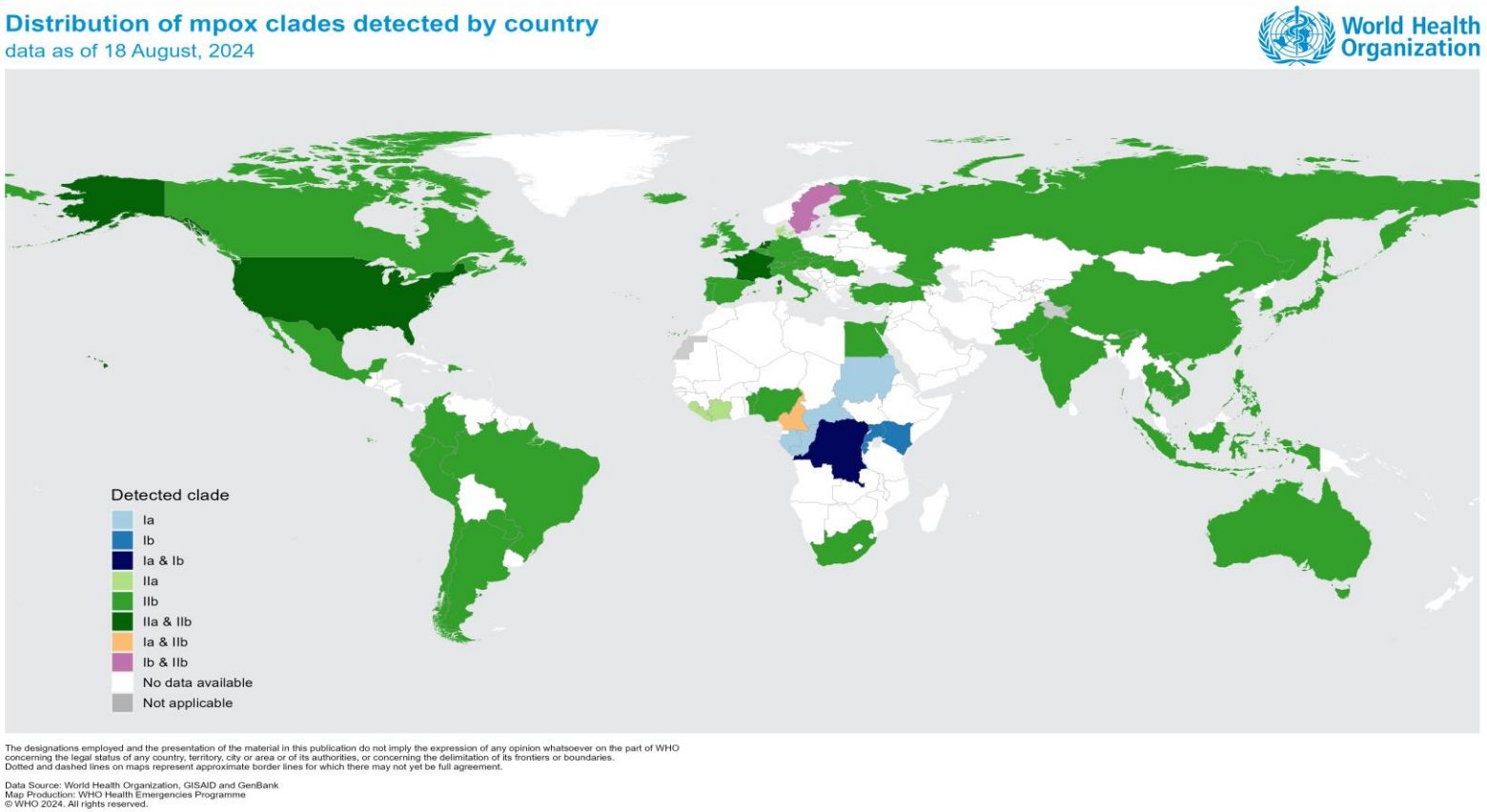
Overview of clinical characteristics of various MPXV clades

Lorenzo Subissi, PhD

WHO Mpox IMST

29 August 2024

Global MPXV (sub)clade distribution



Except Cameroon (clade Ia and IIb), no country has known co-circulation of clade I and II in the community

