Monkeypox and MPHO safety

The Notify MPHO safety group - position statement

Background

Monkeypox virus (MPXV) is a double-stranded, enveloped DNA virus of the *Orthopoxvirus* genus of the family *Poxviridae* that includes another 3 viruses pathogenic to humans: variola major virus, vaccinia virus, and cowpox virus (1). MPXV was discovered in 1958 (2) as a causative agent of a pox-like disease in animals. Animal-to-human transmission was first reported in the Democratic Republic of the Congo (DRC) in 1970 (3). Since then, sporadic local clusters of human infections have been reported in West and Central Africa, mainly in the DRC and Nigeria (4). The first known human cases of monkeypox (MPX) outside Africa were in the USA in 2003 (5). Only a few cases were subsequently imported into the US, UK, Singapore, Israel, and Benin, but they were successfully contained and controlled (6). In early May 2022, the first clusters of MPX cases were reported from several countries where the disease is not endemic and for the first-time sustained chains of transmission have been detected in countries without direct or immediate epidemiological links to areas of West or Central Africa (7). On 23 July 2022, the World Health Organization (WHO) declared monkeypox a Public Health Emergency of International Importance (PHEIC) due to the global spread and uncertainty surrounding the disease (8). The current outbreak of monkeypox in non-African countries affects mainly men who have sex with men (MSM) who have reported recent sex with one or multiple partners. There is currently no signal to indicate sustained transmission beyond these networks (8). As of 12 October 2022, WHO notified a total of 72,198 laboratory-confirmed cases, including 28 deaths, and 1,091 probable cases reported by 109 Member States across all 6 WHO regions (7). In the EU/EEA countries, the total number of confirmed cases was 20 455 on 11 October 2002 with a decrease in the weekly number of new cases from July (9).

The incubation period for MPX can range from five to 21 days (10). Initial symptoms may include fever, headache, chills, weakness, exhaustion, lymphadenopathy, and pain in the back and muscles. Pain and pruritus can be severe and out of proportion to the appearance of the rash. Within three days after the onset of these prodromal signs, a maculopapular rash starts from the site of primary infection and spreads centrifugally to other parts of the body. Palms and soles can be involved. Infected persons can present with a single lesion only and with mucosal lesions (11). Lymphadenopathy is a crucial clinical sign distinguishing MPX from smallpox. Skin lesions develop from the stage of macules to papules, vesicles, pustules, crusts, and scabs, which then fall off (10). Most cases of the current outbreak present with genital or peri-genital lesions, suggesting that transmission probably occurred through close physical contact during sexual activity among young men who have sex with men (MSM) (8). Further spread through secondary contacts including household transmissions is possible. Rarely do patients need hospitalisation including in ICUs. Deaths have also been reported (10).

The zoonotic transmission of the MPX occurs through direct contact with an infected animal's blood, other body fluids, or cutaneous/mucosal lesions. Human-to-human transmission can occur through close direct contact with an infected person's skin or mucosal lesions and respiratory secretions; respiratory droplets in prolonged face-to-face contact and exposure to contaminated fomites can also be involved in the transmission of the virus (1). Report of mother-to-child transmission during pregnancy (12) and viremia detected in infected animals and humans (13-15). Although the asymptomatic infection has been reported, it is not clear whether people without any symptoms can spread the disease or whether it can spread through other bodily fluids. The MPX viral DNA has been found in a range of bodily fluids (semen,

saliva, rectal swab, urine, and faecal samples) during the first 2 weeks of the illness and up to 16 days after the onset of the symptoms (16). In a retrospective analysis of previous outbreaks, prolonged shedding of viral DNA > 14 days after recovery was reported (17). It is not yet known whether infection can spread through these fluids or blood, tissues, and organs. MPX virus is very stable in the environment, it may survive for days to weeks in water, soil, and on refrigerated food (18). MPX transmission from a DNA-positive patient 19 days after symptom onset to a healthcare worker through needlestick injury occurred in Brazil, which suggests the possibility of transmissibility through blood during prolonged viremia in infection (19).

Diagnosis

Diagnosis of MPX is based on the clinical signs and laboratory testing of specimens from skin lesions. Viral DNA can also be detected in blood and other bodily fluids. Since the disease has a limited duration of viremia, scab swabs and aspirated fluid of the lesion are more appropriate than blood samples. WHO recommends a polymerase chain reaction (PCR) as the preferred laboratory test given its accuracy and sensitivity. Although some countries have developed PCR assays for the detection of MPXV (20-22), commercial PCR kits are under development and have limited availability (23-25). An approved/validated screening test for MPHO donors/donations is not available.

