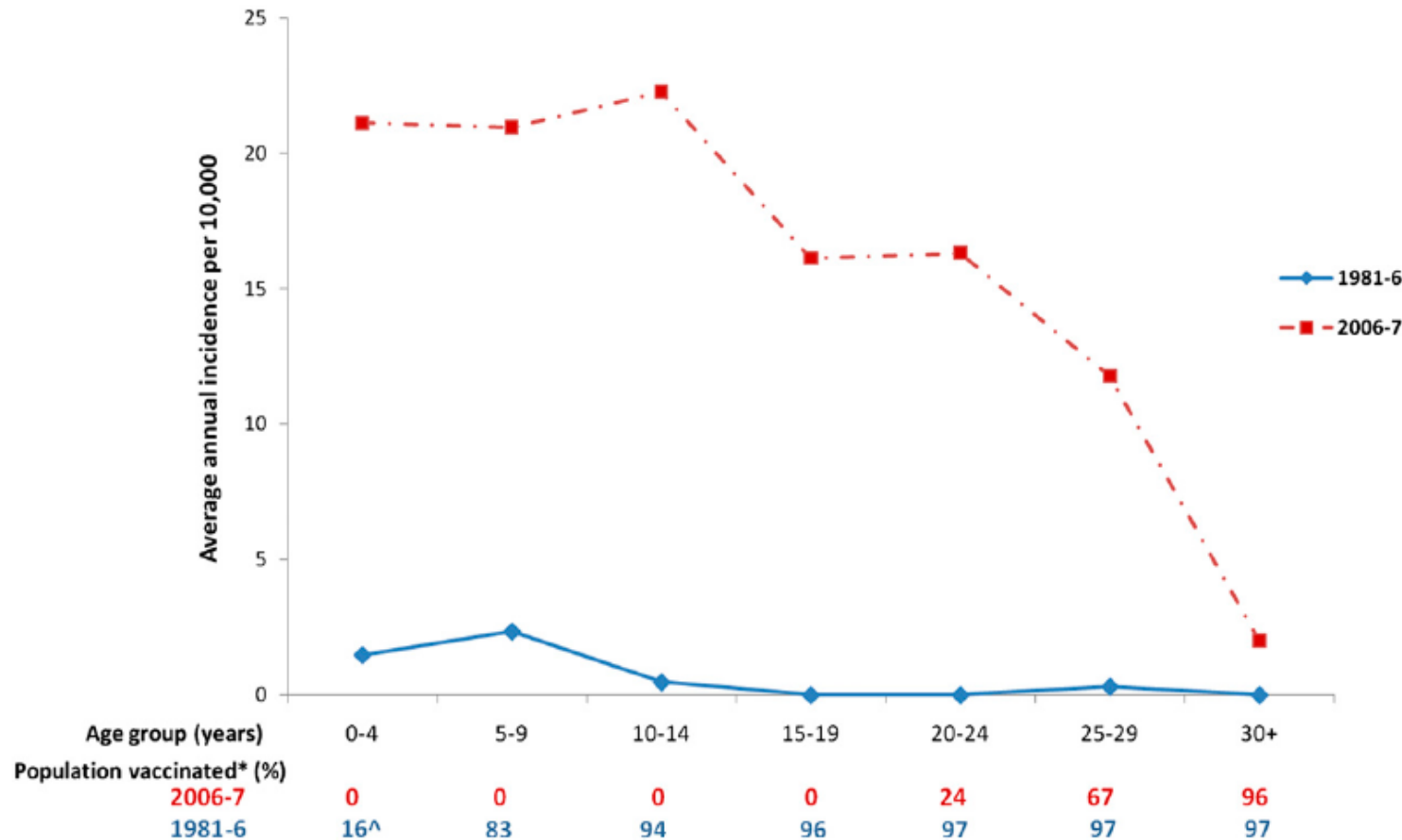


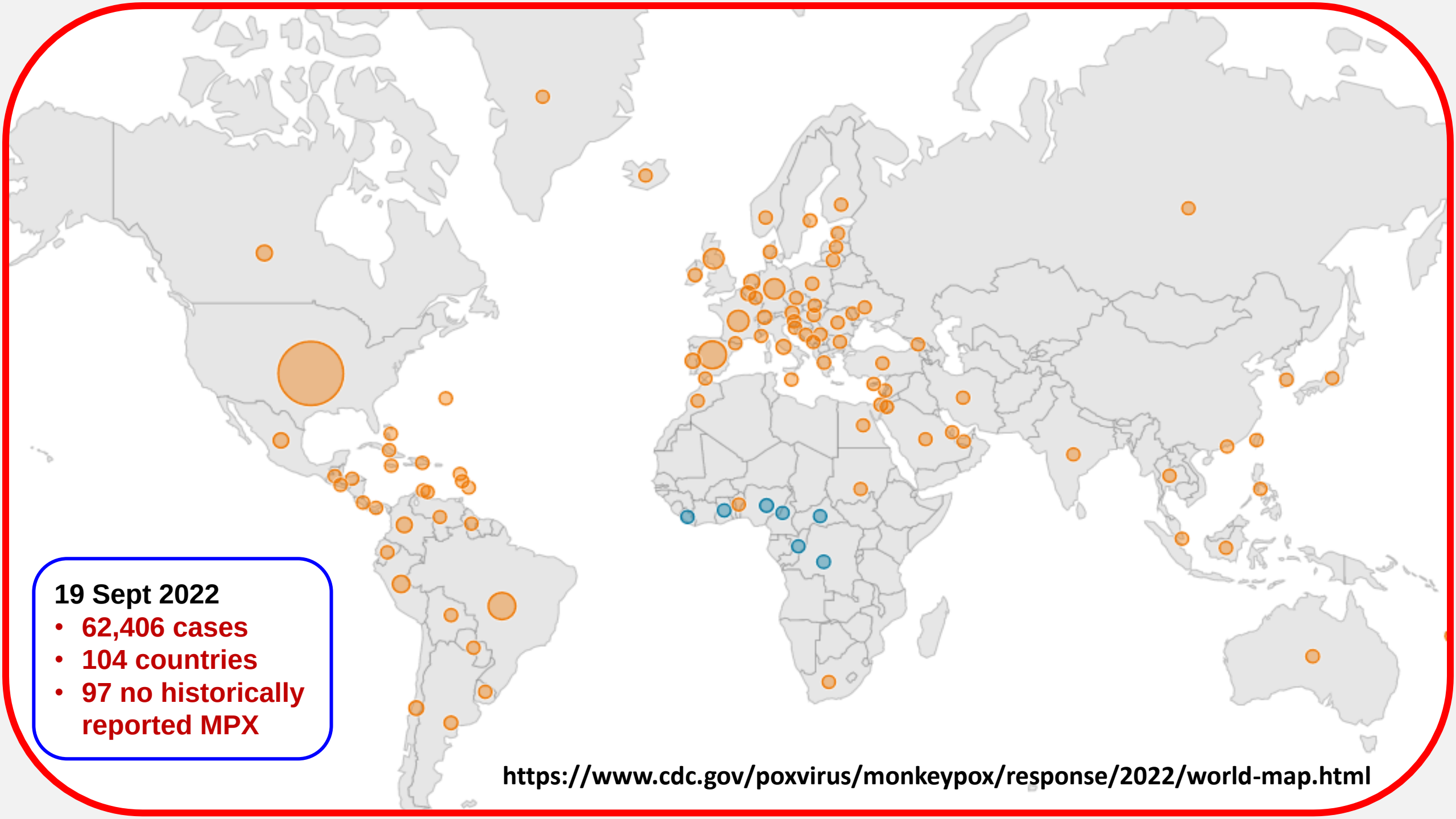
Fig. 4. Comparison of average annual cumulative incidence of human monkeypox by age group Kile Health Zone, Democratic Republic of Congo: 1981–86 vs. 2006–7. *, proportion of the population vaccinated in 2006–7 and in 1981–6 based on vaccination scar surveys in 1981–6 and in 2006. ^, vaccination rate steadily declined from 41.0% in 1981 to 4% in 1985 (13, 33).

“At the end of the smallpox eradication campaign, the Global Commission for the Certification of Smallpox Eradication concluded that continued smallpox vaccination to prevent monkeypox was not justified, despite the cross-protective immunity vaccinia vaccination provided against human monkeypox infection.”

