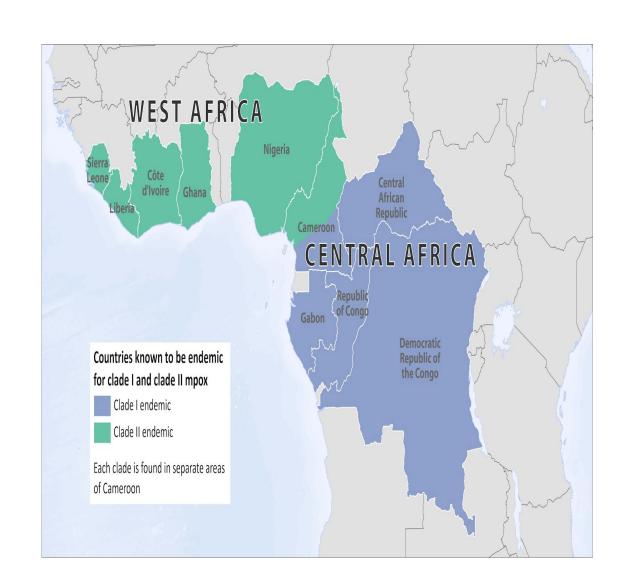
Brief Review of Clade I Mpox: Clinical presentation, Diagnosis and Management

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Epidemiology – Distribution of mpox clades

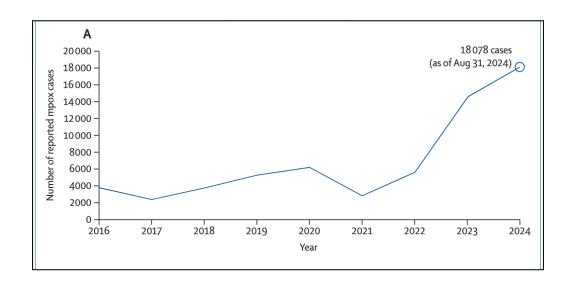
- There are two major clades of Mpox.
- Clade II (a &b) circulates primarily in W. Africa and Clade I (a & b) circulates in Central Africa.
- 2022 global outbreak was caused by clade IIb
- Ongoing outbreaks in Africa caused by clade Ia and Ib



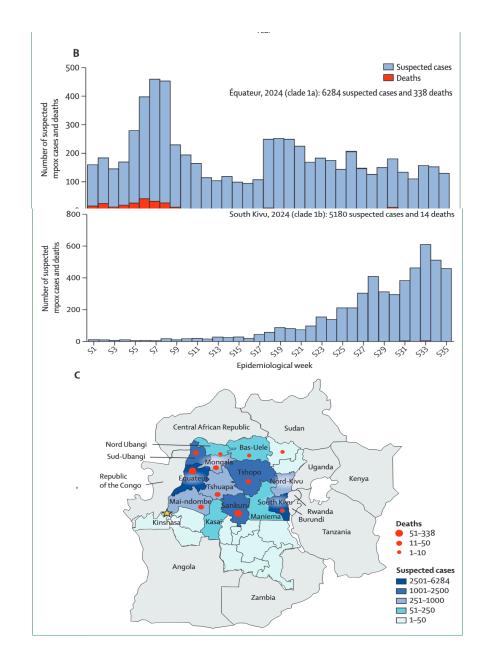
	Clade 1a	Clade 1b	Clade 2a	Clade 2b, lineage A	Clade 2b, lineage B.1
Period	1970-2024	2023	1970-2018	2017–24	2022–23
Geographical distribution	Central Africa (west and central Democratic Republic of the Congo)	East Democratic Republic of the Congo, regional spread	West Africa, some international.	Nigerian 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.

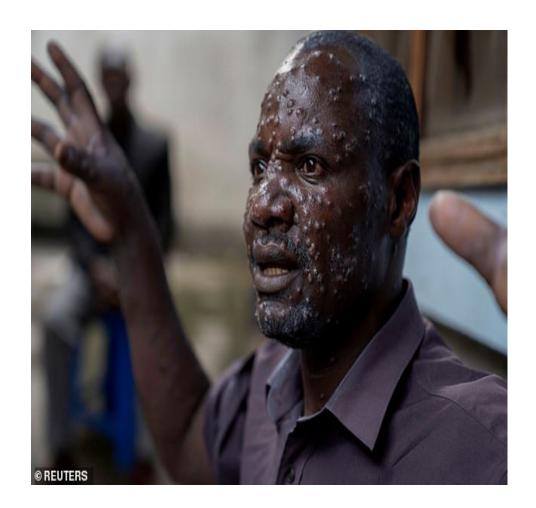


Figure 3: Comparison of disseminated and genital mpox presentations in clades 1a and 1b

(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.



