Position Statement

September 2024

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Mpox Virus (MPXV)

Summary

Human mpox (formerly known as monkeypox) is a zoonotic disease caused by the monkeypox virus (MPXV) and which is endemic in some regions of Central and West Africa. There are two major genetic groups (clades) of MPXV, clade I (formerly known as Central African or Congo basin clade) and clade II (formerly known as West African clade). However, outbreaks have occurred outside of the African continent.

In 2022, a multi-country outbreak of mpox clade IIb was declared and most EU/EEA countries reported clusters of locally acquired cases. The outbreak was driven by human-to-human MPXV transmission via close contact with infected individuals and most cases were in men-who-have-sex-with-men (MSM). As of 08 August 2024, 22,662 confirmed mpox cases have been reported by countries in the EU/EEA as part of the outbreak driven by clade IIb with most cases (93%) reported during the intense period of circulation in 2022. In 2024, 685 mpox cases have been reported by 20 EU/EEA countries indicating continued circulation of mpox (clade II) at low levels.

Up to 31 July 2024 there were 4,018 confirmed/highly probable cases of mpox clade IIb in the UK (3,822 in England, 108 in Scotland, 49 in Wales and 39 in Northern Ireland), several of which were acquired outside the UK and imported. Since January 2023, mpox (clade II) is no longer considered a high consequence infectious disease (HCID) within the UK and the current UK risk is Level 2 (transmission within a defined population group) with flat or negative growth.

Historically, MPXV (clade I) was known to circulate in five Central African Region countries: Cameroon, Central African Republic (CAR), the Democratic Republic of the Congo (DRC), Gabon and the Republic of Congo. However, in 2024 a new outbreak of mpox (clade Ib) was reported from countries in Africa beyond these five countries. Clade Ib emerged in the DRC and has since spread to Rwanda, Uganda, Burundi and Kenya. The increase in mpox is likely to be because of multiple factors including waning population immunity from the discontinued smallpox vaccine and changing environmental and social factors.

In August 2024, the Africa Centres for Disease Control and Prevention (Africa CDC) and the World Health Organization (WHO) declared public health emergencies over a large epidemic of mpox in the DRC and at least 13 other African countries (Figure 1). Until August the Africa CDC has reported 2,863 confirmed mpox cases (all clades combined) and 517 deaths so far in 2024.

MPXV (clade I) is considered a HCID and may be more severe and transmissible then clade II. The first two cases of mpox infection (clade Ib) outside Africa have recently been reported (one case in Sweden and one case in Thailand), both associated with travel and infection in Africa. As of 30 August 2024, no cases of clade Ib mpox have ever been detected in the UK.

