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Supplemental Reference for Monkeypox Virus (MPV) Clade Ib Outbreak

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Situation Overview

- Mpox is a viral illness caused by the monkeypox virus (MPV), with two distinct clades: Clade I and Clade II, with a higher case fatality rate associated with Clade I infection.¹
- Outbreaks of MPV have historically resulted from zoonotic spillover of Clade I MPV in Central Africa and Clade II MPV in West Africa and are considered endemic in different countries in the African continent. Notably, the 2022 MPV outbreak is linked to Clade IIb and cases continue to be reported worldwide.²
- Since late 2023, a large outbreak of mpox has been affecting the Democratic Republic of the Congo (DRC). This outbreak is linked to a new subclade, Clade Ib, which was first identified in the Kamituga Health Zone located in the South Kivu Province in eastern DRC. Clade Ib has since expanded to other African countries and unlike Clade Ia, Clade Ib predominately affects young adults.^{1,3}
- MPV is known to transmit through contact with lesions, body fluids, respiratory droplets, or contaminated material, or through contact with infected animals or consumption of contaminated meat. The current Clade Ib outbreak appears to have sustained human-to-human transmission via close contact, including sexual contact.⁴
- Current vaccines are expected to protect against Clade Ib infection.⁴⁻⁵
- A timeline of events detailing the Clade Ib outbreak can be found below:
 - In September 2023, an ongoing outbreak of MPV was detected in Kamituga Health Zone, a densely populated mining area in South Kivu Province in eastern DRC. In January 2024, this outbreak was identified as a divergent lineage of Clade I, referred to as Clade Ib.³
 - In April 2024, the Republic of the Congo declared a Clade I MPV outbreak and cases of Clade I MPV were confirmed in the Central African Republic. It has not been confirmed if these cases are Clade Ia or Ib; however, the epidemiologic pattern suggests a possible link to the Clade Ib outbreak in DRC.^{1,6}
 - In July 2024, Rwanda, Burundi, Uganda, and Kenya reported cases of MPV that were confirmed to be Clade Ib.⁶⁻⁷
 - On 13 August 2024, Africa Centres for Disease Control and Prevention (CDC) declared a public-health emergency⁸ and on 14 August 2024, the World Health Organization (WHO) designated the Clade Ib outbreak as a Public Health Emergency of International Concern, which releases additional resources for fighting the outbreak.⁹
- As of 21 August 2024, this year a total of 18,737 cases (3,101 confirmed, 15,636 suspected) and 541 deaths (case fatality rate 2.89%) of MPV (combined clades I and II) have been reported from 12 African countries, with Clade Ib reported in Burundi, DRC, Kenya, Rwanda, and Uganda.¹
- Since the Public Health Emergency of International Concern was designated, additional cases of MPV have been detected and suspected outside of Africa in countries with confirmed travel associated Clade Ib cases in Sweden¹⁰⁻¹¹ and Thailand.¹²⁻¹³ No cases of Clade Ib have been reported in the United States.¹⁴

Transmissibility and Infectious Dose - How does it spread from one host to another? How easily is it spread?

- Clade I MPV cases are increasing in DRC, especially in remote forest areas. This is likely due to zoonotic spillover with secondary human-to-human transmission within households.¹⁵⁻¹⁷ A record 14,626 cases of MPV were recorded in the DRC for 2023, indicating potential for a shift towards more sustained human-to-human transmission.³
- The Kamituga MPV outbreak in the DRC has spread rapidly, with 241 suspected cases reported within five months of the first reported case.³

