Surveillance, case investigation and contact tracing for monkeypox

Interim guidance
24 June 2022

World Health Organization

Key points

- A multi-country outbreak of monkeypox is ongoing in several regions of the world and the number of reported cases has markedly increased since May 2022. The overall goal of surveillance, case investigation and contact tracing in this context is to stop human-to-human transmission 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 protect frontline health workers; to identify risk groups; and to tailor effective control and prevention measures.
- The situation is rapidly evolving and WHO expects there will be more cases of monkeypox identified as surveillance continues and expands. Immediate actions focus on: informing those who may be most at risk for monkeypox virus (MPXV) infection with accurate information; offer post-exposure prophylaxis to high and medium risk contacts, stopping further spread; and protecting 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 forward 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 guidance published on 22 May 2022. The guidance has been updated to apply to all countries with potential monkeypox cases, including countries that have historically documented monkeypox transmission and those that have not. The confirmed case definition has been updated to include polymerase chain reaction (PCR) positive cases, regardless of associated symptoms or their absence, in order to more fully characterize pre-symptomatic, pauci-symptomatic or asymptomatic infections. The contact definition has been amended to include more examples of potential exposures, as well as the contact risk levels established by the monkeypox immunization guidance. This guidance also links to recently developed epidemiological tools, including: the minimum data set Case Reporting Form (CRF) for reporting to WHO; an in-depth Case Investigation Form (CIF) for

Member States' use to conduct epidemiologic investigations of cases and contacts; and recent guidance documents for clinical management and infection prevention and control, as well as vaccines and immunization for monkeypox.

This guidance will be updated as additional information about the outbreak becomes available.

Introduction

This guidance serves to provide interim recommendations for the surveillance, case investigation and contact tracing for human monkeypox in the context of the current multi-country outbreak in several regions of the world.[1] This is the first time that cases and sustained chains of transmission have been reported in countries without direct or immediate epidemiological links to areas of West or Central Africa. The number of reported confirmed and probable cases has markedly increased since May 2022.

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 a centrifugal synchronous rash that may involve the oral mucous membranes, conjunctiva, cornea and/or genitalia. Typically, this rash progresses through macules, papules, vesicles, and pustules, before crusting over and desquamating over a period of 2 to 3 weeks. In the context of this outbreak, some patients are presenting with atypical symptoms or progression such as one or a few lesions localized to the genital or perineal/perianal area, asynchronous rash (lesions appearing at different stages of progression), or the appearance of rash prior to the development of typical prodromal or constitutional symptoms (such as fever, fatigue). 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 skin or mucocutaneous 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 and genital), or via the respiratory tract. The infectious period can vary, but generally patients are considered infectious 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 virus transmitted through contact with contaminated bedding.[3]

For respiratory transmission close proximity and longer exposure appear to be necessary. While virus has been found in the semen of affected patients in a few cases to date,[4,5] the role of sexual transmission through seminal or vaginal 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.[6]

The current epidemiological pattern of this outbreak (as of 22 June 2022; see WHO Disease Outbreak News)[1] — the sudden appearance of monkeypox in several countries where this disease has never been reported or where in recent years there have only been cases linked to travel to/from West or Central Africa — is unexpected. Transmission appears to have been amplified by travel and gatherings in several countries. Cases of monkeypox have so far been identified primarily but not exclusively among men, including men presenting to sexual health clinics with genital rash;[1] Most reported cases have not been severe.[4,7,8]

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

Surveillance Case Definitions

The case definitions for use in this outbreak may be reviewed as additional information becomes available.

For further guidance on testing please refer to Laboratory testing for the monkeypox virus: Interim guidance.[9]

Suspected case:

A person of any age presenting since 01 January 2022 with an unexplained acute rash or one or more acute skin lesions

AND

one or more of the following signs or symptoms:

- Headache
- Acute onset of fever (>38.5°C)
- Lymphadenopathy (swollen lymph nodes)
- Myalgia (muscle pain/body aches)
- Back pain
- Asthenia (profound weakness)

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 coinfections have been identified.

