Surveillance, case investigation and contact tracing for monkeypox

Interim guidance 25 August 2022



Key points

- A multi-country outbreak of monkeypox is ongoing in all six WHO regions and the number of reported cases has been increasing since May 2022. The overall goal of surveillance, case investigation and contact tracing in this context is to stop human-to-human transmission and to control the outbreak.
- The key objectives of surveillance and case investigation for monkeypox in the current context are to rapidly identify cases and clusters in order to provide optimal clinical care; to isolate cases to prevent further transmission; to identify, manage and follow up contacts to recognize early signs of infection; to identify risk groups for infection and for severe disease; to protect frontline health workers; and to tailor effective control and prevention measures.
- As the number of cases increases with the expansion of surveillance activities, immediate actions should focus on: informing those who may be most at risk for monkeypox virus (MPXV) infection with accurate information; offering pre- and post-exposure vaccination to at risk population groups; stopping further spread; and protecting vulnerable individuals and frontline workers.
- Clinicians should report suspected cases immediately to local and national public health authorities.
- Probable and confirmed cases of monkeypox should be reported as early as possible, including a minimum dataset of epidemiologically relevant information, to WHO through IHR national focal points (NFPs) under Article 6 of the International Health Regulations (IHR 2005).
- If monkeypox is suspected, case investigation should consist of clinical examination of the patient while using appropriate personal protective equipment (PPE), questioning the patient about possible sources of infection, and safe collection and dispatch of specimens for monkeypox virus laboratory examination.
- As soon as a suspected case is identified, contact identification and contact tracing should be initiated.
- Contacts of probable and confirmed cases should be monitored, or should self-monitor, daily for any sign or symptom for a period of 21 days from last contact with a case or their contaminated materials during the infectious period.
- Quarantine or exclusion from work are not necessary during the contact tracing period as long as no symptoms develop. During the 21 days of monitoring, WHO encourages contacts without any symptoms to rigorously practice hand hygiene and respiratory etiquette, avoid contact with immunocompromised people, children or pregnant women, and avoid any form of sexual contact. Non-essential travel is discouraged.

Changes from earlier version

This is an updated version of the previous interim guidance on Surveillance, case investigation and contact-tracing published on 24 June 2022. On 23 July, the Director General of WHO declared the multi-country outbreak of monkeypox to be a Public Health Emergency of International concern (PHEIC). This interim guidance has been updated with the latest information on symptomatology and epidemiological parameters, and to align with the Temporary Recommendations issued by the Director General.¹ The updated suspected case definition includes known contacts with prodromal signs or symptoms, and both suspected and probable case definitions have been updated to capture additional clinical characteristics such as mucosal lesions. New variables have been added to the minimal dataset of probable and confirmed cases to be shared with WHO. This version of the document contains the first definition of monkeypox-related death for surveillance purposes. It will be updated as further information becomes available.

Introduction

This guidance serves to provide interim recommendations for surveillance, case investigation and contact tracing for human monkeypox in the context of the current global multi-country outbreak.² Since May 2022, the number of monkeypox cases reported globally has been steadily increasing and many countries have reported their first monkeypox case ever.³ This is the first time that sustained community transmission is occurring in areas outside West or Central Africa.

The incubation period of monkeypox has historically ranged from 5 to 21 days.² Typically, the prodromal phase of clinical illness lasts 1-5 days during which time patients may experience fever, headache, back pain, muscle aches, and lymphadenopathy. This is followed by a second phase which typically occurs after the fever subsides, with the appearance of skin and/or mucosal rash, which might include a single or multiple lesions. Typically, the lesions progress through macules, papules, vesicles, and pustules, before crusting over and desquamating over a period of 2 to 4 weeks. In the context of this outbreak, patients are presenting more mucosal lesions than previously described, and often these are localized in the genital or perineal/perianal area as well as in the mouth and on the eyes.⁴ Lesions might appear at different stages of progression and it has been observed that the rash can develop prior to typical prodromal or constitutional symptoms (such as fever, fatigue). Ano-rectal pain and bleeding (e.g. due to proctitis) has also been reported more often in this outbreak. Lymphadenopathy remains a common feature, usually appearing early in the course of illness.