19 Sept 2022

- 62,406 cases
- 104 countries
- 97 no historically reported MPX

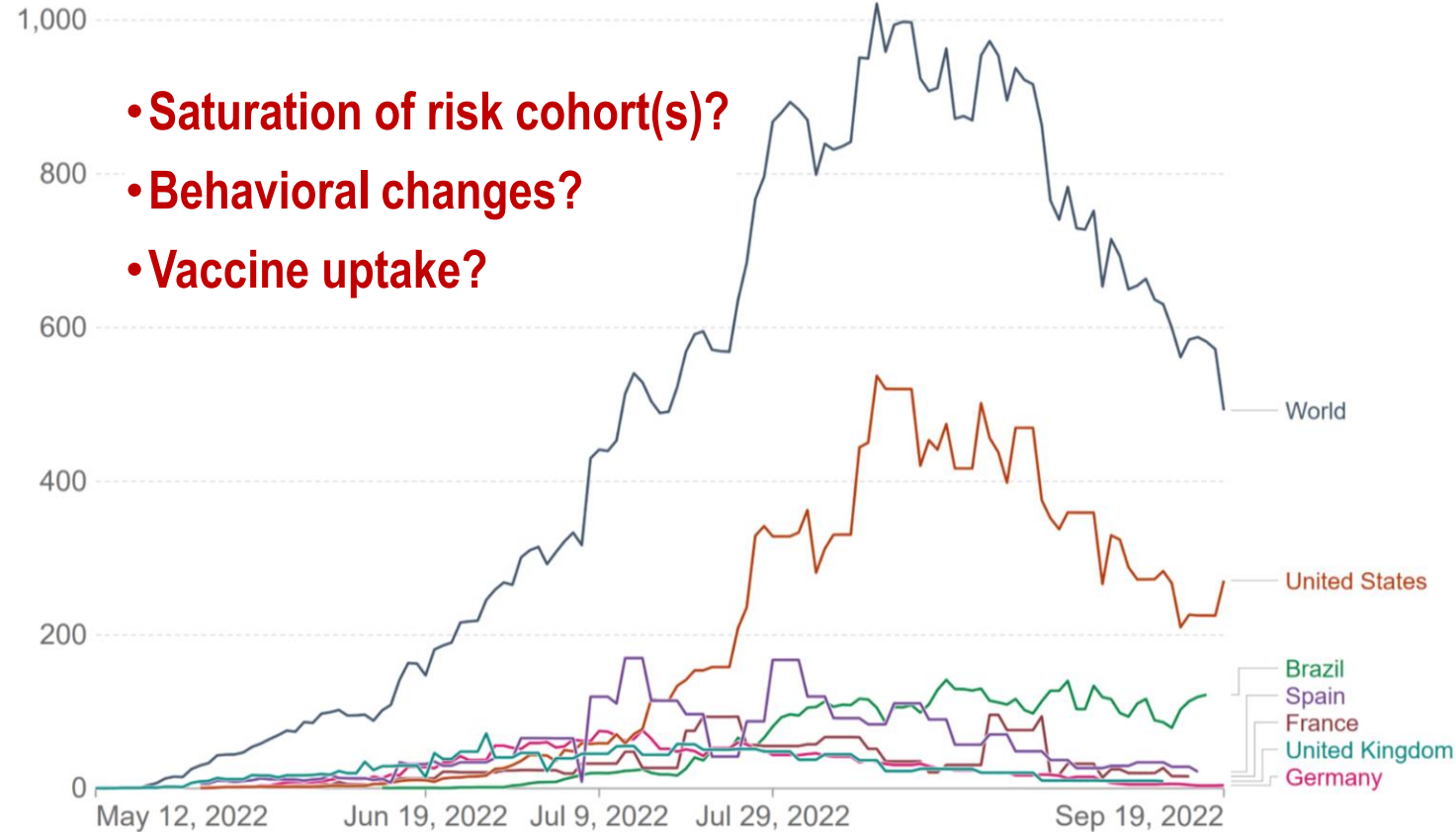
<https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html>



