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 include another 3 viruses pathogenic for 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 was 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, first clusters of MPX cases were reported from several countries where the disease is not endemic. Since then, the number of reported cases has reached almost 16,000 cases in 75 countries predominantly in Europe by 20 July 2022 (7,8). On 23 July 2022 the World Health Organization declared the monkeypox to be a public health emergency of international concern (PHEIC) (9).

The incubation period for MPX can range from five to 21 days (10). Initial symptoms are fever, headache, chills, weakness, exhaustion, lymphadenopathy, pain in the back and muscles. Within three days after onset of these prodromal signs a maculopapular rash starts from the site of primary infection and rapidly spreads centrifugally to other parts of the body. Palms and soles can be involved. 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 households transmissions are possible. Rarely patients need hospitalisation including in ICUs. Deaths have also been reported (10).

The MPX is transmitted to humans through a bite or close contact with an infected animal's blood, body fluids or cutaneous/mucosal lesions. The disease can be transmitted from one person to another through close direct contact with clinically manifested case through face-to-face, skin-to-skin, mouth-to-mouth or mouth-to-skin contact, including sexual contact, respiratory droplets and fomites (e.g. contact with the recently contaminated beddings of infected person) (1). Report of mother-to-child transmission during pregnancy (11) and viremia detected in infected animals and humans (12-14). Although 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. DNA from the monkeypox virus have been found in semen, but it is not yet known whether infection can spread through semen, vaginal fluids, amniotic fluids, breastmilk or blood and other tissues and organs

Diagnosis

Diagnosis of MPX is based on the clinical signs and laboratory testing of specimens from skin lesions and blood. 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 (15-17), commercial PCR kits are

under development and limited availability (18-20). Screening test for MPHO donation is not available.

Treatment

Besides symptomatic therapy and appropriate clinical care an antiviral agent known as tecovirimat that was developed for smallpox was licensed by the European Medicines Agency (EMA) and UK for the treatment of MPX based on data in animal and human studies (21). The tecovirimat should ideally be monitored in a clinical research context with prospective data collection.

Vaccination

Vaccines can be used for postexposure prophylaxis. Imvanex is a vaccine that could potentially be used to prevent monkeypox (22) is already authorised to prevent smallpox in the EU. In the United States, the Jynneos vaccine is authorised to prevent both smallpox and monkeypox (23).

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 experiencing low case numbers. In addition, the consequences of possible transmission of MPXV via MPHO are unknown.

In the 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 donations to be discarded. Enveloped MPXV is effectively inactivated by known and approved pathogen reduction technologies and during plasma fractionation (24 - 26). It is highly certain that pathogen reduced plasma, platelets and some tissues as well as the PMDPs can be considered safe in regard transmission of MPXV.

However, the existence of viremia and reported vertical mother-to-child transmission strongly suggest that virus transmission via MPHO is possible. On the other hand, 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. 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 pre 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 (27) suggests 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 two weeks (14 days) after the end of symptoms and the disappearance of crusted vesicular lesions. If the illness required hospitalization, the grace period is longer (up to three months);

- The implementation of specific selection criteria can help to examine the donation eligibility of persons at risk to be infected (according to WHO);

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

- Eligibility to donate MPHO by donors vaccinated against MPX after exposure depends on the development of the disease 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 principle of weighing the risks and benefits of organs donated for transplantation should be followed;

- 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.

Last update: July 26, 2022

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