Human-to-human transmission of monkeypox can occur through direct contact with infectious lesions of the skin or mucous membranes or body fluids from those lesions, this includes face-to-face, skin-to-skin, mouth-to-mouth or mouth-to-skin contact and respiratory droplets (and possibly short-range aerosols requiring prolonged close contact). The virus then enters the body through broken skin, mucosal surfaces (e. g. oral, pharyngeal, ocular, genital or anal), or via the respiratory tract. The infectious period can vary, but generally patients are considered infectious from the time of symptom onset until skin lesions have crusted, the scabs have fallen off and a fresh layer of skin has formed underneath. Transmission can also occur from the environment to humans from contaminated clothing or linens that have infectious skin particles (also described as fomite transmission). If shaken, these particles can disperse into the air and be inhaled, land on broken skin or mucosal membranes and lead to transmission and infection; one documented health worker infection has been published suggesting monkeypox was acquired through contact with contaminated bedding.⁵ Other two cases in health workers, in France⁶ and in Portugal (reported to WHO), have been infected through an accidental contaminated needle stick injury.

For respiratory transmission, close proximity and extended exposure appear to be necessary. While virus has been found in the semen of affected patients,^{4,7–9} the role of sexual transmission through seminal fluids is not yet well understood.

During pregnancy, virus can cross the placenta causing intrauterine exposure of the foetus and congenital infection of the infant.¹⁰

The sudden appearance of monkeypox in countries where this disease has never been reported or where in recent years there have only been cases linked to travel to/from West Africa — is unexpected. Transmission, initially amplified by travel and gatherings in several countries, has been sustained among men who have sex with men, and this group currently represents those at highest risk of getting infected.³ Most reported cases have not had severe disease, ^{3,4,8,11,12} although many have developed complications and/or required hospitalization for management of severe pain.^{4,11}

Several monkeypox-related deaths have now been reported in countries outside West and Central Africa.³ Some, but not all, patients had underlying risk factors (e.g. being immunocompromised or immunosuppressed). Several, but not all, patients died from encephalitis.

The overall goal of surveillance, case investigation and contact tracing in this context is to break chains of human-tohuman transmission and stop the outbreak.

Transmission from and to animals

Monkeypox is a zoonotic infection which can be transmitted from animals to humans, from humans to humans, and potentially from humans to animals. Current evidence suggests that the 2022 outbreak does not involve multiple zoonotic spillover events, and transmission is sustained through human-to-human spread. Surveillance of monkeypox in animal populations is beyond the scope of this document. Countries are encouraged to report cases of monkeypox in animals to the World Organization for Animal Health (WOAH) with all relevant animal health information as described in Article 1.1.5 of the Terrestrial Animal Health Code, by email to information.dept@woah.org.

Surveillance Case Definitions

The case definitions for use in this outbreak may be reviewed as more evidence becomes available.

For further guidance on testing please refer to Laboratory testing for the monkeypox virus: Interim guidance.¹³

Suspected case:

i) A person who is a contact of a probable or confirmed monkeypox case in the 21 days before the onset of signs or symptoms, and who presents with any of the following: acute onset of fever (>38.5°C), headache, myalgia (muscle pain/body aches), back pain, profound weakness or fatigue.

OR

ii) A person presenting since 01 January 2022 with an unexplained acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions in the ano-genital region or elsewhere on the body. Mucosal lesions may include single or multiple oral, conjunctival, urethral, penile, vaginal, or ano-rectal lesions. Ano-rectal lesions can also manifest as ano-rectal inflammation (proctitis), pain and/or bleeding.

AND

for which the following common causes of acute rash or skin lesions do not fully explain the clinical picture: varicella zoster, herpes zoster, measles, herpes simplex, bacterial skin infections, disseminated gonococcus infection, primary or secondary syphilis, chancroid, lymphogranuloma venereum, granuloma inguinale, molluscum contagiosum, allergic reaction (e.g., to plants); and any other locally relevant common causes of papular or vesicular rash.

N.B. It is not necessary to obtain negative laboratory results for listed common causes of rash illness in order to classify a case as suspected. Further, if suspicion of monkeypox infection is high due to either history and/or clinical presentation or possible exposure to a case, the identification of an alternate pathogen which causes rash illness should not preclude testing for MPXV, as co-infections have been identified.

Probable case:

A person presenting with an unexplained acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions in the ano-genital region or elsewhere on the body. Mucosal lesions may include single or multiple oral, conjunctival, urethral, penile, vaginal, or ano-rectal lesions. Ano-rectal lesions can also manifest as ano-rectal inflammation (proctitis), pain and/or bleeding.

AND

One or more of the following:

- has an epidemiological link¹ to a probable or confirmed case of monkeypox in the 21 days before symptom onset
- Identifies as gay, bisexual or other man who has sex with men
- has had multiple and/or casual sexual partners in the 21 days before symptom onset
- has detectable levels of anti-orthopoxvirus (OPXV) IgM antibody² (during the period of 4 to 56 days after rash onset); or a four-fold rise in IgG antibody titer based on acute (up to day 5-7) and convalescent (day 21 onwards) samples; in the absence of a recent smallpox/monkeypox vaccination or other known exposure to OPXV
- has a positive test result for orthopoxviral infection (e.g. OPXV-specific PCR without MPXV-specific PCR or sequencing)³

Confirmed case:

A person with laboratory confirmed monkeypox virus infection by detection of unique sequences of viral DNA by real-time polymerase chain reaction (PCR)^c and/or sequencing.