62,406 Cumulative cases: Global & U.S.: 19 Sept 2022

Monkeypox: Daily confirmed cases

7-day rolling average

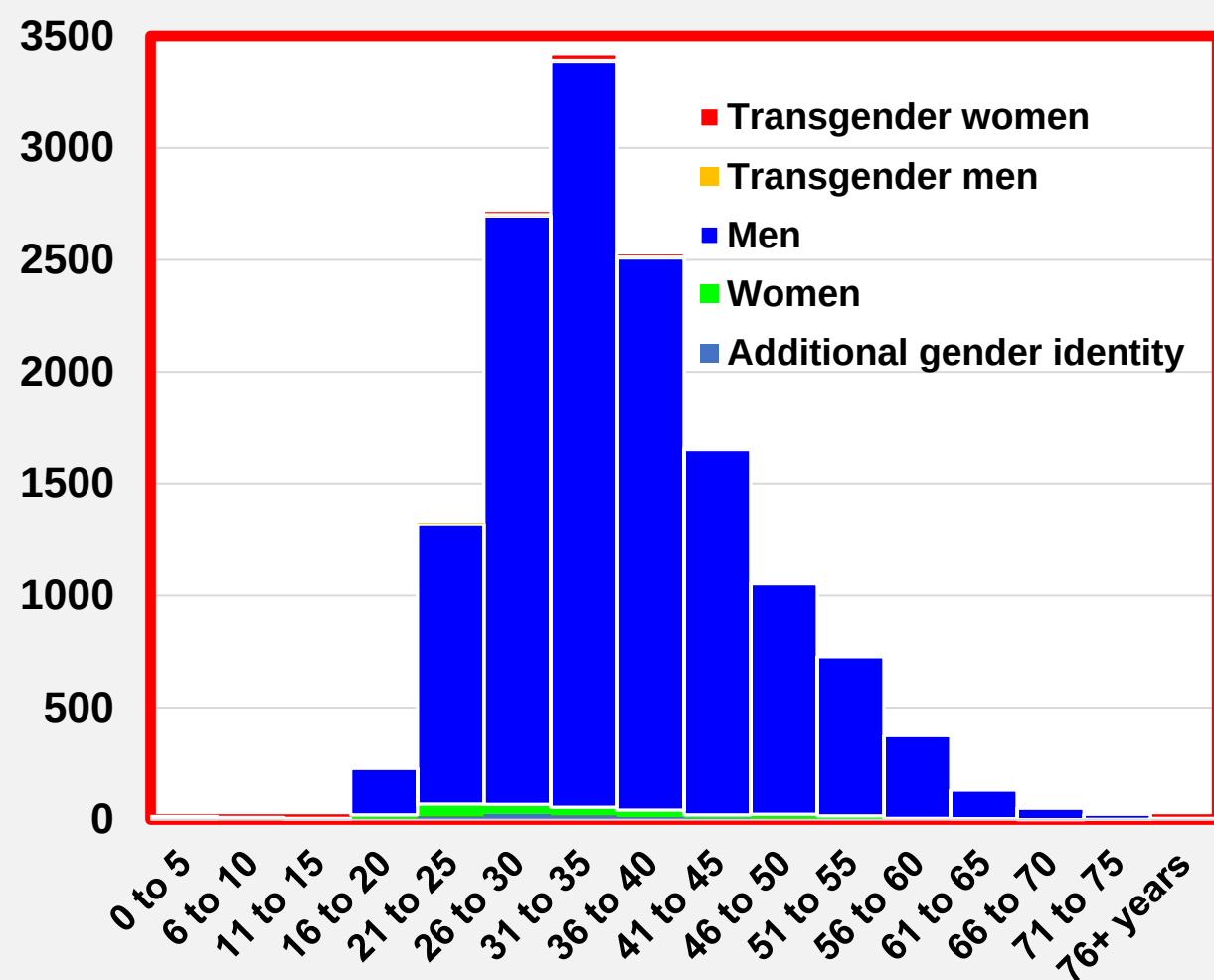


Source: Data produced by the 'Global.health' team — available at github.com/globaldothealth/monkeypox

CC BY

United States	23,893
Spain	6,947
Brazil	6,649
France	3,898
Germany	3,563
United Kingdom	3,552
California	4,656
New York	3,755
Florida	2,398
Texas	2,150
Georgia	1,702
Illinois	1,220