copulations affected 10% adults, 90% children Democratic Regulbit of the Congos 85% adults, 13% children 27% children 70% adults, 20% children 1-20% children 20% collision 1-20% children 1-20% children 20% collision 1-20% children 1-20% children 20% collision 1-20% children 1-20% children 37-41 years 37-42 years	Clae	de 1a	Clade 1b	Clade 2a	Clade 2b, lineage A	Clade 2b, lineage B.1
No No No No No No No No	Population characteristics					
ev 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% apposure to animal pload vaccination in likelihood 100% No No ving with HIV 0.5% 7% Unknown ND 36-67% wing with HIV 0.5% 7% Unknown ND 36-67% weer 44-50% 60% 85% 45-90% 54-72% attigue or myalgia 85% 45-90% 24-81% 48-72% attigue or myalgia 85% 48-79% 25-53% 100 ND ND ore throat or cough 78% 50% ND ND ND weeter eath (-100 lesions) 33% Localised or generalised 66% 48-79% 0-44% stiributiotion Generalised (100%) Localised or generalised 6eneralised (75%) Generalised Localised ifficial Features of lesions 93% 62% 96-98% 20-39% ifficial features of lesions 100%	Populations affected 10		•	,	70% adults, 30% children	
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hildhood systemic spinal of 100% 0% 100% No	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%
reducts / wing with Hill	Smallpox vaccination in childhood	2%	Unknown	Unknown	20%	11–18%
Septemic symptoms	Exposure to animal 100 products	0%	0%	100%	No	No
ever 44–50% 60% 85% 45-90% 54-72% attigue or myalgia 85%	Living with HIV	0.5%	7%	Unknown	ND	36-67%
atigue or myalgia 85% 71% 73-85% 24-81% leadache 24% 65% 48-79% 25-53% or te throat or cough 78% 50% ND ND mymphadenopathy 31-98% (submaxillary, cevicral) 31-98% (submaxillary, cevicral) 31-98% (submaxillary, cevicral) 31-98% (submaxillary, cevicral) 51-98% (submaxillary, cevicral) 51-98	Systemic symptoms					
Angle Angl	Fever 44	4–50%	60%	85%	45-90%	54-72%
Separation Face F	Fatigue or myalgia 85	5%		71%	73-85%	24-81%
S1-98% (submaxillary, cervical) S1-9	Headache 24	4%		65%	48-79%	25-53%
Initial features of He Path	Sore throat or cough 78	8%		50%	ND	ND
No No No No No No No No			42%	71%	57-87% (cervical, 50%)	60% (inguinal)
	Clinical features of the rash					
France 100% 62% 96-98% 20-39% Arms and legs 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 57-68% 55-61% Perianal ND NA ND 34-44% Oropharyngeal 28-52% NA 38% 14-43% evere complications 28-52% NA 38% 3-44 evere complications 6-3% 19% 3-4% evere complications 6-3% 19% 1-125% everta complications 6-3% ND 11-25% everta complications ND ND everta complications <td>Severe rash (>100 lesions) 93</td> <td>3%</td> <td>Unknown</td> <td>20%</td> <td>20-42%</td> <td>0–4%</td>	Severe rash (>100 lesions) 93	3%	Unknown	20%	20-42%	0–4%
Face 100% 62% 96-98% 20-39% Arms and legs 100% 81% 81% 81-91% 50-60% Palms and soles 70-81% 28% NA NA Trunk 70-100% 56% 80-93% 25-57% Genitalia 27% NA NA 67-68% 55-61% Perianal ND NA NA ND 38% 14-43% Perianal ND NA NA ND 38% 14-43% Perianal ND NA NA ND 38% 14-43% Perianal ND NA NA ND ND 34-44% Oropharyngeal 28-52% NA NA 38% 14-43% Perewer complications Percendary bacterial 19% 6-3% 19% 3-4% reception of the complications Perianal NS ND 8 8 ND	Distribution Ger	neralised (100%)	Localised or generalised	Generalised (75%)	Generalised	Localised
Arms and legs 100% 81% 81% 81-91% 50-60% Palms and soles 70-81% 28% NA NA NA NA Trunk 70-100% 56% 80-93% 25-57% 80-93% 25-57% 80-91% 70-100% NA	Primary site of lesions Hea	ad and limbs	Oral and genital	Head and limbs	Site of animal contact	