Discarded case:

A suspected or probable case for which laboratory testing of lesion fluid, skin specimens or crusts by PCR and/or sequencing is negative for MPXV^c. Conversely, a retrospectively detected probable case for which lesion testing can no longer be adequately performed (i.e., after the crusts fall off) and no other specimen is found PCR-positive, would remain classified as a probable case. A suspected or probable case should not be discarded based on a negative result from an oropharyngeal, anal or rectal swab.

These case definitions were developed with a view to balance the importance of detecting cases and interrupting chains of transmission, while avoiding an overly sensitive definition that would overburden public health, diagnostic and treatment resources. Public health authorities may adapt these case definitions to suit local circumstances. All efforts should be made to avoid unnecessary stigmatization of individuals and communities potentially affected by monkeypox.

These definitions are for surveillance purposes and should not be used to guide clinical management. WHO interim guidance for Clinical Management and Infection Prevention and Control for monkeypox has been published separately.⁵

¹ The person has been exposed to a probable or confirmed monkeypox case. Please see below definition of a contact.

² Serology can be used for retrospective case classification for a probable case in specific circumstances such as when diagnostic testing through PCR of skin lesion specimens has not been possible, or in the context of research with standardized data collection. The primary diagnostic test for monkeypox diagnosis is PCR of skin lesion material or other specimen such as an oral or nasopharygeal swab as appropriate. Serology should not be used as a first line diagnostic test.

³ PCR on a blood specimen may be unreliable and should also not be used alone as a first line diagnostic test. If blood PCR is negative and was the only test done, this is not sufficient to discard a case that otherwise meets the definition of a suspected for probable case. This applies regardless of whether the blood PCR was for OPXV or MPXV specific.

Surveillance

The key objectives of surveillance and case investigation for monkeypox in the current context are to rapidly identify cases and clusters of infections as well as the sources of infection as soon as possible in order to: provide optimal clinical care; isolate cases to prevent further transmission; identify, manage and follow-up contacts to recognize early signs of infection; identify risk groups for infection and for severe disease; protect frontline health workers; and tailor effective control and prevention measures.

One case of monkeypox is considered an outbreak. Because of the public health risks associated with a single case of monkeypox, clinicians should report suspected cases immediately to national or local public health authorities regardless of whether they are also exploring other potential diagnoses, according to the case definitions above or nationally tailored case definitions. Probable and confirmed cases of monkeypox should be reported as early as possible, including a minimum dataset of epidemiologically relevant information, to WHO through national IHR focal points (NFPs) under Article 6 of the International Health Regulations (IHR 2005).

Countries and clinicians should be on alert for signals related to patients presenting with monkeypox. It is important to note that patients may present to various community and other health facility settings including but not limited to primary care, fever clinics, sexual health services, infectious disease units, obstetrics and gynaecology, emergency departments, and dermatology clinics. Guidance for clinical management, infection prevention and control, and the safe collection of samples for confirmatory testing should therefore be disseminated widely.^{5,13} In countries detecting cases of monkeypox, epidemiological and transmission patterns should be investigated wherever possible in order to inform ongoing response activities to control the outbreak.

Indicators for monitoring the quality of monkeypox surveillance include:

- 1. Proportion of cases with complete demographic information
- 2. Proportion of suspected cases with laboratory testing performed.
- 3. Proportion of cases with complete clinical and risk factor information.

Indications for monkeypox testing

Any individual meeting the definition for a suspected case should be offered monkeypox testing, where resources allow. In the absence of skin or mucosal lesions, PCR can be done on an oropharyngeal, anal or rectal swab. However, the interpretation of results from oropharyngeal, anal and rectal swabs requires caution; while a positive result is indicative of monkeypox infection, a negative result is not enough to exclude the infection.

Due to the range of conditions that cause skin and mucosal rashes, it can be challenging to differentiate monkeypox solely based on the skin and mucosal clinical presentation, particularly for cases with an atypical presentation. The decision to test should be based on both clinical and epidemiological factors, linked to an assessment of the likelihood of infection. When suspicion of monkeypox infection is high due to history and/or clinical presentation, the identification of an alternate pathogen which causes rash illness should not preclude testing for MPXV, as coinfections have been identified. Given the epidemiological criteria observed in the outbreak, criteria such as being a man who has sex with men, reporting a high number of sexual partners in the prior three weeks, and having attended a gathering where a confirmed case was reported can be suggestive of the need to test for MPXV.