Characteristics of 2022 MPX cases



Gay/bisexual men who have sex with men

HIV-Positive¹

Travel History

Transmission with sex

Hospitalized²

ICU

	Yes	No	Missing
Gay/bisexual men who have sex with men	12,661 (95.0%)	663 (5.0%)	36,305
HIV-Positive ¹	5971 (45.7%)	7108 (54.3%)	36,550
Travel History	1327 (26.5%)	3690 (73.5%)	44,612
Transmission with sex	8430 (90.6%)	878 (9.4%)	40,321
Hospitalized ²	1792 (9.1%)	17,968 (90.9%)	29,869
ICU	11 (0.1%)	8536 (99.9%)	41,082

¹High rates of PrEP use in HIV uninfected MSM with monkey pox (115/172) for whom information available (CDC)

²Hospital admission may have been for isolation or medical treatment, including pain control

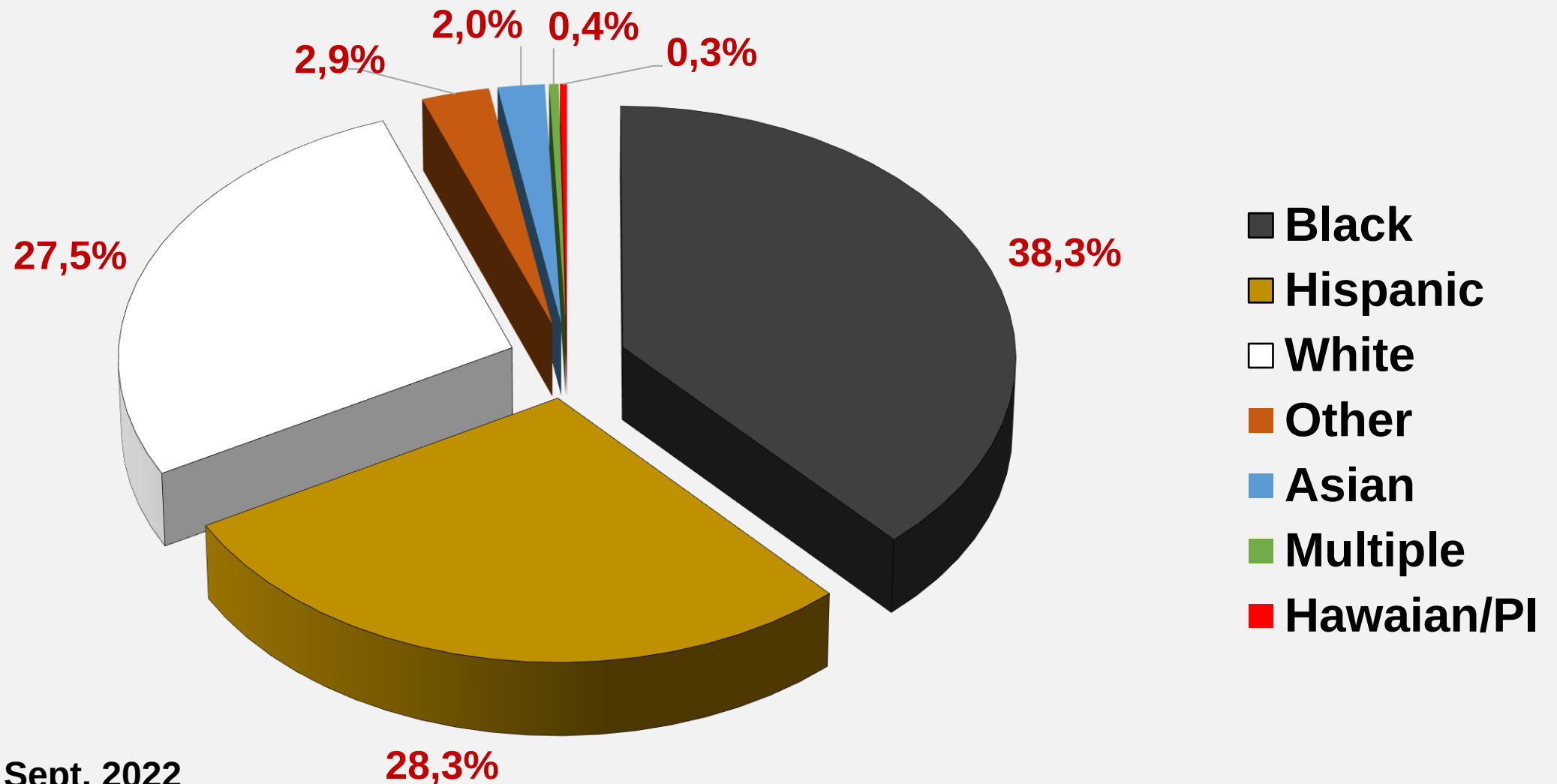
Monkeypox/HIV coinfection

- **HIV-infected patients with good viral suppression & CD4 maintenance/recovery behave like HIV-uninfected**
 - **“People living with HIV on antiretroviral therapy with suppressed viral load are not considered to be immunosuppressed.” However, people with HIV who are not virally suppressed may be at increased risk for severe illness & death from monkeypox.**

**W.H.O. Clinical management & infection prevention & control for monkeypox:
Interim rapid response guidance, 10 June 2022**

- **JYNNEOS, like other nonreplicating vaccines, should be well tolerated & safe with HIV coinfection, but data are STILL sparse**
- **No evidence of adverse interactions of TPOXX with ART or PrEP**

U.S. race/ethnicity: progressive increase among persons of color since May 2022



Monkeypox

- **Febrile prodrome (≈2 days)**
 - May be less common in 2022 epidemic
- **Macule → papule → vesicle → umbilicated vesicle → crust → detachment**
- **Mucosal involvement occurs (oral, rectal): very painful**
- **Pediatric, immunocompromised, pregnant especially at risk for badness**
 - Pneumonia
 - Brain infection (encephalitis)
 - Corneal infection (keratitis)
 - Secondary bacterial infections