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% evere complications 6-3% 19% 3-4% econdary bacterial refection 11% (abnormal lung sounds) 6-3% 19% 3-4% econdary bacterial refection 11% (abnormal lung sounds) 6-3% retropharyngeal abscess 12% bronchopneumonia 0% ecotal (proctitis) 0% ND ND ND ecotal (proctitis) 0% ND ND ND coular 4-6% 6-3% 0.4% 1M eleverlogical 0-4-6% 0.4% 0.4 0.4 eleverlogical 0-4-6%	Face 100	0%		62%	96-98%	20–39%
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% everetecomplications 6-3% 19% 3-4% econdary bacterial frection 19% 6-3% 19% 3-4% respiratory 11% (abnormal lung sounds) 6-3% retropharyngeal abscess 12% bronchopneumonia 0% rectal (proctitis) 0% ND 11–25% rectal (proctitis) 7-8% ND ND rectal (proctitis) 7-8% ND ND rectal (proctitis) 0-6% 0-4% 1% 1-25% rectal (proctitis) 0-6% 0-4% 0-4% 1% rectal (proctitis) 0-4-6%	Arms and legs 100	0%		81%	81–91%	50-60%
Genitalia 27%	Palms and soles 70	0-81%		28%	NA	NA
Perianal ND NA ND 34-44% Oropharyngeal 28-52% NA 38% 14-43% Everer complications econdary bacterial affection 19% 6-3% 19% 3-4% despiratory 11% (abnormal lung sounds) 6-3% retropharyngeal abscess 12% bronchopneumonia 0% destal (proctitis) 0% ND 11-25% destrointestinal 7-8% ND ND obcular 4-6% 6-3% 0-4% 1% devological 0-4-6% 0-4% 0% despital admission 6% 0-4% 0% destrointestinal 1-12% 0-6% 0% 3-6% 0-13%	Trunk 70	0–100%		56%	80-93%	25–57%
Oropharyngeal 28–52% NA 38% 14–43% evere complications econdary bacterial 19% 3–4% econdary bacterial 19% 3–4% despiratory 11% (abnormal lung sounds) 6-3% retropharyngeal abscess 12% bronchopneumonia abscess 0% destrointestinal 7–8% ND ND ND ocular 4–6% 6-3% 0-4% 1% destrointestinal 0-4–6% 0-4% 0% despital admission 6% 24% 26% 1–13% death 1–12% 0-6% 0% 3-6% <0-1%	Genitalia 27	7%		NA	67–68%	55-61%
Part	Perianal ND			NA	ND	34-44%
19% 3-4% 19% 3-4% 19% 3-4% 19% 3-4% 19% 3-4% 19% 3-4% 19% 3-4% 19% 3-4% 19% 3-4% 19% 3-4% 19% 3-4% 19% 3-4% 19% 3-4% 19% 3-4% 19	Oropharyngeal 28	8–52%		NA	38%	14-43%
11% (abnormal lung sounds) 6-3% retropharyngeal abscess 12% bronchopneumonia 0% 0% 0% 0% 0% 0% 0% 0	Severe complications					
abscess tectal (proctitis) 0% ND 11–25% fastrointestinal 7–8% ND ND ocular 4–6% 6-3% 0-4% 1% deurological 0-4–6% 0-4% 0% dospital admission 6% 24% 26% 1–13% death 1–12% 0-6% 0-6% 0-6% 3-6% 20% otata were retrieved from published retrospective cohorts. 3.11,12,172,24,2640,474,84,95° F=women. M=men. NA=not applicable. ND=no data= unknown data.	Secondary bacterial 19 infection	9%		6.3%	19%	3-4%
Fastrointestinal 7–8% ND	Respiratory 13	1% (abnormal lung sounds)		. , ,	12% bronchopneumonia	0%
Ocular 4-6% 6·3% 0·4% 1% Heurological 0·4-6% 0·4% 0% Hospital admission 6% 24% 26% 1-13% Death 1-12% 0·6% 0% 3·6% <0·1%	Rectal (proctitis)	0%			ND	11–25%
Ideurological 0·4-6% 0·4% 0% Idespital admission 6% 24% 26% 1-13% Death 1-12% 0·6% 0% 3·6% <0·1%	Gastrointestinal 7	7–8%			ND	ND
lospital admission 6% 24% 26% 1–13% Death 1–12% 0.6% 0% 3.6% <0.1% death 1–12% extra were retrieved from published retrospective cohorts. 3.11.12.1724-2640.4748.49.50° F=women. M=men. NA=not applicable. ND=no data=unknown data.	Ocular 2	4–6%		6.3%	0.4%	1%
beath 1–12% 0.6% 0% 3.6% <0.1% Itata were retrieved from published retrospective cohorts. 3.11,12,172.42-2640.474.84.95.0° F=women. M=men. NA=not applicable. ND=no data=unknown data.	Neurological (0-4–6%			0.4%	0%
ata were retrieved from published retrospective cohorts, 3-11,12,17,24-2640,47,48,49,50 F=women. M=men. NA=not applicable. ND=no data=unknown data.	Hospital admission 6	5%		24%	26%	1–13%
	Death	1–12%	0.6%	0%	3.6%	<0.1%
ble 2: Clinical presentation and complications of monkeypox virus clades	Data were retrieved from published re	etrospective cohorts. ^{3,11,12,17,24-2640,4} ;	7.48.49.50 F=women. M=men. NA=not ap	plicable. ND=no data=unknov	vn data.	

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.

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