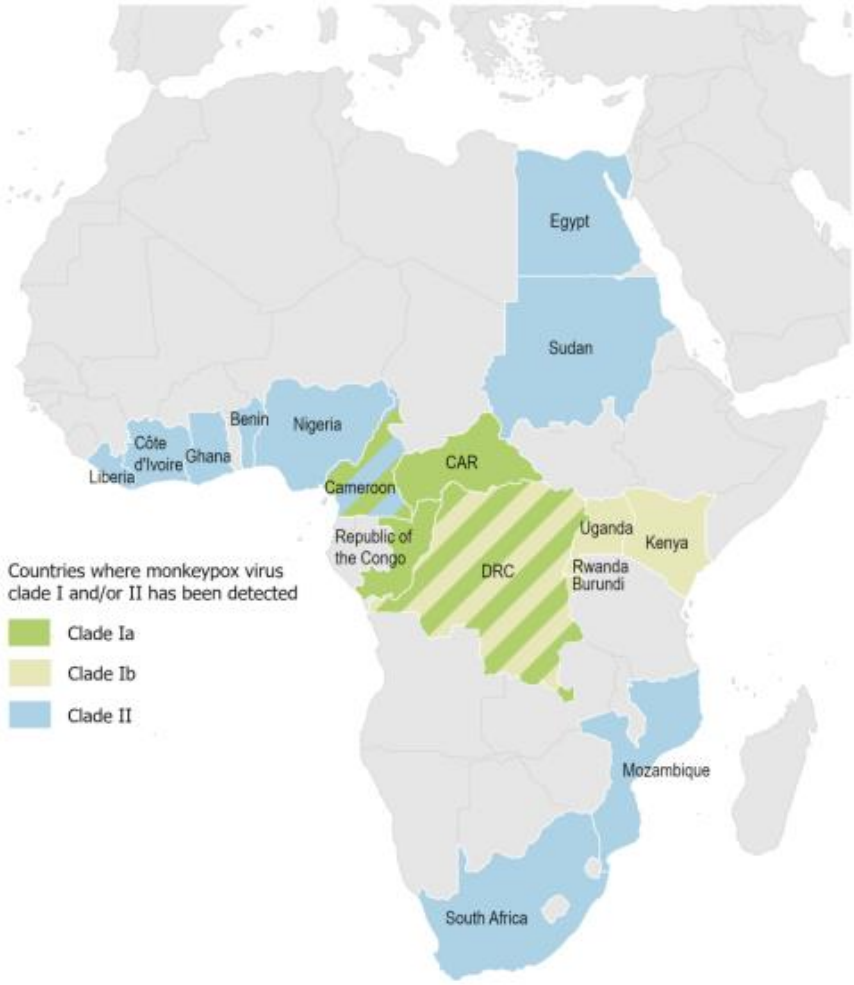

Figure 1. Countries where mpox clade I and/or clade II have been detected (taken from ECDC Risk assessment for the EU/EEA of the mpox epidemic caused by monkeypox virus clade Ib in affected African countries – 16. August 2024).

The risk for recipients of substances of human origin (SoHO), including blood, tissues and cells is considered low:

- Existing donor education and selection criteria should significantly minimise the risk of donation from pre-symptomatic donors and symptomatic donors.
- Post-donation reporting of illnesses enables the discard of donations from potentially infected donors.
- UK Blood and Tissue Establishments have a mechanism in place (through JPAC's Standing Advisory Committee on Transfusion Transmitted Infections (SACTTI) to identify infectious outbreaks/cases and new and emerging pathogens which may threaten the safety of donated products, and to ensure that appropriate actions are taken to mitigate any risk identified.

In addition, the following measures have been taken:

- Specific donor selection guidance for mpox has been added to the UK **Donor Selection Guidelines** (DSG) for blood, tissue and cells.
- The post-donation information list includes specific information for the teams who manage donors who report (or if deceased, have a history of) mpox symptoms and/or diagnosis after donation.
- UK Blood and Tissue Establishments for the four nations will work closely with their respective Public Health Agencies to ensure their involvement with Incident Management Teams.

Background

MPXV is a double-stranded DNA virus of the Orthopoxvirus genus of the family Poxviridae. There are several animal pox viruses and four that are pathogenic for humans: MPXV, variola major virus (VARV), vaccinia virus and cowpox virus (CPXV). VARV is the causative agent for smallpox, which is now eradicated, and vaccinia virus is used in the smallpox vaccine. MPXV infects a wide range of mammalian species, but its natural host reservoir remains unknown (African rodents are the suspected reservoir).

Viruses within the MPXV clade II are less virulent than those in the clade I. Reported case fatality cases range from 1% to 10% for MPXV clade I outbreaks and less than 3% for MPXV clade II.[1] In recent years and prior to the 2022 outbreak, there were only a few isolated cases of mpox in the UK, either imported from countries where mpox is endemic or from contact with infected individuals. Between 2018 and 2021, there have been seven UK cases of mpox (four imported, two household contacts and one healthcare worker).

Symptoms

Mpox begins with fever, headache, muscle aches, chills, swollen lymph nodes and exhaustion. The incubation period is usually 7–14 days but can range from 5–21 days. Generally, within 1–3 days after the appearance of fever, the patient develops a rash, often beginning on the face then spreading to other parts of the body. Lesions progress through macules, papules, vesicles and pustules before the scabs fall off 2–4 weeks later. Mpox can result in severe disease and even death in certain groups (young children, pregnant women, immunosuppressed individuals).

Studies on the multi-country mpox outbreak which started in May 2022 showed an incubation period of 7–8 days although shorter incubation periods of 2–4 days were also observed, possibly due to direct viral inoculation via sexual transmission. Clinical presentation of symptoms was somewhat different than those previously reported in endemic areas; systemic prodromal symptoms (included fever, fatigue, myalgia, and headache) started after the rash in up to half of the cases, while they were completely absent in others. A minority of cases (1–13%) were hospitalised for isolation, pain management, or for complications such as secondary skin infections, abscesses and difficulty in swallowing. Other complications included rectal pain, swelling of the penis, secondary bacterial infections and epiglottitis, myocarditis and encephalitis. Sporadic fatal cases were reported and the overall case fatality rate in the 2022 outbreak was less than 0.1%.

Information on clinical features in the ongoing mpox clade I outbreak is still emerging, but reports suggest that among cases exposed through sexual contact in DRC, some individuals only present with genital lesions, rather than the more typical extensive rash.