 - Adverse pregnancy outcomes
- **Mortality historically from 1-10% (clades II & I respectively)**
 - 2022 outbreak mortality much lower than this: 5 deaths among 42,567 cases in non-endemic countries through 23 Aug. 2022
- **Multiple mutations in 2022 strain (what do these mean?)**

Stages of monkeypox rash



Macules: flat lesions starting where contact with the virus occurred for 1-2 days

Papules: slightly raised lesions for 1-2 days

Vesicles: clear fluid-filled raised lesions for 1-2 days

Pustules: cloudy/opaque fluid filled lesions for 5-7 days

Crusts: may leave scars, pits, & areas without skin pigment after the scabs separate & fall off

Signs & symptoms 2022: U.S.

During illness* (N = 1,007)

Sign/symptom	Yes(No. & %)	No
Rash	1,004 (100.0)	0
Fever	596 (63.3)	345 (36.7)
Chills	550 (59.1)	381 (40.9)
Swollen glands	545 (58.5)	387 (41.5)
Malaise	531 (57.1)	399 (42.9)
Muscle aches	507 (55.0)	415 (45.0)
Headache	469 (50.8)	454 (49.2)
Rectal pain	201 (21.9)	715 (78.1)
Pus/blood in stools	184 (20.5)	713 (79.5)
Abdominal pain	96 (11.5)	742 (88.5)
Rectal bleeding	90 (10.0)	810 (90.0)
Tenesmus	90 (10.0)	809 (90.0)
Nausea/vomiting	83 (9.2)	817 (90.8)

At onset of illness (N = 461)

	Yes	No
	121 (41.6)	170 (58.4)
	120 (41.2)	171 (58.8)
	48 (16.5)	243 (83.5)
	23 (7.9)	268 (92.1)
	24 (8.2)	267 (91.8)
	13 (4.5)	278 (95.5)
	27 (9.3)	264 (90.7)
	0 (0.0)	291 (100)
	0 (0.0)	291 (100)
	1 (0.3)	290 (99.7)
	0 (0.0)	291 (100)
	2 (0.7)	289 (99.3)
	0 (0.0)	291 (100)

*Percents are calculated without missing data

After CDC. *MMWR*. 2022

Monkeypox prevention, treatment & control

- **Vaccination**

- High-risk & exposed prophylaxis with JYNNEOS “smallpox & monkeypox vaccine, live, non-replicating” pre- & up to 14 days post-exposure. Well tolerated
- ACAM-2000. Replication competent live vaccinia if above cannot be used?
 - Associated with myo-pericarditis & many contraindications