For study purposes, countries can retrospectively expand their testing to residuals of specimens collected before May 2022 from patients presenting for sexually transmitted infection (STI) screening and/or with symptoms suggestive of monkeypox.

Reporting

WHO has published and updated the monkeypox Case Reporting Form (CRF)¹⁴ which constitutes the minimum data countries are requested to report to the respective WHO Regional Office, and includes the following information:

- Record ID
- Reporting Country
- Reporting location (subnational ADM1 level)
- Date of notification
- Case classification
- Age, sex, gender, sexual orientation
- Health worker
- Sex worker
- Medical history (pregnancy, immunosuppression, HIV status, HIV PrEP use)
- Smallpox and monkeypox vaccination status and vaccination date
- Clinical signs or symptoms
- Date of onset of first symptoms
- Presence of rash
- Date of rash onset
- Name of concurrent sexually transmitted infections
- Number of sex partners in the last three months
- Monkeypox treatment
- Hospital admission
- Intensive care unit (ICU) admission
- Complications
- Recent travel history (in the 21 days before onset of illness)
- Recent exposure to a probable or confirmed case (in the 21 days before onset of illness)
- Nature of contact with probable or confirmed case (where relevant)
- Contact with animals (in the 21 days before onset of illness)
- Mode of transmission
- Type of specimen collected for diagnosis
- Method of confirmation (where done)
- Genomic characterization and clade (if available)
- Accession number of the genomic sequence uploaded to public database
- Outcome status at time of reporting

Case investigation

During human monkeypox outbreaks, close physical contact, including sexual intercourse, with infected persons is the most significant risk factor for monkeypox virus infection. If monkeypox is suspected, the investigation should consist of:

- (i) clinical examination of the patient using appropriate infection prevention and control (IPC) measures as reported in the specific guidance.⁵
- (ii) questioning the patient about possible sources of infection and the presence of similar illnesses in the patient's community and contacts, both prior to becoming a case (backward contact tracing) to identify the source, and from the beginning of the infectious period through isolation (forward contact tracing) to reduce onward transmission. Current evidence suggest that a case is infectious from the symptom onset to the moment all vesicle scabs fall off.^{15,16}
- ⁽ⁱⁱⁱ⁾ safe collection and dispatch of specimens for monkeypox laboratory examination.¹³

Surveillance, case investigation and contact tracing for monkeypox: interim guidance

In addition to the minimum dataset (CRF), WHO has published and updated the monkeypox Case investigation form (CIF) designed as a tool for Member States and researchers to conduct in-depth epidemiological investigation of suspected, probable and confirmed cases of monkeypox, as well as their contacts, either prospectively or retrospectively. The CIF is designed to address the key unknowns about MPXV transmission in this outbreak, such as infectious period, most efficient route of transmission, clinical presentation and main risk factors for infection and severe disease. The full form is meant for in-country use and the data are not required to be reported to WHO.¹⁴

Exposure investigation should cover the period of 21 days prior to symptom onset. Any patient with suspected monkeypox should be isolated during the presumed and known infectious periods, that is during the prodromal and rash stages of the illness, respectively. Laboratory confirmation of suspected cases is important but should not delay implementation of public health actions.

Retrospective cases found by active search may no longer have the clinical symptoms of monkeypox (they have recovered from acute illness) but may exhibit scarring and other sequelae. It is important to collect epidemiological information from retrospective cases in addition to active ones. Retrospective cases cannot be laboratory confirmed; however, serum from retrospective cases can be collected and tested for anti-orthopoxvirus IgM and/or IgG antibodies to aid in their probable case classification.

Samples taken from persons with suspected monkeypox should be safely handled by trained staff working in suitably equipped laboratories. National and international regulations on transport of infectious substances should be strictly followed during sample packing and transportation. Careful planning is required to consider national laboratory testing capacity. Clinical laboratories should be informed in advance of samples to be submitted from persons with suspected or confirmed monkeypox, so that they can minimise risk to laboratory workers and, where appropriate, safely perform laboratory tests that are essential for clinical care. For more details, please refer to the Laboratory testing for monkeypox virus interim guidance.¹³

Contact tracing

Contact tracing is a key public health measure to control the spread of infectious disease pathogens such as monkeypox virus. It allows for the interruption of chains of transmission and can also help people at a higher risk of developing severe disease to more quickly identify their exposure, so they can monitor their health status and seek medical care quickly if they become symptomatic. Cases should be promptly interviewed as soon as possible to elicit the names and contact information of all potential contacts and identify places visited where contact with other people may have occurred. Contacts of cases should be notified within 24 hours of identification and advised to monitor their health status and seek medical care if they develop symptoms.

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