- Currently at risk: Thailand, Sweden

Mpox clinical presentation

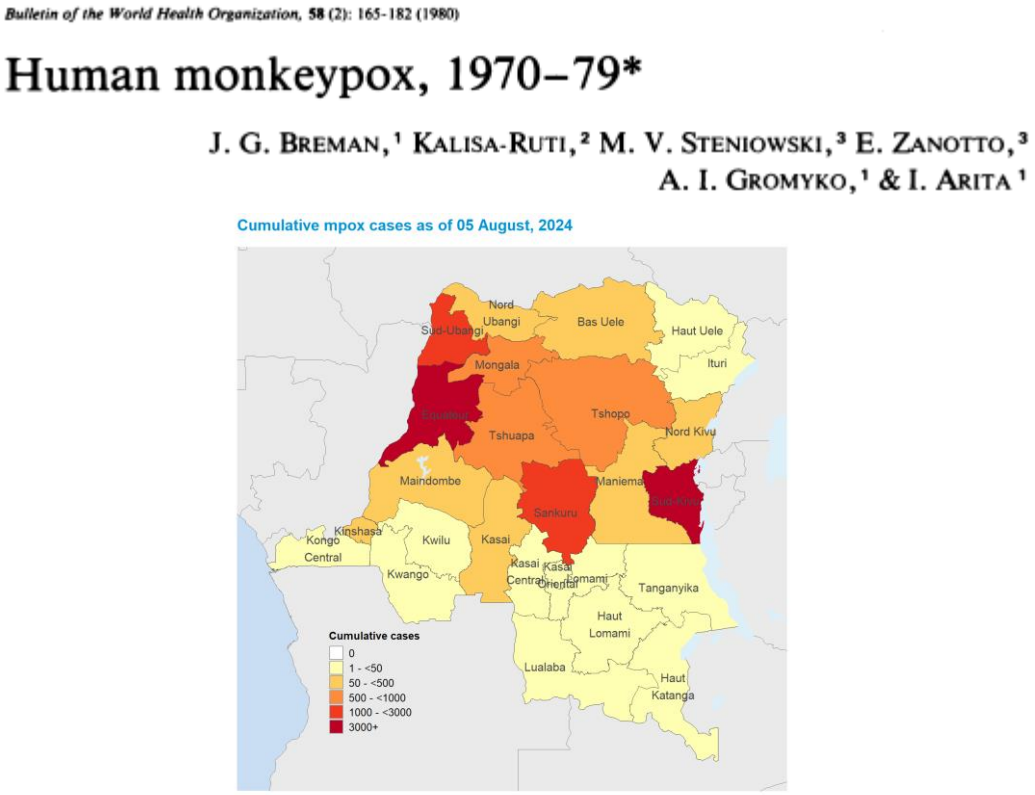
Main factors influencing clinical presentation:

