Brief Review of Clade I Mpox : Clinical presentation, Diagnosis and Management

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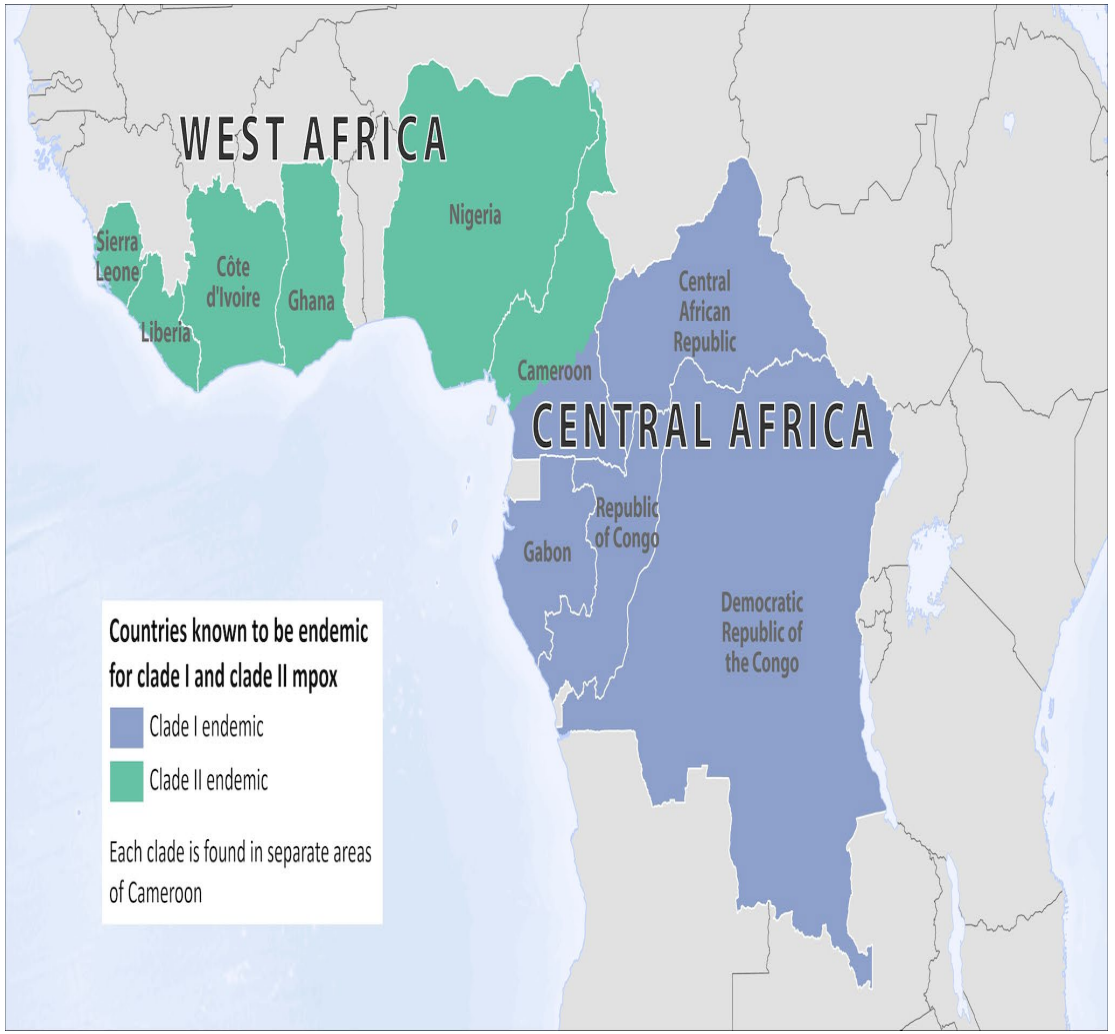
Epidemiology – Distribution of mpox clades

