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Summary of Current Evidence and Information– Monkeypox in Donor Screening and Transplantation

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Purpose

This document is a summary of evidence and information regarding donor screening for monkeypox virus (MPXV) and considerations for organ acceptance from donors with a history of MPXV based on peer-reviewed literature. This resource is subject to revision as new data accumulate and will be reviewed at least biannually for currency. The overarching objective of this document is to compile the latest information known for minimizing the risk of donor-derived MPXV while maximizing donor utilization.

Methods

The OPTN Ad Hoc Disease Transmission Advisory Committee (DTAC) and relevant stakeholders from the Centers for Disease Control and Prevention (CDC), American Society of Transplantation (AST), American Society of Transplant Surgeons (ASTS), Association of Organ Procurement Organizations (AOPO), American Association of Tissue Bank (AATB), US Food and Drug Administration (FDA), and Health Resources & Services Administration (HRSA) reviewed published literature. Specifically, DTAC and

relevant stakeholders assessed the available evidence as it relates to living and deceased donor screening and testing and recovery of organs from living or deceased donors with a history of monkeypox.

Discussion

Background: Current outbreak in US

The US Department of Health and Human Services declared monkeypox to be a public health emergency on August 4, 2022. The CDC, in conjunction with state and local public health partners, continues to confirm cases of monkeypox and provide updated case counts by state. As of September 2nd, 2022, over 19,900 cases have been reported in the US, with additional cases reported daily.

Among monkeypox cases reported to the CDC, and with data available, through July 22, 2022, the median age of infected persons is 35 years (IQR 30-41), and 99% of cases have been detected in men. 94% of infected persons report male-to-male close intimate or sexual contact and 41% are people living with HIV. Data also indicate that racial and ethnic minority groups are disproportionately affected.[i]

While the majority of US monkeypox cases have occurred in men who have sex with men, anyone in close personal contact with someone who has monkeypox is at risk for infection, regardless of gender identity or sexual orientation.

The CDC is continuing to evaluate and address treatment protocols, as no antiviral medications were FDA-approved before the beginning of this outbreak. The CDC has provided more extensive information on treatment protocol options under investigation as of August 2022 in the Morbidity and Mortality Weekly Report (MMWR).

Routes of Transmission

- There have been no confirmed transmissions of MPXV through organ or tissue transplantation or blood transfusions to date. The risk of transmission of MPXV through organ/tissue/blood donation is currently unknown.
- MPXV has been detected in respiratory secretions, blood, urine, seminal fluid, and tissue abscess fluid of infected persons.[ii, iii]
- Monkeypox can spread in the following ways:
    - Direct contact with the rash, scabs, or body fluids of a person with monkeypox infection.
    - Touching objects, fabrics (clothing bedding or towels), and surfaces that have been used by a person with monkeypox.
    - Contact with respiratory secretions of a person infected with monkeypox.
- Infected animals can spread monkeypox to humans via scratch or animal bite.
    - The natural reservoir of MPXV has not been identified, although rodents are the most likely source.[iv]
- Consumption of meat from infected animals may also transmit MPXV.
- Household sampling from a single case of a confirmed infected individual 20 days after symptom onset confirmed MPX DNA on multiple high-contact surfaces. However, no viable virus was detected via culture, with normal household cleaning but no specific decontamination performed.[v]

- In summary, MPX DNA can be identified from multiple sites within the body but the duration of replication-competent virus based on current evidence is uncertain.

Viral Detection and Infectivity

- An infected person is infectious via skin-to-skin contact for 2-4 weeks beginning from the start of symptoms until the skin rash has scabbed off and a fresh layer of intact skin has formed.[vi]
- Because MPX has been detected in blood, tissue, and body fluids, it could be potentially transmitted by organ and tissue transplantation and blood transfusion if the donor is actively infectious at the time of organ donation.
- There is limited information on the duration of MPXV viremia.
- One study described the detection of MPX DNA shedding in upper respiratory tract and blood for at least 3 weeks after initial infection.[ii] The clinical implications of these findings in the context of transplantation are not yet known.
- In animal models, MPX DNA has been detected in ocular, oral, nasal, fecal and blood samples starting at day 3 and up to 28-days post-inoculation. Viable (i.e., infectious) virus was detected from ocular, oral, nasal, and fecal secretions up to 21-days post-inoculation.[vii] The same study identified a peak of blood MPX DNA between days 6-15 post-inoculation, but virus viability was not assessed.
- During the 2003 US monkeypox outbreak, the CDC tested a total of 249 animals by PCR. Thirty-three tested positive for MPXV DNA, and viable virus was isolated from 30 of these. Viable virus was isolated from blood, brain, eyelid, feces, gonad, heart, kidney, liver, lung, lymph node, spleen, skin, tongue and urine.[viii]
- A retrospective study included seven patients in the UK with confirmed monkeypox, admitted between August 2018 and September 2021. MPXV DNA was detected up to 31, 45, 23 days from blood, upper respiratory and urine samples, respectively. There was no testing to determine if the virus was viable.[ix]

