

PUBLIC HEALTH ALERTS | IN PARTNERSHIP WITH CIDRAP

Detection of Community Transmission of Clade Ib Mpox Virus in the United States

Eric C. Tang, M.D., M.P.H.,¹ Monica Haw, M.P.H.,¹ Sonali Kulkarni, M.D., M.P.H.,² Emily Johnson, M.P.H.,³ Crystal M. Gigante, Ph.D.,⁴ Nora Balanji, M.P.H.,³ Ricardo Berumen III, B.S.,¹ Shama Cash-Goldwasser, M.D., M.P.H.,⁴ Jennifer R. Chevinsky, M.D., M.P.H.,⁵ Alex Espinosa, M.S.,¹ Andrea Gallegos, M.S.,⁵ Nicole M. Green, Ph.D.,² Jill K. Hacker, Ph.D., M.P.H.,¹ Faisal S. Minhaj, Pharm.D., M.P.H.,⁴ Erin Nguyen, M.P.H.,² Cliff Okada, M.D., M.P.H.,³ Kathleen Poortinga, M.P.H.,² Will S. Probert, Ph.D.,¹ Kayla Saadeh, M.P.H.,¹ Aisling Vaughan, Ph.D.,^{2,4} Stephanie Wu, B.S.,¹ Debra A. Wadford, Ph.D.,¹ and Kathleen Jacobson, M.D.¹

Abstract

A clade Ib mpox virus (MPXV) outbreak in Central and Eastern Africa has led to multiple travel-associated infections. In October 2025, clade Ib MPXV infection was confirmed in three unvaccinated, hospitalized men in California reporting no international travel. Phylogenetic analysis revealed clustering of these three MPXV infections with one recent travel-associated MPXV infection. This report provides evidence for local transmission of clade Ib MPXV in the Americas, occurring among gay, bisexual, and other men who have sex with men and their social networks.

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Introduction

An mpox (formerly known as monkeypox) outbreak caused by clade Ib mpox virus (MPXV) began in 2023 in the Democratic Republic of the Congo and spread to multiple neighboring countries. Throughout 2024–2025, travel-associated mpox cases in individuals outside Africa have been confirmed — including six in the United States — in the setting of the global clade IIb mpox outbreak that began in 2022. Based on U.S. Centers for Disease Control and Prevention (CDC) data, one of these six individuals was hospitalized. The clinical course of clade Ib is not well described in the United States. For California mpox cases, local and state public health laboratories provide MPXV clade determination. In October 2025, the California Department of Public Health (CDPH) confirmed clade Ib MPXV infection in three unrelated persons in Southern California, none of whom had reported recent travel or contact with one another, suggesting community transmission.

The author affiliations are listed at the end of the article.

Investigation and Outcomes

In early October, CDPH identified clade Ib MPXV in a hospitalized resident in Long Beach (CA0102) based on results of a laboratory-developed test¹ and whole-genome sequencing.

The identification of clade Ib MPXV led to CDPH outreach to the Long Beach Department of Health and Human Services for investigation. Two days later, Los Angeles County

Eric C. Tang can be contacted at eric.tang@cdph.ca.gov or at the Office of Sexually Transmitted Infections and Hepatitis C Virus, California Department of Public Health, 850 Marina Bay Parkway, Bldg P, 2nd Fl, Richmond, CA 94804.

Department of Public Health (LACDPH) was notified of suspected mpox in another hospitalized patient (CA0103); specimens sent to LACDPH from this and one other patient with mpox (CA0104) were positive for non-variola orthopoxvirus but negative for clade II MPXV. Specimens from CA0103 and CA0104 were sent to CDPH and confirmed to be clade Ib.

These three newly identified clade Ib MPXV infections were in cisgender men, 25–40 years of age, who were either gay or bisexual or within associated social networks. For all three, symptoms began mid-to-late September. None reported sexual contact within the 21-day maximum incubation period for mpox; however, each patient reported other intimate or skin-to-skin contact (e.g., hugging, cuddling). One man was diagnosed with sexually transmitted coinfections at the time of mpox diagnosis. All were hospitalized (including one in the intensive care unit) with mpox-associated conditions, including secondary skin or soft-tissue bacterial infections and airway compromise and were discharged to isolate and recover; all patients received hospital care prior to the clade I determination. One man was severely immunocompromised. None were previously vaccinated against mpox, and none received tecovirimat or other mpox-directed treatment. All patients recovered with supportive care.