- route of exposure
- infectious dose
- host immune response
- clade

Ogoina et al 2023 10.1016/j.cmi.2023.09.004

Clade Ia characteristics from epi/clinical studies

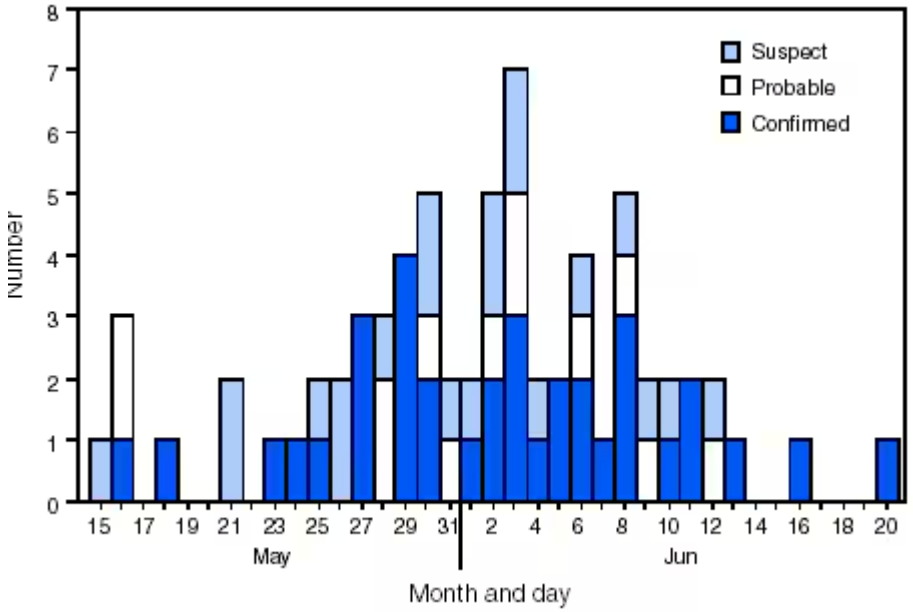
- Study period: 1970-2024 (suspected and confirmed cases in the DRC)
- Mode of transmission : zoonotic (60-75%, Mixed-animal contact and bush meat consumption) human to human (40-35% household non-sexual contact)
- Incubation period 12 days (range 7-31 days)
- >90% children <15y/o
- Hospitalisation rate unclear
- 0.6% of people living with HIV in one study (1998)
- Primary rash site: Face (82%)
- Largely centrifugal distribution, same stage evolution, separate lesions, 51% > 100 lesions
- Lymphadenopathy 80% (usually submaxillary and cervical)
- Febrile prodrome: 80%
- 25%—genital rash
- Anorectal lesions not reported
- Mortality 5-10.%; mostly among children; Mortality in the PALM-007 trial (optimal care); 1.7%



Jezek et al 1987 doi 10.1093/infdis/156.2.293; Bunge et al 2022 10.1371/journal.pntd.0010141; Ogoina et al 2023 10.1016/j.cmi.2023.09.004; Whitehouse et al 2021 10.1093/INFDIS/JIAB133; Breman et al 1980 PMID: 6249508

Clade IIa characteristics from epi/clinical studies

- No evidence from endemic areas available
- Data from 79 cases (35 lab confirmed) from the 2003 US outbreak
- 100% of the transmission was zoonotic, linked to prairie dogs (imported from Ghana)
- Incubation period 12 days (range 1-31)
- Median age 28 years (range 1-51); 70% adults, 50% males
- 26% admitted in the hospital
- HIV status not reported
- Primary rash related to site of animal contact
- Largely centrifugal distribution, same stage evolution, separate lesions. 20% > 100 lesions
- Lymphadenopathy 69% (56% cervical)
- Febrile prodome: 73%
- No deaths



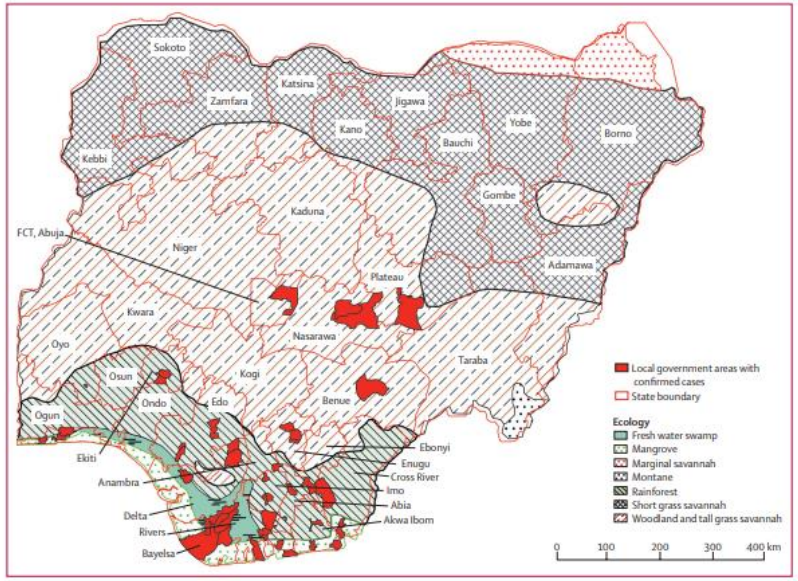
Epi curve of the clade IIa US outbreak in 2003

•Ogoina et al 2023 10.1016/j.cmi.2023.09.004; Huhn et al 2005 10.1086/498115 CDC MMWR 2003 PMID: 12855947

Clade IIb characteristics from epi/clinical studies

Evidence from Nigeria (lineage A, zoonotic transmission also involved)

