

Monkeypox FAQ

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A multi-country outbreak of monkeypox started in May 2022 when several cases were reported from regions not endemic for the virus infection ¹. Since then, thousands of cases have been reported in at least 75 countries and territories across the world ². On July 21, 2022, the World Health Organization declared the monkeypox outbreak as a public health emergency of international concern.

This communication is intended to inform the transplant community of the potential risk caused by monkeypox to our transplant patients. While there have been no published data on monkeypox in transplant recipients, there is an imminent threat to this immunocompromised group of patients, if the ongoing human-to-human spread continues.

This document provides a summary of information from the literature that may be relevant to the transplant community. As more information becomes available, particularly as it relates to transplantation, this document will be updated.

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What is monkeypox?

Monkeypox is a zoonotic disease caused by an enveloped double-stranded DNA virus (known as monkeypox virus) that belongs to the *Orthopoxvirus* genus of the *Poxviridae* family.

There are two distinct genetic clades of monkeypox virus: the more virulent central African (Congo Basin) clade and the less virulent west African clade.

The current multi-country outbreak is due to the west African clade.

How is monkeypox transmitted?

Animal-to-human transmission of monkeypox can occur from direct contact with the blood, bodily fluids, or cutaneous or mucosal lesions of infected animals³. The natural reservoir of monkeypox has not been identified, although rodents are the most likely source⁴. It has been detected in many animals including squirrels, Gambian rats, different species of nonhuman primates and others.

Human-to-human transmission of monkeypox can result from close contact with respiratory droplets and by direct contact with infected body fluids, and skin or mucosal lesions³. Since respiratory droplets generally cannot travel more than a few feet, prolonged face-to-face contact is required for transmission. Indirect contact with an infected material through fomites, such as clothing, bedding, towels, and contaminated surfaces, has been documented⁵. Transmission can also occur through the placenta from mother to fetus or during close contact during and after birth.

Because the virus can be detected in blood and body fluids, theoretically, monkeypox virus could be potentially transmitted by organ transplantation if the donor is actively infectious at the time of organ donation. There is limited information on the duration of monkeypox viremia or its tissue tropism. Prolonged upper respiratory tract viral DNA shedding has been observed even after skin lesion resolution, and monkeypox viral DNA has been detected in the urine, blood, and deep tissue abscess⁶. The clinical implications of these findings in the context of organ transplantation are not yet known.

What is the illness caused by monkeypox virus?

After exposure to an infected person, the average incubation (asymptomatic) period before the onset of symptoms is 5-21 days.

A prodrome of fever, lymphadenopathy, and other non-specific symptoms such as malaise, headache, and myalgia may occur. During the current outbreak, these prodromal symptoms have been variable.

After 1-4 days of prodromal symptoms, a maculopapular rash appears, often on the face, and then spreads to other parts of the body. Representative photos of the skin rash are available (<https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html>)⁷. The rash becomes deep-seated, vesicular, pustular and umbilicated. The lesions are notably at the same stage of development at each site. The lesions crust over, scabs and fall off over a period of 2 to 4 weeks. During the current outbreak, lesions have also begun in the anogenital region, which may be confused with genital herpes, syphilis, or other sexually transmitted diseases¹.

While data of the clinical course of monkeypox in transplant recipients are lacking, there is concern that they could have a more virulent course than non-immunosuppressed hosts. This is based on the observation of more severe complications in immunocompromised HIV-infected patients⁸.

Case fatality rate of monkeypox in the general population is reported between 1 and 11%.

Efforts to develop a registry of monkeypox cases and outcomes in transplant recipients are ongoing.

What are other conditions that may be mistaken as monkeypox?

There are common diseases affecting transplant recipients and other patients that may be easily mistaken as monkeypox. These include syphilis, chancroid, herpes labialis, herpes genitalis, chickenpox or herpes zoster. Co-infection with monkeypox and other sexually transmitted infections has been reported^{1,9}.

There should be a low threshold for monkeypox because of its implications for infection control and prevention. Earlier [testing](#) will allow for a more rapid initiation of treatment, if indicated.

Testing for other infections, such as herpes and syphilis, should be performed in the proper clinical context.

When is monkeypox contagious?

An infected person is generally infectious to others from the onset of symptoms (during the prodrome) until the monkeypox lesions have crusted and a layer of healthy skin has formed underneath. The illness typically lasts 2-4 weeks ⁷.

There is currently no information on the duration of infectivity from viremia or prolonged respiratory DNA detection. One study has reported few patients with monkeypox virus DNA detected in blood for at least 3 weeks ⁶. However, there is no information on whether this represents viable infectious virus.