Probable case:

A person meeting the case definition for a suspected case

AND

One or more of the following:

- has an epidemiological link [prolonged[a] face-to-face exposure in close proximity, including health workers without appropriate PPE (gloves, gown, eye protection and respirator)[3]; direct physical contact with skin or skin lesions, including sexual contact; or contact with contaminated materials such as clothing, bedding or utensils] to a probable or confirmed case of monkeypox in the 21 days before symptom onset
- has had multiple or anonymous sexual partners in the 21 days before symptom onset has detectable levels of anti-orthopoxvirus (OPXV) IgM antibody[b] (during the period of 4 to 56 days after rash onset); or a four-fold rise in IgG antibody titre 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)[c]

[a] Evidence is currently lacking as to the duration of exposure necessary for infection by the respiratory route, including how it relates to the severity of the index case's disease. Characterization of this parameter is one of the goals of the case investigation form described below.
[b] 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.
[c] 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.

Confirmed case:

Laboratory confirmed monkeypox virus by detection of unique sequences of viral DNA by real-time polymerase chain reaction (PCR)[c] and/or sequencing.

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

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.

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.[3]

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; to isolate cases to prevent further transmission; to identify, manage and follow-up contacts to recognize early signs of infection; to protect frontline health workers; to identify risk groups; and to tailor effective control and prevention measures based on the most commonly identified routes of transmission.

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 IHR national 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 health care 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.[3,9] 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; severely ill suspected cases should be tested if at all possible. Due to the range of conditions that cause skin rashes, it can be challenging to differentiate monkeypox solely based on the 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 man (MSM), 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.

Reporting

WHO has published a Case reporting Form (CRF)[10] 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
- Medical history (pregnancy, immunosuppression, HIV status)
- Smallpox vaccination status and vaccination date
- Clinical signs or symptoms
- Date of onset of first symptoms
- Presence of rash
- Date of rash onset
- Concurrent sexually transmitted infections
- Monkeypox treatment
- Hospital admission
- Intensive care unit (ICU) admission
- 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
- Mode of transmission
- Type of specimen collected for diagnosis
- Method of confirmation (where done)
- Genomic characterization (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 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.[3]

(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.[11,12]

(iii) safe collection and dispatch of specimens for monkeypox laboratory examination.[9]

In addition to the minimum dataset (CRF), WHO has published a 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, such as the highest-risk behaviours, and exposure times necessary for respiratory transmission. The full form is meant for in-country use and the data are not required to be reported to WHO.[10]

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 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.[9]

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 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. Case-patients should be interviewed to elicit the names and contact information of all such persons, as well as to identify places visited where contact with other people may have occurred. Contacts should be notified within 24 hours of identification.

In the current context, as soon as a suspected case is identified, contact identification and contact tracing should be initiated, while further investigation of the source case is ongoing to determine if the case can be classified as probable or confirmed; in the event that the case is discarded, contact tracing may be aborted.

Definition of a contact

A contact is defined as a person who, in the period beginning with the onset of the source case's first symptoms and ending when all scabs have fallen off, has had one or more of the following exposures with a probable or confirmed case of monkeypox:

- direct skin-to-skin physical contact (such as touching, hugging, kissing, intimate or sexual contact)
- contact with contaminated materials such as clothing or bedding, including material dislodged from bedding or surfaces during handling of laundry or cleaning of contaminated rooms
- prolonged face-to-face respiratory exposure in close proximity
- respiratory exposure (i.e., possible inhalation of) or eye mucosal exposure to lesion material (e.g., scabs/crusts) from an infected person
- The above also apply for health workers potentially exposed in the absence of proper use of appropriate personal protective equipment (PPE)

Based on the recommendation to offer smallpox or monkeypox vaccine for post-exposure prophylaxis, WHO has established three levels of risk for contacts of a monkeypox case as follows:[13]

High risk

Direct exposure of skin or mucous membranes to skin or respiratory secretions of a person with confirmed, probable or suspected monkeypox, their body fluids (e.g., lesion vesicular or pustular fluid) or potentially infectious material (including clothing or bedding) if not wearing appropriate PPE. This includes:

- inhalation of droplets or dust from cleaning contaminated rooms
- mucosal exposure due to splashes from body fluids
- physical contact with someone who has monkeypox, including direct contact during sexual activities. This includes face-to-face, skin-to-skin or mouth-to-skin contact or exposure to body fluids or contaminated materials or objects (fomites)
- normally sharing a residence (permanently or occasionally) during the presumed incubation period with a person who has been diagnosed with monkeypox, or
- a penetrating sharps injury from a contaminated device or through contaminated gloves.

Medium risk

- no direct contact but close proximity in the same room or indoor physical space as a symptomatic monkeypox patient, if not wearing appropriate PPE.[2]

Lower or minimal risk

- contact with a person with confirmed, probable or suspected monkeypox or an environment that may be