Contact tracing and 21-day symptom monitoring was conducted for 133 individuals — including 124 health care workers and 9 individuals with high- or intermediate-risk contact exposures — and 1 received MVA-BN vaccine (JYNNEOS) (Bavarian Nordic) postexposure prophylaxis. No known contacts became symptomatic or tested positive for MPXV. Wastewater surveillance in the Los Angeles area, which covers the zip codes where these three individuals live, has not detected clade I MPXV since implementation in September 2024.

CDPH coordinated expedited testing of specimens from all 64 remaining individuals in California with known MPXV infection without clade determination from August 1, 2025 through October 31, 2025: 57 out of 64 (89%) were clade II positive and 7 out of 64 (11%) were unavailable for additional testing. Of all individuals with confirmed clade II MPXV infection (n=201) that occurred between August and October 2025, 7 people (3.5%) were hospitalized; the specimen from 1 hospitalized patient was unavailable for additional testing and therefore could not have clade confirmed.

Public health interviews found no epidemiologic links among these men. However, phylogenetic analysis of viral

sequence data revealed genetic clustering of the three cases of clade Ib MPXV infection reported in California with a previous travel-associated infection (Fig. 1). That infection occurred in one patient (CA0101) who traveled internationally for several weeks, experienced symptom onset within the incubation period of mpox after travel, was diagnosed with mpox outside of California, and self-reported having fully recovered before returning home to California in late August.

Preliminary Conclusions and Actions

This report represents evidence of community transmission of clade Ib MPXV in the Americas and suggests the virus may be circulating undetected among gay, bisexual, and other men who have sex with men and their social networks. Phylogenetic analysis suggests four 2025 California MPXV infections most likely resulted from a single introduction of clade Ib MPXV to the United States followed by local transmission, and less likely from separate introductions of identical viruses given no travel reported in the three men in whom symptoms developed in September. However, genetic data alone cannot substantiate direct transmission linkages, and the lack of epidemiologic linkages supports undetected transmission in Southern California.

Four of five individuals in California with clade Ib MPXV infection required hospitalization, none were previously vaccinated, and all recovered with supportive care. Comparatively, approximately 5% of unvaccinated individuals with mpox in 2025 from clade IIb MPXV in California have been hospitalized.³ While small numbers preclude any conclusions about clade Ib severity, data from the current outbreak in Central and Eastern Africa estimate a case fatality rate of less than 0.5%.⁴ Future studies are needed to investigate a potential difference in morbidity by clade.

Vaccination remains a key preventive measure, as JYNNEOS vaccination has been associated with a decreased risk of clade IIb infection,^{5–7} clinical progression,⁸ and hospitalization,⁹ and is presumed to be effective against clade Ib; the vaccine is approved by the Food and Drug Administration for prevention of mpox regardless of clade in adults aged 18 years and older determined to be at high risk for smallpox or mpox infection.¹⁰ These data highlight the importance of vaccination for those at risk for exposure to MPXV — including gay, bisexual, and other men who have sex with men. This is particularly important