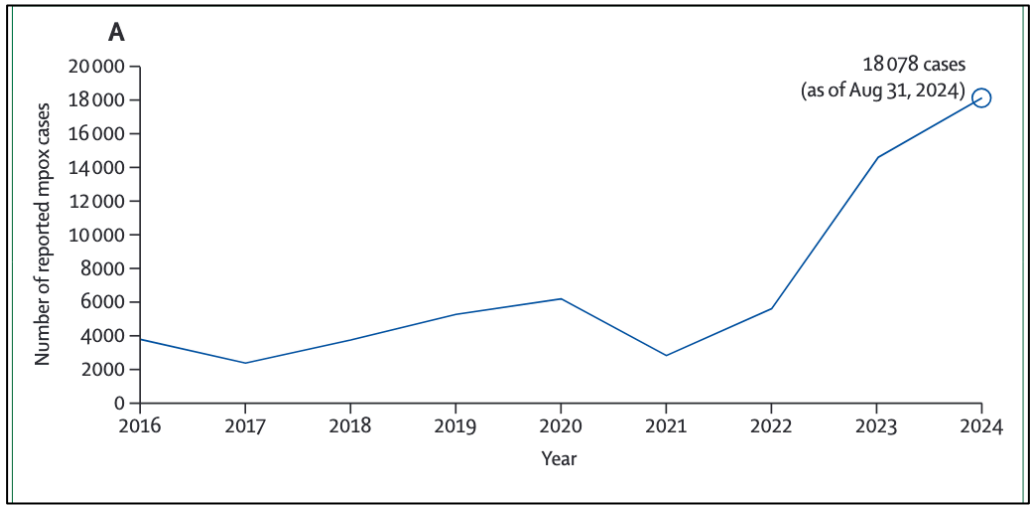
- There are two major clades of Mpox.
- Clade II (a &b) circulates primarily in W. Africa and Clade I (a & b) circulates in Central Africa.
- 2022 global outbreak was caused by clade IIb
- Ongoing outbreaks in Africa caused by clade Ia and Ib