Treatment

Besides symptomatic therapy and appropriate clinical care, tecovirimat, an antiviral agent that was developed for smallpox was licensed by the European Medicines Agency (EMA) and the UK for the treatment of MPX based on data in animal and human studies (26). The use of tecovirimat should ideally be monitored in a clinical research context with prospective data collection.

Vaccination

Vaccines can be used for pre and post-exposure prophylaxis. Imvanex is a vaccine that could potentially be used to prevent monkeypox (27) and is already authorised to prevent smallpox in the EU. In the United States, the Jynneos vaccine is authorised to prevent both smallpox and monkeypox (28).

The overall risk of MPXV infection

ECDC assessed the overall risk of MPXV infection as moderate for people having multiple sexual partners (including some groups of MSM) and low for the broader population The likelihood of MPX spreading further in networks of people (such as MSM) with multiple sexual partners in the EU/EEA is considered high, and the likelihood of MPX spreading among the broader population is assessed as very low (9).

Risk of MPX transmission through MPHO

No cases of MPXV transmission through MPHO have been documented, thus the MPHO-associated risk of MPXV transmission is currently considered theoretical. The likelihood of the virus entering the MPHO supply and further transmission is low in countries implementing standard safety interventions and specific deferral of donors having multiple sexual partners (including some groups of MSM) in 21 days before donation or experiencing low case numbers. In addition, the consequences of possible transmission of MPXV via MPHO are unknown.

In populations where the incidence of MPXV is low, standard donor education and selection criteria to prevent pathogen transmission should significantly minimise the risk of donation by infectious donors. Post-donation disease reporting will allow potentially infected blood donations to be discarded. Enveloped MPXV is effectively inactivated by known and approved pathogen reduction technologies and during plasma fractionation (29 - 31). It is highly certain that pathogen-reduced plasma, platelets, and some processed tissues (eg. cortical or cancellous bone), as well as the PMDPs, can be considered safe regarding the transmission of MPXV.

However, the existence of viremia and reported vertical mother-to-child transmission strongly suggest that virus transmission via MPHO is possible. The increasing incidence in affected populations and the spread of infection to new countries, as well as the existence of asymptomatic cases, increase the likelihood that the virus escapes the standard preventive interventions and enters the MPHO supply. In addition, viable MPXV was isolated from rectal swabs (32), which suggests that the virus may be transmitted through faecal microbiota (FMT) products, although the risk of such transmission is unknown. These facts, together with the uncertainties about the survival of the virus in donated MPHO, clinical course after possible MPHO transmission, viremia of unknown duration during the disease, and its presence in incubation and post-symptomatic periods or asymptomatic cases, strongly indicate the need to implement certain precautionary measures, especially in countries with an increasing number of cases. Finally, new data and evidence are urgently needed to address these uncertainties, which may contribute to more accurate risk assessment and the use of appropriate MPHO safety interventions.

Specific MPHO precautionary measures

To prevent possible transmission of MPXV through MPHO, The Notify MPHO safety group (33) suggest implementing the following agent-specific precautionary measures:

- A person diagnosed with MPX is not eligible to donate MPHO during the clinical course of the disease and for a minimum of two weeks (14 days) after the resolution of symptoms and the disappearance of crusted vesicular lesions. If the illness required hospitalization, a longer period needs to be observed (up to three months);

- Implementation of specific selection criteria may help to examine the eligibility for a donation by persons at risk of MPXV infection, and to detect currently or recently MPXV-infected persons;

- Close contacts that include sexual partners, those living in the same household, and persons involved in caring for a person with MPX who have not used appropriate personal protective equipment should be deferred from donations of blood, cells and tissues for the period of maximal or double average incubation from the date of exposure;

- Determining the eligibility of potential organ donors who have been in contact with MPX cases is based on the assessed risk of exposure and consultation with an infectious disease specialist. Decisions on organ acceptance should follow the principle of weighing the risks and benefits of organs donated for transplantation;

- Eligibility to donate MPHO by donors vaccinated against MPX after exposure depends on the time since exposure, the clinical course, and the nature of the vaccine. The approved JYNNEOS vaccine is a live non-replicating vaccine that does not require post-vaccination deferral for MPHO donation.

- Reinforcing the post-donation reporting in the period of 14 days after blood and some cells and tissues donation;

- The screening of MPHO donors before donation seems to be of limited value, however, it may shorten the deferral period of persons recovered from the illness.

Currently, the MPX outbreak is developing quite dynamically, so it is necessary to follow the developments and closely monitor the national/local epidemiological situation and assess the risk to MPHOs accordingly.

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