- Based on available epidemiological data, Clade Ib has been spreading rapidly among adults through close physical contact which includes sexual contact.¹⁸
 - The Kamituga outbreak appears to be associated with sexual transmission as a primary mode of transmission. Most cases presented with genital lesions and in 29% of confirmed and suspected cases individuals indicated sex work as a profession.³
 - The higher local contact rates due to sexual transmission could be related to the concentration of sex workers associated with the mining industry in the region.¹⁹⁻²¹ More data is needed to confirm that Clade Ib is predominantly spread via sexual transmission.
- The reproduction number estimated for MPV Clade Ib is 1.4 - 1.6, which is higher than the current estimated reproduction number of the MPV Clade Ia outbreak in the DRC (1.2 - 1.3).²¹
- The infectious dose of Clade Ib is currently unknown. MPV Clade Ib has mostly affected adolescents and young adults, unlike Clade Ia.^{7, 15, 22} This could be a byproduct of the region where Clade Ib appears to have originated; however more data are needed. In a case study focused on hospitalizations within the Kamintuga region, only 25% (79/371) cases were children under 15 years of age with the majority of patients between 16 and 26 years old.²³
 - In a review of 108 confirmed mpox cases, the median age of individuals was 22 years, 51.9% were female and 29% were sex workers.³
 - The single most predominant profession of the male respondents was gold mining (20%).¹⁹

Incubation Period and Clinical Presentation – How long until symptom onset? What are initial symptoms?

- In a case study assessing MPV cases at the Kamituga hospital, skin rash, fever, headache, and swollen lymph nodes were listed as the most common symptoms, having been reported by 88%, 74%, 72%, and 70%, respectively, of the entire cohort. Additionally, two patients (one male and one female) reported being asymptomatic.¹⁹ This is consistent with symptoms present in other MPV clades.²⁴
- Males displayed symptoms of skin rash, chills or sweats, genital lesions, headache, and muscle pain more frequently than females.¹⁹
- As of April 2024, eight MPV patients admitted at the Kamituga hospital were pregnant women and four patients experienced abortion. While none of these fetuses have had confirmation of MPV, during the 2022 MPV Clade IIb outbreak MPV DNA was detected in the placenta and in the fetus, suggesting the possibility of materno-fetal transmission. More data is needed to confirm if this is occurring with Clade Ib infection.^{23, 25-26}

Clinical Diagnosis – Are there tools to diagnose infected individuals? When during the infection are they effective?

- Polymerase chain reaction (PCR) detection and diagnostic techniques remain effective for Clade Ib.²⁷
- The US CDC recommends that patients who travel from DRC receive Clade-specific testing.²⁸

Fatality Rate - How likely is it that those infected will die from MPV?

- The current case fatality rate in DRC estimated at ~ 4.6% is higher compared to Clade IIb (~ 1%) but lower than Clade Ia (~10%) outbreaks.^{3,29} The case fatality rate for the 2022 US Clade IIb MPV outbreak was 0.1%.³⁰
- As of 21 August 2024, no deaths from Clade 1b have been reported in Rwanda, Kenya, or Uganda.⁶

Genomics - How does the disease agent compare to previous strains?

- MPV is a member of the Orthopoxvirus genus of the Poxviridae family of enveloped viruses, with a linear double-stranded DNA genome of around 200 kb.³¹
- The distinct MPV Clade Ib lineage linked to the Kamituga Health Zone was revealed through genomic analysis in January 2024. Clade Ib is divergent from previously sequenced Clade I strains in DRC and increases the known diversity of Clade I by 54%.^{3, 32}
- Clade Ib appears to be mutating at an accelerated rate as compared to Clade Ia, where the former has nearly 150 nucleotide substitutions compared to the 96 nucleotide substitutions for Clade Ia.³
- Clade Ib contains a large ~1kbp deletion within a region typically used for identifying Clade I viruses.³ PCR techniques remain effective for Clade Ib.²⁷
- 55.5% (5/9) of the reconstructed mutations in Clade Ib are consistent with APOBEC3-mediated cytosine deamination. This is significantly higher than the observed 8% in reservoir hosts and suggests human-to-human transmission.³
- Clade Ia MPV cases continue to be observed in the DRC outside the Kamituga region and appear to mostly result from independent spill over events with their own subsequent transmission. There is no evidence that transmissibility has otherwise changed and is assumed these cases are not Clade 1b as they do not share the same genetic markers.³

What else do we know?

- Other aspects of MPV Clade Ib infection are either presumed or confirmed to agree with those previously described for MPV. Additional information can be found in the [DHS S&T Master Question List for Monkeypox Virus](#).

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