- Evidence from 2017-2019 (confirmed/probable cases)
- Transmission mode unknown (61.8%), human-to-human (30%) suspected zoonotic (8.2%)
- Incubation period 9.5 days (range 3-34)
- Median age 29 years (range 0-50); 80% adults, 70% males
- 20% of hospitalized patients were people living with HIV
- Mixed picture—65% centrifugal distribution, 52.5% separate lesions, 62.5% regional monomorphism, 60% > 100 lesions
- Lymphadenopathy 69% (50% inguinal, 50% cervical)
- Febrile prodrome: 57%
- 68%—genital rash
- Mortality 3-5% mostly among young adults with advanced HIV

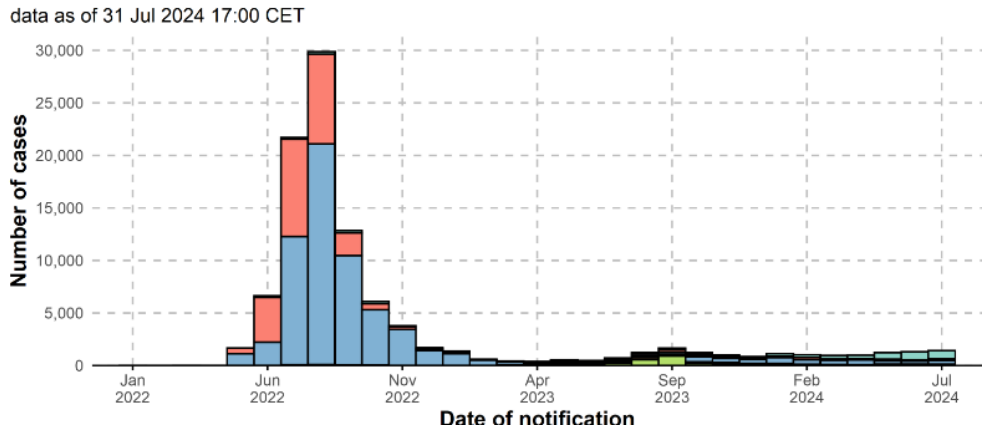


Yinka-Ogunleye et al 2019 10.1016/S1473-3099(19)30294-4; Ogoina et al 2023 10.1016/j.cmi.2023.09.004 Ogoina et al 2020 10.1093/cid/ciaa143

Clade IIb characteristics from epi/clinical studies

Evidence from the global outbreak (lineage B.1, only human to human transmission reported)

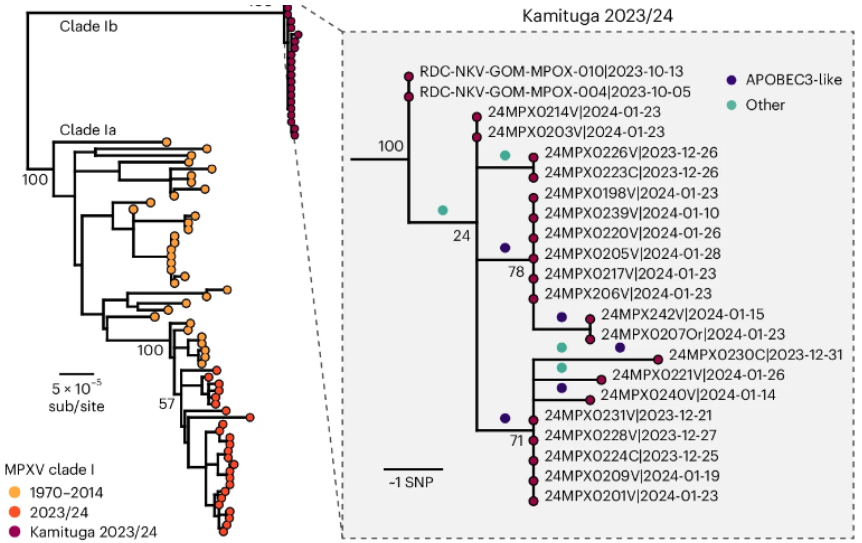
- Evidence from 2022-2023
- Sexual transmission
- Incubation period 7 days (range 3-20)
- Median age 35 y (range 15-58);>99% adults, >98% males
- 42-48% people living with HIV
- 7-11% of patients hospitalised
- Primary rash site: Anogenital (70–87%)
- Localized to anogenital area. Largely pleomorphic. 64% < 10 lesions
- Lymphadenopathy: 53% (47% inguinal)
- Febrile prodrome: 42-57%
- Mortality 0.19%, mostly among adult GBMSM with unsuppressed and advanced HIV infection