Infection and viraemia

Unlike respiratory viruses (e.g. SARS-CoV-2), MPXV does not spread easily between individuals. Human-to-human transmission occurs through close contact with infectious material from skin lesions of an infected person, through respiratory droplets in prolonged face-to-face contact, and through virus-contaminated fomites such as bedding or clothing. Emerging evidence indicates that infected people may transit MPXV up to four days prior to symptom onset. A secondary attack rate of approximately 8% (range 0–11%) for unvaccinated household contacts has been estimated. In the 2022 multi-country outbreak, the presentation of the lesions in certain cases indicate that transmission occurred during sexual contact. Furthermore, people living with HIV/AIDS (PLWHA) accounted for 38–50% of the mpox clade II cases worldwide.

In infected individuals MPXV DNA has been detected in blood. A retrospective review of mpox symptomatic cases treated in UK between August 2018 and September 2021 demonstrated MPXV DNA in the bloodstream in six of seven individuals, with viraemia fluctuating for 27–29 days in two of the cases. Furthermore, virus was detected in blood after the clearance of rash in two cases.[1] MPXV DNA was detected in upper respiratory tract swabs in all seven cases and for at least three weeks in three patients.[1] In an mpox outbreak in the US, 14 blood samples collected 21 days after the appearance of rash were negative for MPXV DNA. There are no good data on viraemia in asymptomatic (most, if not all, cases are thought to develop symptoms) or pre-symptomatic individuals. Virus can be detected in the blood, tissues and organs of MPXV-infected animals.

Study groups in the 2022 mpox clade II outbreak have reported asymptomatic infection (between 1.3% and 1.8% never experience symptoms). However, there are no good data on viraemia in asymptomatic individuals and role of asymptomatic cases in transmission is currently unclear.

Risk of MPXV transmission through substances of human origin (SoHO)

The survival of MPXV in blood components, tissues and cells is unknown although the virus is known to be robust. No cases of MPXV transmission through SoHO have been documented, although transmission from mother to baby during pregnancy has been documented. Transmission of MPXV through SoHO is considered likely until proven otherwise, although currently the overall likelihood of MPXV being present in a donation and onward transmission to recipients is low due to the low case numbers in the population and the risk mitigation processes that are already in place in UK Blood and Tissue Establishments.

Precautionary measures adopted by UK Blood and Tissue Establishments

The JPAC Donor Selection Guidelines ensure safe and consistent donor selection processes. These guidelines already include information on the identification and deferral of donors with acute infections. These are sufficient to deal with donors who provide information which would suggest symptomatic mpox infection. It is unlikely that symptomatic donors would attend to donate, but there is the potential for a live donor who is symptom free but with virus circulating in the bloodstream, or a deceased donor who had mild unidentified symptoms antemortem, to donate. However, this is considered an unlikely event and the existing measures currently in place in UK Blood and Tissue Establishments are currently thought sufficient to the point at which any risk of donations from mpox infected individuals is negligible.

Questions, asked to all UK donors at each donation, regarding illness, infection or fever in the preceding two weeks should potentially screen out symptomatic individuals and the question regarding contact with anyone with an infectious disease in the last four weeks will potentially screen out known contacts. The **ECDC Rapid Risk Assessment: Monkeypox multi-country outbreak** recommends that contacts of an

mpox case should be deferred from blood, organ or bone marrow donations for a minimum of 21 days from the last day of exposure.

Public health management of known contacts of mpox infected individuals for 21 days (which includes isolation for contacts) will also prevent this group of individuals from presenting as donors. UK Public Health Agencies are working closely with colleagues across the wider health service to spread awareness and ensure clinicians are available to identify possible cases and associated contacts. All donors are asked to think about any recent behaviours such as travel or new sexual partners that might affect their eligibility to donate blood.

As of September 2024, National Travel Health Network and Centre (NaTHNaC) pre-travel advice and leaflets will be handed out to people coming off direct flights with electronic notice boards in case of people travelling via indirect routes.

Another important safety measure, which has been used for many years by the UK Blood and Tissue Establishments and other organisations that recover/collect/handle SoHO, is to ensure that any live donor with symptoms appearing post-donation immediately contacts the appropriate service and reports the symptoms. All donors are reminded to report any illness arising in this 14-day period after donation. This reminder is given at the point of donation, and for blood donors, at every donation. Full details of the symptoms and accurate timings are required. This requirement applies to blood donors, living tissue donors and stem cell/cord blood donors. If the components/donations have been administered/transplanted, the clinician responsible for the recipient would be informed.