Who is at risk of monkeypox?

Any person is at risk of monkeypox if they have close contact with an active case (e.g., blood or other body fluids, skin lesions, anogenital or oral lesions, or infected fomites).

During the current outbreak, the majority of cases have been reported to occur among men who have sex with men ¹. However, cases have started to occur outside of this group, including children, potentially as a result of human-to-human transmission through direct contact with infected lesions and fomites.

Travel to a [high-risk area](#) within the past 21 days (incubation period) is a risk factor, especially if there was close contact with an active case, or exposure to an infected animal during the travel ².

When to suspect monkeypox?

Monkeypox should be suspected in any transplant patient who presents with a suspicious rash (<https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html>) ⁷ or other symptoms **and** have an epidemiologic risk factor within the last 21 days, including:

1. Contact with persons with probable or confirmed monkeypox.
2. Close or intimate contact with persons in a social network that is experiencing monkeypox activity.
3. Contact with wild animal or pet known to harbor monkeypox virus.

How do you prevent monkeypox?

Education. Raising awareness and educating transplant patients and their caretakers about measures they should undertake to reduce exposure to the virus (such as close and intimate contact) is the main prevention strategy. Transplant patients should be reminded that close contact with an infected person is the most important risk factor for monkeypox.

Post-exposure prophylaxis. [Post-exposure prophylaxis](#) is recommended to a person with known or suspected high-risk exposure to monkeypox-infected blood, body fluids or close skin contact with an infected person¹⁰.

High-risk exposures include the following:

1. Unprotected contact with infected skin, mucous membranes, fluid and blood (e.g., skin to skin and sexual contact).
2. Unprotected contact with contaminated materials such as shared utensils, clothing, towels, or bedding.
3. Unmasked face-to-face exposure to an infected person within 6 feet for 3 hours or longer (without wearing surgical mask or PPE), or exposure to a patient within 6 feet of a procedure that may create aerosols from oral secretions or skin lesions (without wearing PPE).

Expanded post-exposure prophylaxis. [Expanded post-exposure prophylaxis](#) is recommended, as vaccine supply allows, to high-risk persons with high potential for exposure^{10, 11}. This indication will likely expand once there is sufficient supply of the vaccine

Pre-exposure prophylaxis. Pre-exposure prophylaxis is recommended to high-risk groups, such as laboratory personnel working directly with monkeypox and healthcare workers caring for or likely to be exposed to patients with monkeypox^{10, 11}. This indication will likely expand once there is sufficient supply of the [vaccine](#).

What vaccines and other therapeutics are available for the prevention of monkeypox?

Modified vaccinia Ankara vaccine.

The modified vaccinia Ankara vaccine (MVA; available as JYNNEOS in US, Imvamune in Canada, Imvanex in Europe) is recommended as post-exposure prophylaxis to eligible patients, including transplant patients, under an Investigational New Drug protocol, after consultation with public health authorities¹². Transplant and

immunosuppressed patients are a priority group for post-exposure vaccination ¹⁰. Though MVA is a live attenuated virus vaccine, it cannot replicate in human cells, and considered safe in transplant recipients ¹³. The vaccine should preferably be given within 4 days, although it may be given up to 14 days after exposure, if no rash is present. MVA is a two-dose vaccine, given 4 weeks apart. Adverse effects to vaccination are injection site reaction (pain, redness, swelling, itching), muscle pain, headache and fatigue.

In contrast, the smallpox vaccine, ACAM2000, is a live replicating virus and is **contraindicated** in transplant and immunocompromised patients ¹⁴. This live virus vaccine should also NOT be given to persons living with an immunocompromised transplant recipient. Severe complications have been reported in immunocompromised patients who received smallpox vaccination with a replication-competent vaccinia virus ¹⁴.

Vaccinia Immune Globulin Intravenous (VIGIV).

For persons who are not eligible for MVA vaccine (e.g., severe immunodeficiency in T-cell function), prophylactic vaccinia immune globulin intravenous (VIGIV) may be considered for postexposure prophylaxis ¹¹.

Data are limited to support the efficacy of MVA and VIGIV against the current monkeypox virus outbreak. Given the sparse evidence for postexposure prophylaxis efficacy, shared decision-making between the patient, transplant provider, and transplant infectious disease specialist is recommended.

Who is eligible for post-exposure prophylaxis?