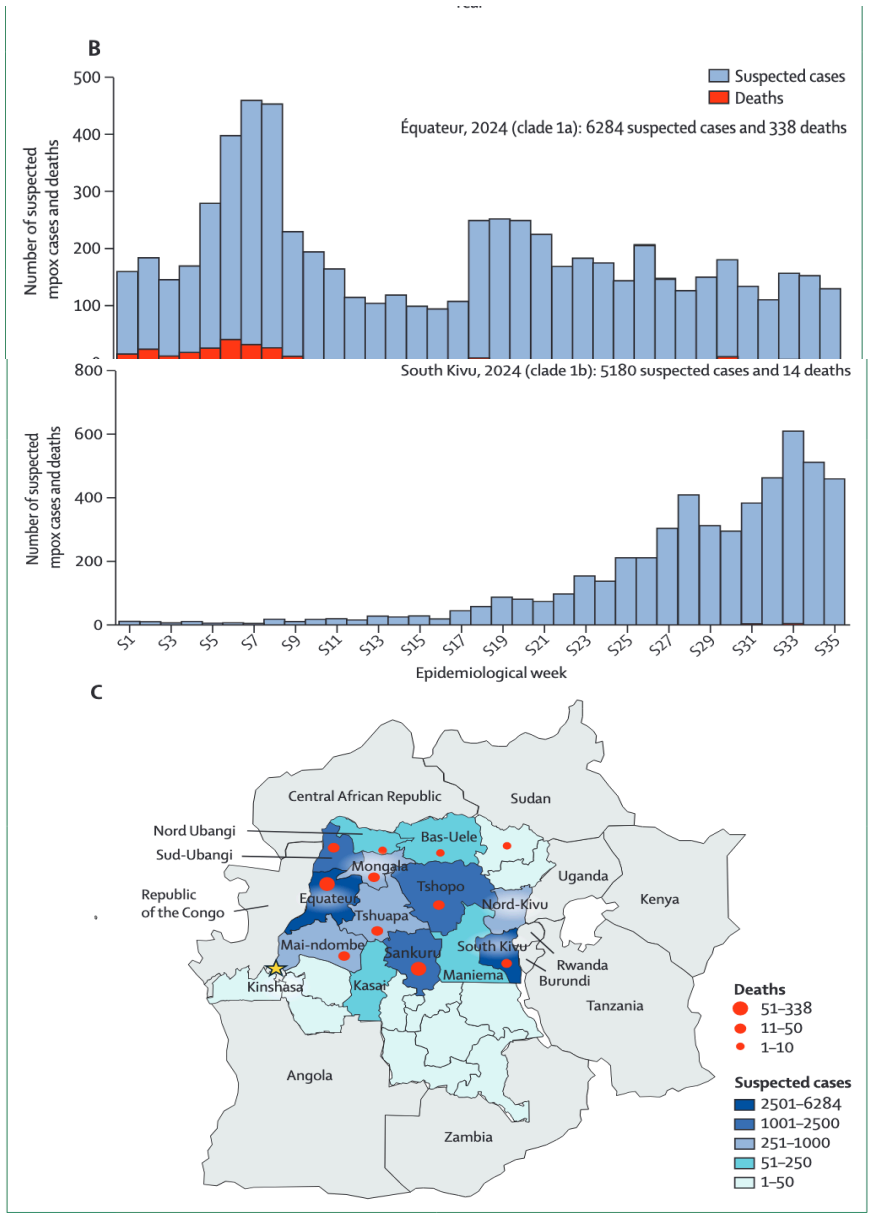


	Clade 1a	Clade 1b	Clade 2a	Clade 2b, lineage A	Clade 2b, lineage B.1
Period	1970–2024	2023	1970–2018	2017–24	2022–23
Geographical distribution	Central Africa (west and central Democratic Republic of the Congo)	East Democratic Republic of the Congo, regional spread	West Africa, some international.	Nigerian outbreak 2017–19	Global since 2022
Transmission dynamics[10,11,13,24,25]	Zoonotic (>70%), little human-to-human spread	Human-to-human spread	Zoonotic (100%)	Zoonotic and widespread human-to-human spread	Sexual contact
Historical trends	Low incidence until 2010, then rise	Emerged in 2023, spreading	Sporadic cases and localised outbreaks in west Africa (1970–2018); notable outbreak in the USA in 2003	2017 Nigeria outbreak; remains actively spreading	2022 global outbreak; remains actively spreading
Demography	Mostly children	Mostly adults	Adults and children	Mostly adults	Mostly adult men who have sex with men
Genomics[4,9,26]	High diversity, multiple zoonotic introductions; infrequent *APOBEC3*-type mutations (8% of all mutations)	Low diversity little spread; substantial mutations observed; frequent *APOBEC3*-type mutations (55% of all mutations)	High diversity, multiple zoonotic introductions; low *APOBEC3* activity (13% of all mutations)	Very frequent APOBEC3-type mutations (90·8% of mutations)	High diversity; frequent *APOBEC3* mutations (84·8% of observed mutations)

Table 1: **Epidemiology and transmission of monkeypox virus clades**

Epidemiology – Ongoing outbreaks of Clade I Mpox





- DRC outbreak escalated toward the end of 2023
- In 2024 August, emergence of large outbreak in south kivu
- Identification of clade I b
- So far > 50,000 suspected cases, 900+ deaths
- Cases reported in neighboring African countries to the DRC
- Exported cases of clade Ib reported in European countries and North America

Clinical features of Clade I Mpox

- Across all clades, systemic symptoms, such as fever, fatigue, and headache are common.
- Clade I infections are more severe that clade II mpox infections.
- In clade Ia cases from Democratic Republic of the Congo, skin lesions were primarily concentrated on the head, arms, and legs, spreading in a centrifugal pattern
- > than 90% of patients presented with more than 100 lesions
- 70–80% typically experienced lymphadenopathy
- Severe complications, including secondary bacterial infections with sepsis (20%) and involvement of the respiratory (11%) or gastrointestinal tracts (8%), are common.

