UK Health Security Agency

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Event:	Outbreak of Clade I mpox in the African Region: update to high consequence infectious disease case definition
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Authorised by	Meera Chand, Deputy Director of TARZET Dominic Mellon, Regional Deputy Director for HP Ops Derren Ready, Deputy Director of Science Emma O'Brien, Comms
Contact	1. Clinicians should initially discuss suspected clade I mpox cases with their local infection specialists 2. Infection specialists seeking clinical advice on suspected clade I mpox cases should contact the Imported Fever Service (IFS) on 0844 778 8990 to discuss testing and management. Clinicians seeking information regarding testing from the Rare and Imported Pathogens Laboratory (RIPL) should telephone 01980 612348 (available 9am to 5pm, Monday to Friday). 3. Health protection teams seeking urgent public health advice may contact the EIZ team in hours via EpiIntel@ukhsa.gov.uk (9am-5pm weekdays) or CEI duty doctor via +44 20 7123 0333 out of hours.
IRP Level	N/A (non-incident notification)

Instructions for Cascade

- Devolved Administrations to cascade to Medical Directors and other DA teams as appropriate to their local arrangements
- Regional Deputy Directors to cascade to Directors of Public Health
- Local authorities are requested to send this briefing note to commissioned sexual health services
- UKHSA microbiologists to cascade to non-UKHSA labs (NHS and private laboratories) and NHS Trust infection leads
- NHS Trust infection leads to cascade to relevant local services (e.g. Emergency Medicine, General Medicine, Acute Medicine, Infectious diseases, Microbiology, Virology, Genitourinary Medicine)
- The British Association of Sexual Health and HIV; British HIV Association, Faculty of Sexual and Reproductive Healthcare

Summary:

- Clade I mpox virus (MPXV) is a high consequence infectious disease (HCID) which may be more severe and transmissible than the clade II mpox, which has been present in the UK since 2022.
- Clade I mpox virus (MPXV) has historically only been reported in five countries in Central Africa. There is now increasing transmission of clade I mpox in the Democratic Republic of Congo (DRC), and cases are also being reported from other surrounding countries in Central and East Africa.
- The countries reporting laboratory-confirmed Clade I mpox (historic or current) include: the DRC, Republic of Congo, Central African Republic, Burundi, Rwanda, Uganda, Kenya, Cameroon and Gabon. The countries where there may be a risk of Clade I mpox exposure (base on sharing a border with the DRC) currently include: Angola, South Sudan, Tanzania, and Zambia. Given the rapid spread of Clade I in the African region,

please check the UKHSA mpox pages regularly for any updates to the countries included in the list above.

- There is evidence of sustained sexual transmission of clade I MPXV in the DRC. Sexual transmission should not be used to infer whether an mpox case is likely to be clade I or II.

Clinicians are asked to:

1. Be alert to the possibility of clade I mpox in all patients with suspected mpox if there is a link to the specified countries in the African region (as listed above).
2. Have a low threshold for testing for mpox in patients with clinically compatible presentations with a travel history irrespective of sexual history.
3. Isolate patients meeting the following criteria as a high consequence infectious disease and contact the Imported Fever Service to discuss urgent testing and typing:

   Confirmed or clinically suspected mpox cases but clade not yet known and:
   there is a travel history to the DRC or specified countries where there may be a risk of clade I exposure, or a link to a suspected case from those countries (listed above), within 21 days of symptom onset and/or
   there is an epidemiological link to a case of Clade I mpox within 21 days of symptom onset

4. Discuss any patient with suspected mpox and severe or disseminated disease with IFS, even if no travel history is identified.
5. Notify the local Health Protection teams on suspicion of Clade I mpox.

All confirmed Clade I mpox cases will be managed as HCID through the specialist HCID network.

Laboratories are requested to send all mpox positive samples tested locally **to RIPL** for clade differentiating tests **regardless of whether Clade I is suspected**. UKHSA will contact Trusts for samples for any mpox cases for which samples have not been received for clade typing.

Background: There are two known clades of MPXV: Clade I and Clade II. Transmission of mpox to humans can be due to zoonotic transmission or person-to-person spread. Historically, Clade I MPXV was associated with zoonotic transmission and known to circulate in 5 African countries; Cameroon, Central African Republic, the DRC, Gabon and the Republic of Congo. Infection with Clade I MPVX has been reported to cause more severe mpox disease with a higher case fatality rate. Between 25 July and 5 August 2024, confirmed Clade I MPXV cases have been reported from Burundi, Kenya, Rwanda and Uganda for the first time, which has expanded the geographical footprint of Clade I MPXV in the African Region. Clade II cases have been reported from Benin, Cameroon, Cote D'Ivoire, Ghana, Liberia, Nigeria and South Africa in 2024.

In 2023, the DRC reported the highest annual number of Clade I MPXV cases, with a geographical expansion of the outbreak and the first reports of sexual transmission of Clade I MPXV. So far in 2024, the suspected case numbers being reported are higher than in the equivalent 2023 period. In South Kivu province, in the east of the DRC, sexual transmission of clade I MPXV has been reported, including infection of female sex workers. Clade I MPXV remains a high consequence infectious disease (HCID) in the UK. An mpox variant, now known as clade Ib, detected in South Kivu has been identified that may render currently available clade-typing assays unreliable for clade I MPXV. Additional testing pathways have been developed at the Rare and Imported Pathogens Laboratory (RIPL) as an interim measure and will be supplemented by whole genome sequencing where possible. Clade I MPXV has never been identified in the UK and the overall risk of Clade I MPXV to the UK population is considered low. However, given the ongoing outbreaks, it is important to remain alert to cases that have a link to specified countries or with an unusual presentation compared to Clade IIb mpox cases, which have been seen in the UK since 2022. The operational case definition has been updated following the recent changes in mpox epidemiology.