- **Behavioral adjustments**

- **Vaccinia immune globulin (passive antibodies) available for treatment**

- **Tecovirimat for severe infection or high risk of progression to severe**

- Protected NHP from fatal monkeypox virus infection
- EUA for use during the current outbreak
 - U.S. RCT planned to start enrollment in Sept.
- Cidofovir or brincidofovir
- Trifluorothymidine or vidarabine drops for ocular complications

- **Isolation & quarantine**

**Pain
Control**

TPOXX (tecovirimat)

- ACT-UP *et al* & HIV—need for rapid access leads to EUA regs
- FDA-approved for treatment of (closely related, lethal) smallpox for efficacy demonstrated under the “animal rule” using non-human primates for monkeypox & rabbits for rabbitpox
 - Smallpox (eradicated in nature) was a life-threatening illness. Definitive trials were unethical & infeasible cf. monkeypox
- Safety was evaluated in healthy human volunteers at relevant doses & durations
- RCTs in planning for Central Africa (clade I) before current epidemic may not be directly applicable
- ACTG RCT trials to start in Sept. for U.S. clade IIb infections
- Expanded access availability in CDC-held emergency IND



Impact of monkeypox on select behaviors?

- **GBMSM in U.S. are taking steps to protect themselves & their partners from monkeypox**

Online survey Aug. 8-15

2022 Monkeypox Supplemental Survey.

<https://emoryamis.org/>



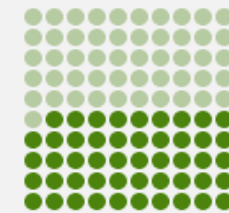
48%

Reduced number of sex partners



50%

Reduced one-time sexual encounters



49%

Fewer partners from dating apps/sex venues

Monkeypox & transfusion?

- **No reported or alleged transfusion transmission**
- **“DNA-emia”, as viremia proxy, in a proportion of human infections**
 - Little data on presence of infectious virus in humans (that available is negative)
 - Virtually no data on presymptomatic viremia/DNA-emia
- **IV transmission & infectious viremia documented in NHP & other animal models**
- **2003 outbreak in US (34 confirmed cases)**
 - No *mandated* donor interventions
 - CBER: no recommendations except deferral for recent smallpox vaccination (which was/is recommended for monkeypox exposure)
- **Donors must be well & the skin of the donation site must be inspected & intact**
 - No validated donor history questions or education materials
 - No screening assays suitable for donors, but NAT companies are engaged

Parker S & Butler RM. *Future Virol.* 2013.

Adler H et al. *Lancet ID.* 2022.

Johnson RF et al. *J. Virol.* 2011.

Noe S et al. *Research Square.* 2022. DOI: <https://doi.org/10.21203/rs.3.rs-1725831/v1>

Infectivity of I.V. inoculation with cell culture-derived virus

Intravenous *Macaca fascicularis* challenges with Congo Basin strain (Zaire 79)

Dose	Fever onset (duration)	Weight loss (%)	Lesion onset (maximum lesion count)	Mortality/ euthanasia (days of death)	Blood vDNA detected [†] (duration of detection)	Infectious virus from swabs (duration of detection)	Ref.
10 ⁷	Day 3	4–10	Day 3–6 (>1000)	2/6 (by day 18)	Day 6 (to day 27)		[23]
10 ⁷		2–6	Day 5–6 (>2500)	4/4 (5, 7, 7, 7)	Day 5–7 (to day 7)		[48]
10 ⁶		4–8	Day 6 (>1200)	4/6 (12, 12, 12, 14)	Day 6–9 (to day 14)		[48]
10 ⁷	Day 3 (to day 7)	1–10	(>250)	8/8 (by day 9)		Throat from day 2–6 Blood from day 5	[102]
10 ⁷		6–11	Day 4 (>1000)	4/6 (9, 9, 11, 14)	Day 4 (to day 28)		[103]
10 ⁷			Day 3–4 (>1500)	3/3 (11, 12, 13)	Day 4 (to day 13)		[104]
10 ⁷			Day 5–8 (>1400)	3/3 (9, 13, 13)	Day 4 (to day 12)		[105]
10 ⁷	Day 3 (to day 9)	7–10	By day 6 (>750)	3/4 by day 15	Day 4 (to day 15)		[106]
10 ⁷			By day 6 (TNTC)	5/5 (11, 11, 11, 13, 15)	Day 4 (to day 15)		[107]
10 ⁷	Day 3 (to day 12)	>4	Day 6 (>200)	3/3 (9, 11, 15)	Day 3 (to day 15)		[49]

TNTC: Too numerous to count; vDNA: Viral DNA.