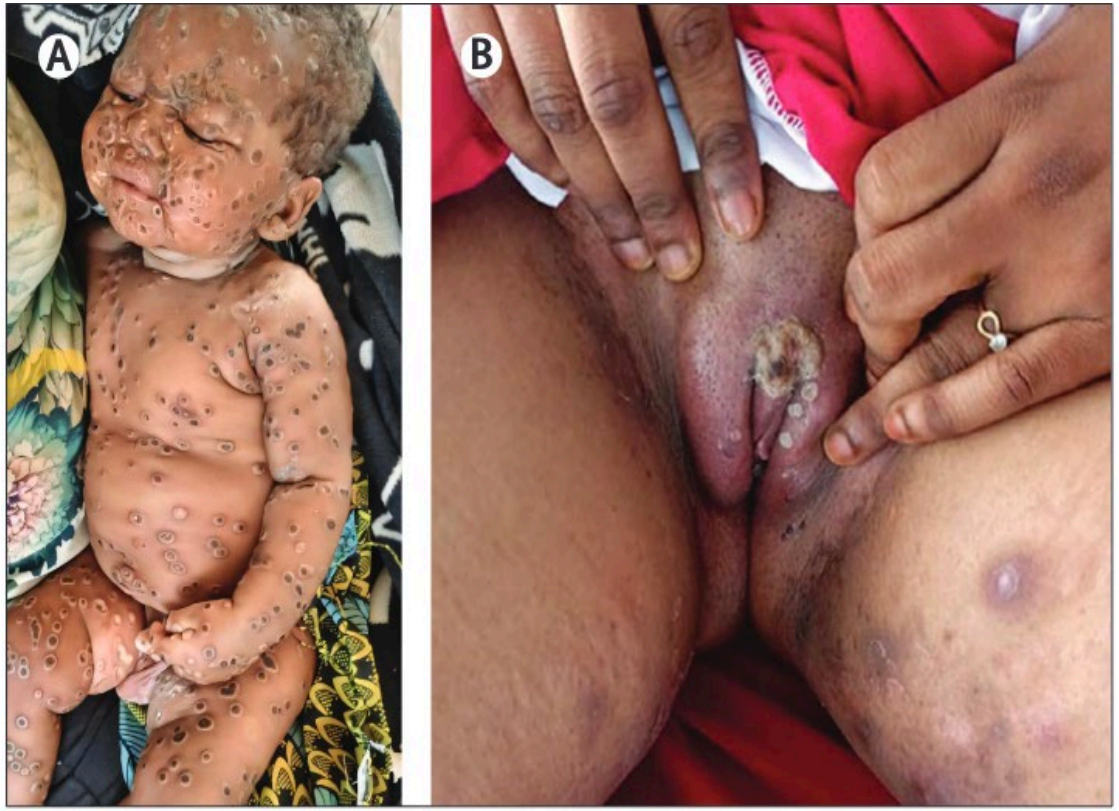


***Figure* 3: Comparison of disseminated and genital mpox presentations in clades 1a and 1b**

(A) A child with disseminated mpox lesions associated with clade 1a, showing widespread umbilicated vesicles on the torso and limbs. (B) A woman patient with genital mpox lesions associated with clade 1b, characterised by vulvar coalescent whitish vesicles with umbilicated centre.

Clinical Features of Clade I Mpox

- In clade 1b, first described in 2023, the median age of affected individuals is 22 years.
- 50% of infected individuals are women and 30% are sex workers, although children are also affected.
- Genital lesions were reported in 63–85% of cases.
- Although 91% of patients were hospitalized, primarily for isolation, only 10% experienced severe respiratory issues.
- Infections have been associated with increased risk for pregnancy loss and case fatality is higher in children and in immunocompromised persons like in Clade II infections.

	Clade 1a	Clade 1b	Clade 2a	Clade 2b, lineage A	Clade 2b, lineage B.1
Population characteristics					
Populations affected	10% adults, 90% children	Democratic Republic of the Congo: 85% adults, 15% children	73% adults, 27% children	70% adults, 30% children	80–99% adults, 1–20% children
Mean age	14 years	22 years	--	26–32 years	37–41 years
Sex	M: 50–64%; F: 26–50%	M: 48%; F: 52%	M: 53%; F: 47%	M: 53–78%; F: 22–47%	M: 97–100%; F: 0–3%
Smallpox vaccination in childhood	2%	Unknown	Unknown	20%	11–18%
Exposure to animal products	100%	0%	100%	No	No
Living with HIV	0·5%	7%	Unknown	ND	36–67%
Systemic symptoms					
Fever	44–50%	60%	85%	45–90%	54–72%
Fatigue or myalgia	85%	--	71%	73–85%	24–81%
Headache	24%	--	65%	48–79%	25–53%
Sore throat or cough	78%	--	50%	ND	ND
Lymphadenopathy	51–98% (submaxillary, cervical)	42%	71%	57–87% (cervical, 50%)	60% (inguinal)
Clinical features of the rash					
Severe rash (>100 lesions)	93%	Unknown	20%	20–42%	0–4%
Distribution	Generalised (100%)	Localised or generalised	Generalised (75%)	Generalised	Localised
Primary site of lesions	Head and limbs	Oral and genital	Head and limbs	Site of animal contact	Oral, anal, and genital (70–87%)
Face	100%	--	62%	96–98%	20–39%
Arms and legs	100%	--	81%	81–91%	50–60%
Palms and soles	70–81%	--	28%	NA	NA
Trunk	70–100%	--	56%	80–93%	25–57%
Genitalia	27%	--	NA	67–68%	55–61%
Perianal	ND	--	NA	ND	34–44%
Oropharyngeal	28–52%	--	NA	38%	14–43%
Severe complications					
Secondary bacterial infection	19%	--	6·3%	19%	3–4%
Respiratory	11% (abnormal lung sounds)	--	6·3% retropharyngeal abscess	12% bronchopneumonia	0%
Rectal (proctitis)	0%	--	--	ND	11–25%
Gastrointestinal	7–8%	--	--	ND	ND
Ocular	4–6%	--	6·3%	0·4%	1%
Neurological	0·4–6%	--	--	0·4%	0%
Hospital admission	6%	--	24%	26%	1–13%
Death	1–12%	0·6%	0%	3·6%	<0·1%

