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RAPID REVIEW

TRANSFUSION

Monkeypox and the safety of the blood supply

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1 | INTRODUCTION

Monkeypox virus (MPXV), typically endemic in Africa, is currently an international public health crisis following its rapid and expansive spread. Diagnostic testing, treatment with antivirals, and vaccines are currently available, which provide a significant opportunity to slow and contain the infection. Transfusion-transmission of MPXV has not been reported but donor centers and hospitals should be aware of the potential risks.

2 | MONKEYPOX CHARACTERISTICS AND CURRENT OUTBREAK

MPXV is an orthopoxvirus that is causing an expanding worldwide outbreak of monkeypox in 2022, with spread to more than 32,000 individuals and 82 non-endemic countries at time of this writing. Classic monkeypox is characterized by a prodrome of fever, headache, and lymphadenopathy, followed by the development of mucocutaneous lesions from which virus is shed at high levels. Mortality outside of Africa during the current outbreak has been significantly less than previously reported rates for the two major clades of MPXV (Central Africa, Clade I; and West Africa Clade IIa and IIb). The 2022 outbreak strain is predominantly Clade IIb.[1]

To date, the vast majority of reported infections have been in men who have sex with men (MSM) in Western Europe and the United States, although diagnostic testing has been limited to date and there may be biases in test seeking behaviors.[2] Diagnostic testing is generally performed using PCR testing of skin lesion swabs, which often carry $>10^8$ copies/swab.

Similar to variola virus (smallpox), MPXV is thought to spread from the site of inoculation systemically via monocytic cells through lymphatic as well as hematogenous routes.[3] Viral DNAemia is common in both animal models as well as human cases. Recent reports of human monkeypox cases have detected approximately 10^5 viral DNA copies/ml whole blood, which mirrors that seen in animal models.[4–6] The relationship of DNAemia to infectious viremia is not established. Notably, MPXV has never been cultured from the blood of humans but has been cultured from the blood of prairie dogs in experimental infection.[6,7]

Diagnostic testing in the United States is authorized by the Food and Drug Administration, and is done by MPXV DNA detection by real-time PCR amplification. It is widely available in public health and commercial laboratories. The preferred sample is a swab obtained from the skin lesion. Testing on alternative samples, for

Abbreviations: FDA, United States food and drug administration; MPXV, Monkeypox virus; MSM, Gay and bisexual men who have sex with men.

example, blood, saliva, or cerebrospinal fluid is not yet validated.

3 | VACCINE

Smallpox vaccines are being recommended as pre- and postexposure prophylaxis of monkeypox for defined populations. JYNNEOS, a replication incompetent, live attenuated, modified Ankara vaccinia vaccine is FDA-approved for preexposure or post-exposure prophylaxis for MPXV, though it has not been directly tested for efficacy in humans for monkeypox or smallpox. Its effectiveness against monkeypox is inferred from immunogenicity data in humans and efficacy data in animal challenge studies suggesting approximately 85% effectiveness in preventing monkeypox cases. ACAM2000 is an FDA-approved, replication competent, live attenuated vaccinia virus vaccine available from the US Strategic National Stockpile for the prevention of smallpox. This vaccine is contraindicated in immunocompromised individuals and those with eczema, given a concerning side effect profile and the possibility of viral transmission, thus potential blood donors with exposure to this vaccine are recommended for deferral. ACAM2000 is not widely recommended at this early stage of the outbreak, except in rare individuals with contraindications to JYNNEOS.

4 | IMPLICATIONS FOR TRANSFUSION MEDICINE

Transfusion transmission of MPXV has not been recognized. The presence of infectious virus in blood components from infected but otherwise qualified donors has not been studied, nor has its survival after contemporary processing and storage. The impact of universal leukoreduction is unknown, as is the capacity of parenteral inoculation to establish infection in humans. Disease transmission by intravenous inoculation has been successful in animals, including nonhuman primate models.[8]

Donors must be well on the day of donation, undergo a limited skin examination and have their temperature taken in the donor room. In the United States, MSM are specifically deferred for 3 months after the most recent sexual contact to reduce the risk of collecting HIV infected window period donations. This interval is believed to be beyond the duration of a putative infectious viremia and high adherence to this donor criterion effectively mitigates risk where donors continue to be directly questioned about MSM activity. Currently, the Food and Drug administration recommends no donor deferral for donors receiving prophylactic JYNNEOS vaccine (in contrast to ACAM2000) and has required no other interventions.[9] Pathogen reduction processes in wide use are active against orthopoxviruses.[10]

In much of the world, the MSM deferral has been discarded and replaced by individual donor risk assessments. These recognize the importance of other behaviors, as opposed to sexual preference, in disease transmission risk, for example, multiple recent and new sex partners and sexual practices. In the context of the current epidemiology of the outbreak, overwhelmingly affecting MSM, it may be necessary in such venues to add specific inquiries regarding potential exposures to monkeypox, as has been recommended by the European Centers for Disease Control.[11] The FDA considers that current donor screening strategies are sufficient to determine blood donor eligibility and does not recommend additional questions to evaluate possible exposure to MPXV.[12] Whether this will change during the evolution of the epidemic remains undetermined and the recent description of asymptomatic infections[13] and transmission beyond MSM will demand vigilance. Despite the fact that there are no cases of transfusion transmitted MPXV, the potential for MPXV viremia brings the theoretical risk of transmission through transfusion. There are currently no specific recall and lookback recommendations. Until more evidence is available to definitively determine the risk of transmission through transfusion, it may be prudent to counsel, clinically observe, and consider serial investigational and appropriate diagnostic testing of recipients of a unit from a donor who developed MPXV within 3 weeks after the donation.

CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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