Thornhill et al 2022 10.1056/NEJMOA2207323; Ogoina et al 2023 10.1016/j.cmi.2023.09.004 Okoli et al 2024 10.1007/s15010-023-02133-5; Liu et al 2023 10.3390/pathogens12010146; Laurenson-Shafer et al 2022 10.1016/S2214-109X(23)00198-5; https://worldhealthorg.shinyapps.io/mpx_global/#2_Situation_in_Africa

Clade Ib characteristics from emerging epi/clinical studies

- Study period 2023-2024, Kamituga, DRC (mining area with a lot of movement)
- Data from 139 cases in total from two studies
- Transmission mode: close contact, including sexual contact (29% female sex workers)
- Median age 22 years (IQR 18-27); 52% female, 15% children < 15 years;
- 91% hospitalized for isolation purposes, 10% bedridden
- Of those whose HIV status was known, only 7% of cases living with HIV
- 85% patients had genital lesions in one study, 63% had anogenital lesions in the other study
- 61% cases sexually active with more than one partner within the last six months
- Mortality in one study 1.4% (with latest surveillance data 0.7%)
- A lot we still do not know!



Vakaniaki et al 2024 10.1038/s41591-024-03130-3; Masirika et al 2024 10.1101/2024.03.05.24303395

Newly affected countries with Clade Ib

July - August 2024

Country	# confirmed cases	Distribution
Burundi	258	Dispersed in the country
Rwanda	4	3 in capital; 1 in border district
Uganda	4	Multiple districts
Kenya	2	PoE with Tanzania
Sweden	1	Travel history to Africa
Thailand	1	Travel history to Africa

No deaths have been reported so far by any of the countries

What we are learning

- **Spreading in the DRC** since September 2023, in absence of zoonotic exposure.
- **Sexual contact** has amplified the transmission quickly in certain networks and areas.
- **Unclear driver of transmission** in children **(**50% of children <15 affected in Burundi): behavioral?
- **Functional characterization** of clade Ib in the lab needed

Summary of differences across (sub)clades

Characteristics	Clade Ia	Clade IIa	Clade IIb (lineage A)	Clade IIb (lineage B.1)	Clade Ib	Relevant comparison
transmission	Z (60-75%), H2H (40-35%); recent estimate?	100% zoonotic	10% zoonotic, 30% H2H, 60% unknown	99% H2H	99% H2H?	Clade Ia and IIa mainly Z
Age and sex	90% <15y	70% adults	80% adults, 70% males	>99% adults; >98% males	85% adults in DRC; 50% in Burundi	Sexual transmission described for clade Ib and IIb
Primary site of lesions	Face	Site of animal contact	N/A	Anogenital (70-87%)	40% oral, 60-85% genital	Linked to mode of transmission
Distribution and number of lesions; 51% > 100	Mostly centrifugal	Mostly centrifugal	Mixed (65% centrifugal)	Localised (anogenital)	Mixed	Data on Clade Ib still emerging
HIV	0.6% (1998)	N/A	22%	42-48%	7%?	Association with HIV seems less relevant for clade I?
Lymphadenopathy	80% (submaxillary, cervical)	70% (50% cervical)	70% (50% cervical, 50% inguinal	50% (50 % inguinal)	42% (site unknown)	Decreasing in newly emerging (sub)clades
Febrile prodrome	80%	73%	57%	42-57%	60% fever	Highest for clade Ia
Mortality	5-10%	0%	3-5%	0.19%	0.7%	Lower for clade Ib?

Conclusions

- Clade Ib data is still emerging, and it remains unclear whether data from Africa will be generalizable to other settings (due to behavioural/cultural differences)

- Comparing results from observational studies in different countries with different designs, objectives, standard of care, etc makes it very challenging to make firm conclusions; important to complement epi/clinical studies with evidence on virological characteristics from lab studies

Thank you