Operational case definition
The following patients should be managed as HCID cases (pending confirmation of clade type where appropriate):

- Confirmed mpox case where clade I has been confirmed
- Confirmed or clinically suspected mpox case but clade not yet known and:
    - there is a travel history to the DRC or specified countries where there may be a risk of clade I exposure, or a link to a suspected case from those countries (listed below), within 21 days of symptom onset and/or
      there is an epidemiological link to a case of Clade I mpox within 21 days of symptom onset

The countries identified on this list are those where clade I cases have been reported, as well as countries bordering those with ongoing Clade I transmission. They include the DRC, Republic of Congo, Central African Republic, Burundi, Rwanda, Uganda, Kenya, Cameroon, Gabon, Angola, South Sudan, Tanzania, and Zambia. This case definition and country list is available here. Given the rapid spread of Clade I in the African region, please check the UKHSA mpox pages regularly for any updates to the countries included.

The following patients should be managed using standard mpox precautions (NIPCM), and do not require HCID precautions:

- confirmed as Clade II MPXV, or
- confirmed or clinically suspected mpox but clade not known, and all of the following conditions apply:
    - there is no history of travel to the DRC or specified surrounding countries within 21 days of symptom onset
    - there is no link to a suspected case from the DRC or specified surrounding countries within 21 days of symptom onset

When assessing a patient for suspected mpox, clinicians should assess the travel and contact history as above. All cases meeting the operational definition of an HCID should be discussed with the Imported Fever Service (0844 778 8990). Cases where the clade is unknown, but who have a travel or contact history as above, should be discussed with the Imported Fever Service as soon as possible to ensure appropriate testing and escalation.

Implications & Recommendations for UKHSA Regions

Suspected mpox cases who may meet the operational definition of a HCID should be discussed with the Imported Fever Service. The epidemiological situation will remain under close review and operational definitions may be updated as further information emerges.

Implications & Recommendations for Local Authorities

Public health leads in local authorities should be aware of the updated operational case definition and are requested to send this briefing note to commissioned sexual health services.

Implications & Recommendations for UKHSA sites and services

Samples sent directly to RIPL for mpox testing will have clade typing performed routinely if positive. Where testing for mpox is performed locally, all positive samples **must be sent to** RIPL for clade testing, regardless of whether there are potential links to clade I or travel from the African region. https://www.gov.uk/guidance/monkeypox-diagnostic-testing An mpox variant, now known as clade Ib, detected in one region of the DRC has been identified that may render currently available clade-typing assays unreliable for clade I MPXV. Additional

testing pathways have been developed at the Rare and Imported Pathogens Laboratory (RIPL) as an interim measure and will be supplemented by whole genome sequencing where possible.

In either circumstance, if the operational case definition is met cases should be discussed with the IFS to expedite testing.

Implications & Recommendations for NHS

Clinicians should be alert to the possibility of clade I mpox if there is a link to the specified countries in the African region, and those treating patients with suspected mpox who may meet the operational definition of an HCID (as outlined above) should discuss with the Imported Fever Service (0844 778 8990) to expedite testing and ensure appropriate escalation. Patients with severe disease should also be discussed with the IFS. Clinicians are asked to notify the local Health Protection teams on suspicion of Clade I mpox.
All samples from all individuals testing positive for mpox (regardless of whether there are potential links to clade I or travel from the African region) must be sent to the UKHSA RIPL for clade testing. https://www.gov.uk/guidance/monkeypox-diagnostic-testing Guidance on returning healthcare workers from the above list of countries will be released soon.

If Clade I MPXV infection is suspected from initial case investigation, the local Infection Prevention and Control team should be contacted, and the patient should immediately be isolated in a negative-pressure, single room or a single room with dedicated medical equipment. Positive pressure single rooms should not be used. Suspected or confirmed Clade I mpox cases should be managed as a HCID requiring transmission-based precautions and enhanced personal protective equipment (PPE) as outlined in the National Infection Prevention and Control Manual.

Where suspected cases meeting the operational case definition present in primary care, General Practitioners should contact their local infection service for advice, including appropriate arrangements for transfer into secondary care and immediate precautions in the setting. The case should be notified to the local Health Protection Team on suspicion of infection as above.

If clade I MPXV infection is confirmed, the HCIDN and public health responses should be activated through the usual procedures. If clade testing is initially indeterminate and further testing (including sequencing) is required, the treating clinicians should discuss the risk assessment with the IFS. If there are clinical and / or epidemiological risk factors, the case should be managed as an HCID pending further testing, and the HCIDN and public health response activated.

References/ Sources of information

1. https://www.gov.uk/guidance/hcid-status-of-monkeypox
   https://www.gov.uk/guidance/monkeypox-diagnostic-testing
2. https://www.gov.uk/guidance/imported-fever-service-ifs
3. Eurosurveillance | Ongoing mpox outbreak in Kamituga, South Kivu province, associated with monkeypox virus of a novel Clade I sub-lineage, Democratic Republic of the Congo, 2024