[†] Does not include detection at day 0 following intravenous challenge.

Other critters: various routes & doses

- Chimps
- Baboons
- Capuchins
- Spider monkeys
- Prairie dogs
- Squirrels
- Mice
- Guinea pigs
- Rats
- Opossums

Are you well & healthy today?

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

- GBMSM GC/CT samples with no MPX symptoms screened with PCR

- 4/224 positives

De Baestelie I et al. *Nat. Med.* 2022

Annals of Internal Medicine

LETTERS

OBSERVATIONS: BRIEF RESEARCH REPORTS

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

MPXV-specific PCR was performed using a previously published protocol (4).

During the study period, 706 MSM visited our clinic, 383 had symptoms suggestive of MPXV infection (40% had anal lesions), and MPXV infection was confirmed in 271 of those with symptoms (Table). Screening for *C trachomatis* and *N gonorrhoeae* infection was not performed when MPXV infection was suspected because of laboratory biosafety restrictions (5). Of the 706 MSM, 323 had

- GC/CT samples MPX symptom-free GBMSM screened with PCR

- 13/200 positives

Ferre VM et al. *Ann. Int Med.* 2022

EID fact sheet

- The need for specific interventions to minimize a theoretical risk of transfusion transmission of MPXV during the unique 2022 epidemic is undetermined.
- Donors must be **well on the day of donation**, undergo a limited skin examination, & have their temperature taken in the donor room.
- **In the US, MSM are specifically deferred for three months** after the most recent such contact to reduce the risk of collecting donations from recently HIV-infected donors. This interval is believed to be well beyond the duration of a putative MPXV infectious viremia & high adherence to this donor criterion effectively mitigates any risk where donors continue to be deferred for MSM activity*
- **In much of the world, the MSM deferral has been discarded & replaced by individual donor risk assessments.** These recognize the importance of behaviors, as opposed to sexual preference, in disease transmission risk, e.g., multiple recent & new sex partners & traumatic sexual practices. In the context of the current epidemiology of the outbreak, overwhelmingly affecting MSM, it may be necessary in such venues to add specific inquiries regarding potential exposures to MPXV, as has been recommended by the European Centers for Disease Control.

*And for receipt of PrEP

https://www.aabb.org/docs/default-source/default-document-library/regulatory/interim-monkeypox-virus-fact-sheet.pdf?sfvrsn=6dbca696_4

Whither monkeypox—discussion points for TTD

- At this stage of the U.S. outbreak, are specific measures necessary to prevent phlebotomy of infected donors e.g., written materials, direct questioning, enhanced examination, donor testing?
 - For donors of SOHO the ECDC recommends that...
“...potential donors should be carefully interviewed regarding contacts with infected (confirmed or suspected) MPX cases, infected animals or travels to affected areas....”
- (At least) 21-days deferral if donor volunteers contact with monkeypox?
- Deferral of infected until all lesions healed (reepithelialized)?
- Consignee notification of prior donations from infected &/or contacts & advice to hospitals on how to respond?

TTD to monitor the evolving epidemic & update membership PRN

Big questions—the science agenda at NIAID

- Are all infections symptomatic?
- Viral kinetics & duration of infectivity?
- Attack rates in contacts?
- Immunological correlates of protection?
- Is immunity after infection permanent, like for smallpox?
- How long does vaccine immunity last?
- How much does vaccine modify disease at ≤ 4 days or > 4 days?
- ID vs. SC vaccines?
- Characterize infection in patients with immune compromise?
- What is/are the animal reservoir/s?
- Antiviral & vaccine clinical research (including in Africa)?

Thanks for the invite
lkatz@mvrbc.org