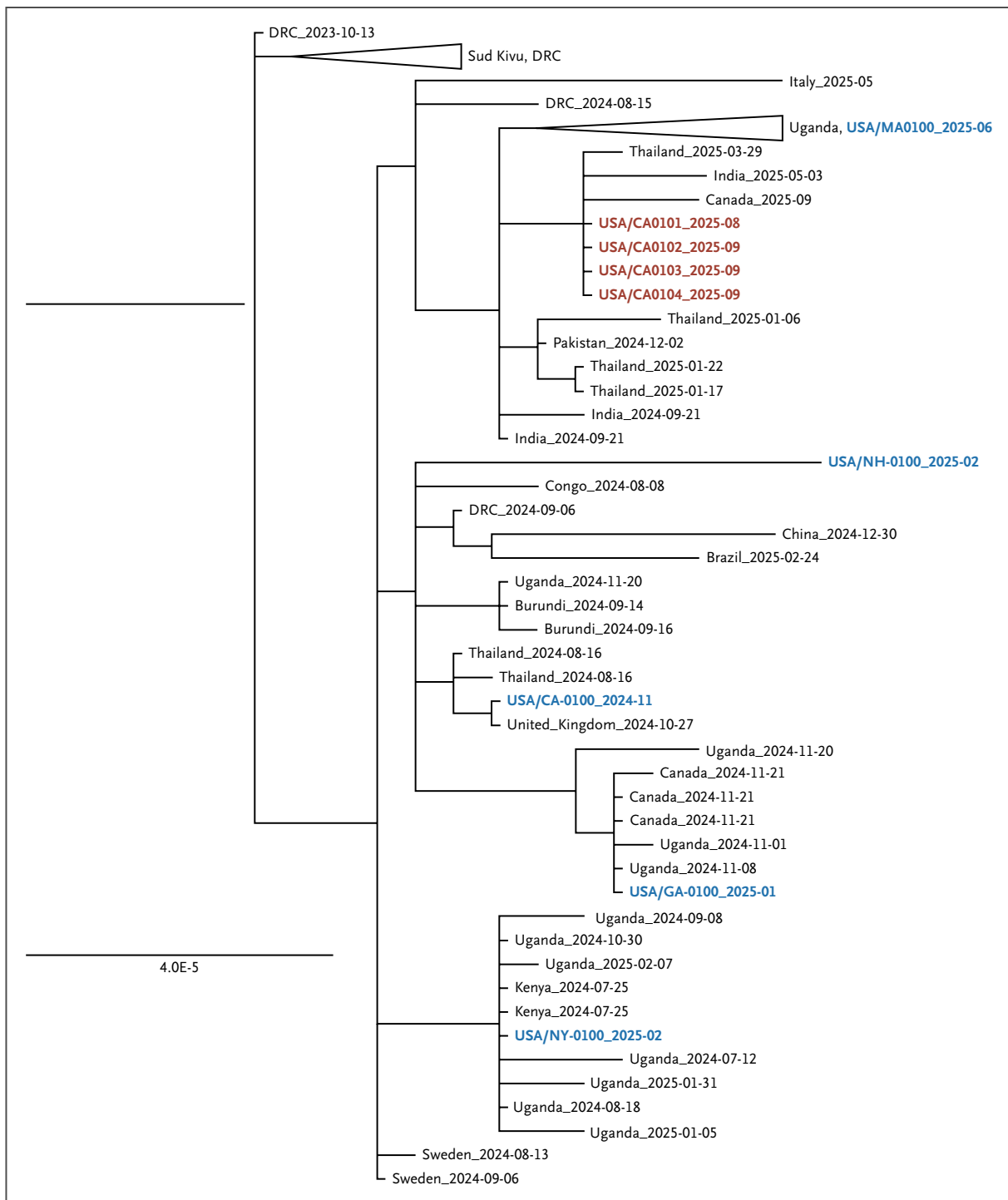


Figure 1. Phylogenetic Analysis of MPXV from Recent Clade Ib Mpox Cases by Maximum Likelihood.

MPXV sequences from individuals identified as CA0101, CA0102, CA0103, and CA0104 (brown text) exhibited high viral sequence identity. This finding is distinct from other travel-associated clade Ib MPXV sequences from individuals in the United States (highlighted in blue text), including from the first person in California and the United States with clade Ib mpox (CA0100),² which all clustered separately in the phylogeny, supporting separate introductions into the United States. The scale bar shows substitutions per site; branches with support below 70% based on 1000 bootstrap replicates were collapsed into a polytomy; phylogenetic analysis performed using RAXML-NG on whole-genome alignment after removal of low complexity regions and the right genomic terminus; dates reflect year and month of specimen collection. GenBank accession numbers: PQ662929.1, PX442285.1, PX480709.1, PX480730.1, PX480710.1. DRC denotes Democratic Republic of the Congo; and MPXV, MPOX Virus.

for those who are immunocompromised, have HIV, or are at risk for more severe disease outcomes.¹¹

In summary, locally acquired clade Ib MPXV infections in individuals requiring hospitalization have been identified in Southern California among persons who had not traveled outside of the United States and were unvaccinated; undetected clade Ib mpox disease and transmission are likely, although no other individuals with clade Ib MPXV infection have been identified through the end of November 2025. This report calls attention to the importance of collaboration between commercial laboratories and health departments to ensure clade-specific testing and highlight the need for health departments and clinicians to remain vigilant, to assess for mpox risk and symptoms, to test patients with compatible signs and symptoms, and to increase vaccination of at-risk groups to prevent further spread of clade Ib MPXV.

Disclosures

Author disclosures are available at evidence.nejm.org.

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This activity was reviewed by the California Health and Human Services Agency and the CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy (see e.g., 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.)

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Author Affiliations

¹ California Department of Public Health, Richmond, CA, USA

² Los Angeles County Department of Public Health, Los Angeles, CA, USA

³ Long Beach Department of Health and Human Services, Long Beach, CA, USA

⁴ Centers for Disease Control and Prevention, Atlanta, GA, USA

⁵ Riverside University Health System — Public Health, Riverside, CA, USA

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