Travel deferrals for imported cases of mpox are mitigated in blood and tissue donation by a 4-month malaria deferral for visitors to countries where mpox is endemic. This does not apply to hematopoietic stem cell transplantation. As the main event in the current outbreak relates to UK acquired infection and not to importation from endemic countries, this is unlikely to substantially increase risk.

JPAC's Standing Advisory Committee on Transfusion Transmitted Infection (SACTTI) performs regular horizon scanning on behalf of JPAC to identify infectious outbreaks, new and emerging pathogens which may threaten the safety of donated products, and to ensure that appropriate actions are taken to mitigate any risk identified. A monthly Emerging Infections Report (EIR) compiled by the NHSBT/UKHSA Epidemiology Unit includes information provided by a range of national and international evidence sources such as the UKHSA EpiIntel reports, the European Centre for Disease Control (ECDC) and the European Infectious Diseases (EID) Monitor group of the European Blood Alliance (EBA). Rapid alerts are also channelled through the same route to ensure immediate and appropriate action, if required.

Additional measures adopted by the UK Blood Services

A new mpox entry has been created for all DSGs. Changes to the A-Z index will signpost donation staff to the correct page for information on donor and donor contact deferral. Donors can be accepted after recovery from confirmed or suspected mpox infection if:

- It is at least 28 days since the diagnosis of mpox was made, and
- It is at least 14 days since recovery and the donor remains well, and
- It is at least 14 days since all skin lesions have healed, and
- It is more than seven days since completing any antiviral or antibiotic therapy, and
- The donor has been discharged from all follow up (including public health surveillance), and
- The donor is not subject to deferral for sexual behaviour, travel history or other risk factors.

The same conditions apply for deceased and live tissue donors.

Individuals who have been identified by public health teams as a close contact of an individual with mpox can be accepted to donate if:

- If it is more than 21 days since last contact,
- The donor has no symptoms of mpox, and
- The donor has completed any isolation period, and
- The donor has been discharged from all follow-up (including surveillance by public health).

Furthermore, post-donation information was updated to include specific information for the teams who manage donors who report (or if deceased have a history of) mpox symptoms and/or diagnosis after donation. All components/donations from donors who are infected with MPXV (classified as proven or probable according to **case definition criteria** set by UKHSA) within 21 days of donation/procurement, will be removed from inventory. Local processes for public health notification will be followed if any component has been transfused. If the donor has retrospectively reported contact with mpox in the 21 days before their donation, the donation will be placed on hold and UK Blood and Tissue Establishments will seek public health advice to determine the risk for the recipient. National pathways for clinical diagnosis of mpox must be followed.

Donor care staff will be advised to be alert for donors who have (or if deceased have a history of) rash and illnesses consistent with mpox regardless of sexual behaviour, travel history or other risk factors but **case definition criteria** must be used for consistency.

UK Blood and Tissue Establishments for the four nations will work closely with their respective Public Health Agencies to ensure their involvement with Incident Management Teams. UKHSA (Porton Down) have established a mpox PCR assay that is able to distinguish clade Ib from clade II with same day turnaround 24/7.

Several unknowns still exist regarding this outbreak and UK Blood and Tissue Establishments will continue to monitor developments closely and update the position statement as new data and information become available.

Treatment and vaccination

Since 22 July 2022, the third-generation non-replicating smallpox vaccine Imvanex – Modified Vaccinia Ankara - Bavarian Nordic (MVA-BN) has been authorised in the EU for protection against mpox in adults. **UK mpox vaccination advice (pre- and post-exposure)** is available from UK Health Security Agency (UKHSA).

Information on treatment; anti-virals, prevention of secondary bacterial infections and post-exposure prophylaxis of close contacts is detailed in the ECDC risk assessments; **ECDC Rapid Risk Assessment: Monkeypox multi-country outbreak** and **Risk assessment for the EU/EEA of the mpox epidemic caused by MPXV clade 1 in affected African countries**.

Individuals receiving vaccine will have been assessed as high-risk exposure and will be under isolation. These donors should not present for donation, or if they do, donor selection guidelines would capture these individuals.

Generic Donor Selection Guidance is that recent vaccination may require deferral depending on the vaccine administered and the particular vaccination programme. Vaccines are defined on the basis of

the nature of the vaccine, i.e. vaccines containing live or attenuated virus (eight weeks for smallpox vaccination) and those not containing live agents (no deferral required if donor is well and not undergoing any isolation). At this time, the 21-day deferral for contacts will take precedence.

References

1. Alder et al., Clinical features and management of human monkeypox: a retrospective observational study in the UK, *The Lancet Infectious Diseases* (2022). Published online May 24, 2022. **doi.org/10.1016/S1473-3099(22)00228-6** (accessed 02/10/24)

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