Screening Considerations: Deceased Donors

- Based on the biology of disease, clinical data, and data in animal studies, there may be a risk of disease transmission to recipients of organs from donors with active monkeypox.
- Standard physical examination of a potential donor will determine if they present with regional lymph node swelling or a rash, which is a common presentation for MPXV. [x,xi]
    - In a donor with suspected MPXV lesions, infectious disease consultation may be appropriate to guide further evaluation and management.
- Current donor medical history screening questions in the universal Donor Risk Assessment Interview (uDRAI) can obtain information on risk factors for MPXV exposure or infection
    - In addition, the American Association of Tissue Banks (AATB) has released a bulletin that contains donor risk assessment questions that may be used to obtain information specific to screening for risk of MPXV
- Persons infected with MPXV may remain asymptomatic for up to 21 days before showing symptoms. The risk of transmission from infected, asymptomatic individuals is unknown.
- For donors with a history of MPXV infection, if the donor is asymptomatic and all of the scabs on the skin lesions are healed the likelihood that they have any replication-competent virus is low.

- While active lesions are present or incompletely healed, the risk of transmission to potential recipients may be increased. DNA has been isolated from different sample types (blood, upper respiratory and urine sample types) after lesions have healed, but infectivity has not been established.
- The Modified virus Ankara vaccine (MVA)(JYNNEOS) is the primary vaccine being used in the US during this outbreak. It is made from a highly attenuated, nonreplicating vaccinia virus. Thus, donors receiving this vaccine are not at risk of transmitting vaccine-strain Vaccinia virus.
- ACAM2000 is a replication-competent smallpox vaccine. Vaccinia virus can be recovered from the skin at the vaccination site for a mean duration of 7.8 days, with a range of 0 to 18 days. Peak immunity is expected to be reached 4 weeks after administration.
    - Viremia is unlikely once the immune response is initiated.
    - Viremia has been more readily detected in people with moderate to severe complications of vaccinia virus infection. These complications include generalized vaccinia, eczema vaccinatum and progressive vaccinia.
- Evidence suggests that the decision to recover organs could include the following:
    - The recipient risk of mortality or further complications while delaying transplantation and remaining on the waitlist.
    - Current unknown outcomes.
    - Infectious disease experts can offer subject matter expertise when accepting organs from these donors
- CDC provides recommendations for healthcare worker vaccination for MPXV
- The FDA has released considerations for tissue donation regarding MPXV

Safety of the OPO, Recovery Team and Transplant Programs

- Donors with unrecognized monkeypox infection are possible sources of transmission to healthcare personnel, including OPO staff and recovery team members.
- Risk of transmission to healthcare personnel is reduced by standard precautions, personal protective equipment (**to include an N95 respirator and contact precautions**), environmental control tactics, and waste management; for more specifics, see here.
- Potential donors with prior monkeypox infection are no longer contagious via skin contact once skin lesions are completely re-epithelialized.
- There have been few reports of transmission to healthcare personnel, but currently these are rare.[xii]
- CDC provides recommendations for post-exposure vaccination for healthcare workers

Screening Considerations: Living Donors, Impact on Living Donor Safety

- Although most cases of monkeypox have been diagnosed in men who have sex with men, anyone in close contact with a person infected with monkeypox is at risk for infection, regardless of gender identity or sexual orientation.
- Screening and educating potential living donors for possible exposure or illness is a strategy to reduce the risk of transmitting MPXV to recipients.
    - Educate potential living donors regarding increased risk behaviors for contracting MPXV.

  - Examination of the genitals and perianal area could identify MPXV lesions.
- The optimal timing of living donation after recovering from monkeypox is unknown. Factors to be considered could include:
  - Safety of the living donor. The risk of surgical complications following monkeypox is unknown.
  - Risk of transmission to the recipient. While active lesions are present or incompletely healed, the risk of transmission to potential recipients may be increased. DNA has been isolated from different sample types (blood, upper respiratory and urine sample types) after lesions have healed, but infectivity has not been established.
  - Waiting list mortality of the intended recipient.
- Individuals infected with MPXV may be asymptomatic for up to 21 days after their exposure. Obtaining a careful history to identify contact exposures to monkeypox or engagement in activities that have increased risk of infection[xiii] is crucial.
  - Potential living donors who have been exposed to monkeypox could consider deferring donation until 21 days following their last exposure while monitoring for symptoms.[xiv] The risk of such wait time should be weighed against the morbidity and mortality risk for the potential recipient.
- Potential living donors who live in the same household as a person infected with monkeypox could consider self-quarantining prior to donation to reduce the risk of additional exposure.

Testing Considerations: Available testing, accessibility, specimen information

- Testing may be coordinated through the Laboratory Response Network, local public health departments, and certain commercial laboratories.
- Nucleic acid testing (NAT) of skin lesions may provide the most definitive results for monkeypox.
- There is significant cross-reactivity between orthopoxvirus antibodies, so positive serologic tests do not definitively indicate exposure to monkeypox.
- The CDC has published guidance on preparation and collection of specimens

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