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Monkeypox

Fact Sheet

Monkeypox outbreak at a glance

Monkeypox is a viral zoonotic disease that is endemic in Central and West Africa. Since 13 May 2022, cases of monkeypox have been reported to WHO from 12 Member States that are not endemic for the monkeypox virus, across three WHO regions, namely the Region of the Americas, the European region, and the Western Pacific region. The identification of clusters of monkeypox cases in several non-endemic countries with no direct travel links to an endemic area is atypical. Based on currently available information, cases have mainly but not exclusively been identified amongst men who have sex with men (MSM) seeking care in primary care, secondary care, and sexual health services.

Historically, vaccination against smallpox has been shown to be protective against monkeypox. Immunity from smallpox vaccination will be limited to older persons since populations worldwide under the age of 40 or 50 years no longer benefit from the protection afforded by prior smallpox vaccination programs.

The infectious agent

Monkeypox is caused by the monkeypox virus, a member of the Orthopoxvirus genus in the family Poxviridae. It is an enveloped double-stranded DNA virus and there are two distinct genetic clades of the monkeypox virus – the Central African (Congo Basin) clade and the West African clade. The Congo Basin clade has historically caused more severe disease and was thought to be more transmissible.

Reservoir

The animal species identified as being susceptible to the monkeypox virus are rope squirrels, tree squirrels, Gambian pouched rats, dormice, non-human primates, and other species. The natural reservoir of the monkeypox virus has not yet been identified, though rodents are the most likely. Further studies are needed to identify how virus circulation is maintained in nature.

Transmission

Monkeypox is transmitted to humans through close contact with an infected person or animal, or with material contaminated with the virus.

Animal-to-human (zoonotic) transmission can occur from direct contact with the blood, bodily fluids, or cutaneous or mucosal lesions of infected animals. Eating inadequately cooked meat and other animal products of infected animals is a possible risk factor. People living in or near forested areas may have indirect or low-level exposure to infected animals.

Human-to-human transmission can result from close contact with respiratory secretions, skin lesions of an infected person or recently contaminated objects. Transmission via droplet respiratory particles usually requires prolonged face-to-face contact. Transmission can also occur via the placenta from mother to fetus (which can lead to congenital monkeypox) or during close contact during and after birth. While close physical contact is a well-known risk factor for transmission, it is unclear at this time if monkeypox can be transmitted specifically through sexual transmission routes. Studies are needed to better understand this risk.

Incubation period

The incubation period (interval from infection to onset of symptoms) of monkeypox is usually from 6 to 13 days but can range from 5 to 21 days.

Symptoms

Monkeypox is usually a self-limited disease with symptoms lasting from 2 to 4 weeks. Severe cases can occur. In recent times, the case fatality ratio has been around 3-6%.

The infection can be divided into two periods:

- The invasion period (lasts between 0-5 days) is characterized by fever, intense headache, lymphadenopathy (swelling of the lymph nodes), back pain, myalgia (muscle aches) and intense asthenia (lack of energy). Lymphadenopathy is a distinctive feature of monkeypox compared to other diseases that may initially appear similar (chickenpox, measles, smallpox)
- Skin eruption usually begins within 1-3 days of the appearance of fever. The rash tends to be more concentrated on the face and extremities rather than on the trunk. It affects the face (in 95% of cases), and palms of the hands and soles of the feet (in 75% of cases).

Also affected are oral mucous membranes (in 70% of cases), genitalia (30%), and conjunctivae (20%), as well as the cornea. The rash evolves sequentially from macules (lesions with a flat base) to papules (slightly raised firm lesions), vesicles (lesions filled with clear fluid), pustules (lesions filled with yellowish fluid), and crusts which dry up and fall off. The number of lesions varies from a few to several thousand. In severe cases, lesions can coalesce until large sections of skin slough off.

Severe cases occur more commonly among children and are related to the extent of virus exposure, patient health status and nature of complications. Underlying immune deficiencies may lead to worse outcomes. Complications of monkeypox can include secondary infections, bronchopneumonia, sepsis, encephalitis, and infection of the cornea with ensuing loss of vision. The extent to which asymptomatic infection may occur is unknown.

Clinical diagnosis

The clinical differential diagnosis that must be considered includes other rash illnesses, such as chickenpox, measles, bacterial skin infections, scabies, syphilis, and medication-associated allergies. Lymphadenopathy during the prodromal stage of illness can be a clinical feature to distinguish monkeypox from chickenpox or smallpox.