Data were retrieved from published retrospective cohorts.[3,11,12,17,24-26,40,47,48,49,50] F=women. M=men. NA=not applicable. ND=no data. --=unknown data.

Table 2: **Clinical presentation and complications of monkeypox virus clades**

Mpox clinical presentation across clades

Diagnostic Considerations for Clade I Mpox

- Relevant epidemiologic exposures
- Clinical rash suspect for mpox infection (papular rash with central umbilication).
- Confirmatory diagnostics is detection of virus DNA by PCR from swabs obtained from lesions.
- Clade 1b is associated with specific diagnostic challenges, as it can be missed by some PCR assays due to deletions in the C3L gene, leading to false negatives.
- If non-variola orthopoxvirus PCR is positive but clade IIb PCR is negative, this should prompt referral of the sample to CDC for clade I specific testing and sequencing.

Clinical Management of Mpox – Updates

- Mpox treatment primarily involves supportive care to manage symptoms and complications, such as pain relief, hydration, and treating secondary infections.
- Tecovirimat, widely used during the 2022 outbreak, acts by inhibiting the function of envelope proteins required for viral replication.
- PALM-007 study in in DRC showed that Tecovirimat did not shorten the course of illness compared to supportive care for Clade I infections
- STOMP trial in the US assessed Tecovirimat in Clade IIb infections. Study stopped for futility.
- Role of tecovirimat and other antivirals for the treatment of severe infections in immunocompromised individuals needs to be assessed.

Clinical Management of Mpox –Updates

- Management of severe cases should be in conjunction with a CDC consultation.
- CDC encourages the state health department and diagnosing clinician to contact the CDC Emergency Operations Center (EOC) at 770-488-7100 and request a clinical mpox consult after clade I mpox is diagnosed, regardless of the severity of illness.
- Antiviral combos (tecovirimat, cidofovir, brincidofovir) or biologics

(vaccinia immunoglobulin IV) can be used for treatment based on expert opinion and guidance on a case-by-case basis.

Vaccines – Considerations relevant for Clade I Mpox

- All available vaccines are currently based on attenuated vaccinia-virus strains rather than the monkeypox virus itself.
- MVA-BN vaccine has shown effectiveness in preventing clade 2b mpox based on observational studies. A case-control study across 12 US jurisdictions estimated the vaccine effectiveness at 75·2% after one dose and 85·9% after two doses.
- Data on the efficacy of MVA-BN in the context of clade 1 monkeypox virus are currently scarce but. This is the mainstay for vaccine prevention in ongoing outbreaks.
- Continue to offer vaccinations to individuals who meet criteria for vaccination and consider for travelers going to countries with active outbreaks.

Public Health Considerations

- Clade I Mpox outbreaks in Africa remain a public health emergency of international concern.
- Clinicians should have a heightened awareness especially in patient presenting with relevant epidemiologic context.
- Engage referral laboratory facilities like the CDC promptly for confirmatory testing and management
- Continue to offer mpox vaccines to those who meet criteria.

References:

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4. **2022-24 Mpox (Monkeypox) Outbreak: Global Trends**, https://worldhealthorg.shinyapps.io/mpx_global/