Laboratory diagnosis

Confirmation of monkeypox depends on the type and quality of the specimen and the type of laboratory test. Polymerase chain reaction (PCR) is the preferred laboratory test given its accuracy and sensitivity. For this, optimal diagnostic samples for monkeypox are from skin lesions – the roof or fluid from vesicles and pustules, and dry crusts. Where feasible, a biopsy is an option. PCR blood tests are usually inconclusive because of the short duration of viremia relative to the timing of specimen collection after symptoms begin and should not be routinely collected from patients.

As orthopoxviruses are serologically cross-reactive, antigen and antibody detection methods do not provide monkeypox-specific confirmation. Serology and antigen detection methods are therefore not recommended for diagnosis or case investigation where resources are limited.

Retrospective cases cannot be laboratory confirmed; however, serum from retrospective cases can be collected and tested for anti-orthopox virus antibodies to aid in their case classification.

Treatment

Clinical care for monkeypox should be fully optimized to alleviate symptoms, manage complications and prevent long-term sequelae. Patients should be offered fluids and food to maintain adequate nutritional status. Secondary bacterial infections should be treated as indicated.

While one vaccine (MVA-BN) and one specific treatment (tecovirimat) were approved for monkeypox, in 2019 and 2022 respectively, these countermeasures are not yet widely available.

Prevention

1. Reducing the risk of human-to-human transmission

Surveillance and rapid identification of new cases are critical for outbreak containment. During human monkeypox outbreaks, close contact with infected persons is the most significant risk factor for monkeypox virus infection. Health workers and household members are at a greater risk of infection. Health workers caring for patients with suspected or confirmed monkeypox virus infection, or handling specimens from them, should implement standard infection control precautions. If possible, persons previously vaccinated against smallpox should be selected to care for the patient.

Samples taken from people and animals with suspected monkeypox virus infection should be handled by trained staff working in suitably equipped laboratories. Patient specimens must be safely prepared for transport with triple packaging in accordance with WHO guidance for the transport of infectious substances.

2. Reducing the risk of zoonotic transmission

Over time, most human infections have resulted from a primary, animal-to-human transmission. Unprotected contact with wild animals, especially those that are sick or dead, including their meat, blood and other parts must be avoided. Additionally, all foods containing animal meat or parts must be thoroughly cooked before eating.

3. Preventing monkeypox through restrictions on animal trade

Some countries have put in place regulations restricting the importation of rodents and non-human primates. Captive animals that are potentially infected with monkeypox should be isolated from other animals and placed into immediate quarantine. Any animals that might have come into contact with an infected animal should be quarantined, handled with standard precautions and observed for monkeypox symptoms for 30 days.

4. Vaccination

Vaccination against smallpox was demonstrated through several observational studies to be about 85% effective in preventing monkeypox. Thus, prior smallpox vaccination may result in milder illness. Evidence of prior vaccination against smallpox can usually be found as a scar on the upper arm. At the present time, the original (first-generation) smallpox vaccines are no longer available to the general public.

5. Public health response

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 that their health status can be monitored and they can seek medical care faster if they become symptomatic. In the current context, as soon as a suspected case is identified, contact identification and contact tracing should be initiated. Case patients should be interviewed to elicit the names and contact information of all such persons. Contacts should be notified within 24 hours of identification.

Any patient with suspected monkeypox should be investigated and if confirmed, isolated until their lesions have crusted, the scab has fallen off and a fresh layer of skin has formed underneath.

In non-endemic countries, one case 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. Cases should be reported immediately, according to the case definitions below. Probable and confirmed cases should be reported immediately to WHO through IHR national focal points (NFPs) under the International Health Regulations (IHR 2005).

The current case definitions as of 25 February 2025 are as follows. Case definitions will be updated as necessary.

- **Suspected case**

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

OR

ii) 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 anorectal 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 mpox or MPXV 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 anorectal 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 link to a probable or confirmed case of mpox in the 21 days before symptom onset
- has had multiple and/or casual sexual partners in the 21 days before symptom onset
- has a positive test result for orthopoxviral infection (e.g., OPXV-specific PCR without MPXV-specific PCR or sequencing)

○ **Confirmed case**

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