Any person, including transplant recipients, with high-risk exposures, such as:

1. Unprotected contact with infected skin, mucous membranes, fluid, blood (including skin to skin and sexual contact).
2. Unprotected contact with contaminated materials such as shared clothing, towels, bedding, and other infected fomites.
3. Unmasked face-to-face exposure to a person within 6 feet for 3 hours or longer (without wearing surgical mask or PPE), or exposure to a patient within 6 feet of a procedure that may create aerosols from oral secretions or skin lesions (without wearing PPE).

How do you diagnose monkeypox?

Any patient suspected to have monkeypox should have a confirmatory laboratory diagnostic test with the use of molecular diagnostic test such as real-time polymerase chain reaction (PCR) assay or Next-Generation sequencing of specimens (swab) obtained from skin lesions ¹⁵.

If the molecular test is suspected as false-negative, repeat the molecular test using a properly collected swab specimen. If an alternative test is desired, serology may be requested from the CDC.

How do you treat monkeypox?

Most immunocompetent patients with monkeypox will develop mild disease and recover without medical intervention.

Supportive clinical care should be provided to patients to alleviate symptoms, manage complications, and prevent long-term sequelae ¹¹.

There is no FDA-approved treatment for monkeypox virus. A few investigational drugs are available for treatment, under the guidance of public health and infectious disease specialists ¹¹. Given sparse evidence for treatment efficacy of these investigational drugs, shared decision-making between the patient, primary transplant provider, and transplant infectious diseases specialist is recommended.

Criteria for treatment:

High-risk patients, including children, and those with severe disease are eligible for treatment.

- Transplant and other immunocompromised patients, regardless of disease severity
- Patients with severe disease (e.g., confluent and hemorrhagic symptoms, encephalitis)
- Patients with disease involvement of sensitive anatomical areas such as the eyes and the anogenital region

Drugs for treatment:

Tecovirimat (TPOXX), an antiviral drug that was developed for use in patients with smallpox ¹⁶, has been suggested as treatment of monkeypox. Immunocompromised patients, including transplant recipients, belong to the priority group for treatment.

However, tecovirimat is not widely available, and its use should ideally be monitored in a clinical research context. Tecovirimat is a weak inducer of cytochrome P450 (CYP)3A and CYP2B6 and may theoretically slightly reduce tacrolimus and sirolimus levels. Tecovirimat is contraindicated in patients with creatinine clearance <30 ml/minute.

Cidofovir and brincidofovir have also been suggested and were used in some reported cases of monkeypox ⁶. In the US, they are available under an expanded access protocol from the CDC ¹¹.

Vaccinia Immunoglobulin Intravenous (VIGIV) is available under expanded access protocol from the CDC for the treatment of monkeypox.

What do transplant patients do if they live with someone with probable or confirmed monkeypox?

Transplant patients who are household members of a person with a probable or confirmed monkeypox should avoid contact with the infected person until the rash has fully resolved and skin has reepithelialized ¹⁷.

Transplant patients and other household members should not share potentially contaminated items such as utensils, beddings, linens, towels.

The infected patient should isolate and avoid contact with uninfected household members and should cover all exposed skin lesions. They should avoid or limit the use of spaces and items that are shared with other household members.

The transplant recipient should discuss with their providers if they are eligible for treatment or post-exposure prophylaxis. A transplant recipient living with someone with active monkeypox is potentially exposed and may benefit from post-exposure prophylaxis.

What are recommendations for infection prevention and control in transplant centers?

Transplant center leadership should discuss with their [institutional Infection Prevention and Control department](#) for guidance, as specific practices may vary¹⁸.

What is the risk of donor-derived infection?

Because monkeypox virus can be transmitted by body fluids, there is a theoretical risk of transmission from infected living or deceased donors to transplant recipients.

The pre-procurement evaluation of living and deceased donors should include questions to assess the risk of monkeypox exposure or active infection. The physical examination of living and deceased donors should assess for skin and mucosal lesions, including the anogenital regions, and suspected lesions be tested for monkeypox. It should be noted that genital lesions and vesicular skin lesions have a broad differential diagnosis and expert opinion should be sought prior to turning down deceased donors on this basis.

Organs from donors with confirmed active monkeypox should **not** be used based on current limited information. This is an interim recommendation that is subject to change as new data becomes available.

Confirmed monkeypox infected patients should defer donation until at least all lesions has scabbed and skin re-epithelialization has occurred. However, there is a report of prolonged upper respiratory tract viral DNA shedding even after skin lesion resolution ⁶. The clinical implication of this prolonged respiratory shedding is unknown at this time.

Living donors with recent exposure and are asymptomatic should consider deferring organ donation until they are beyond the 21-day incubation period and have remained asymptomatic.

Risk-benefit discussion is strongly recommended among the patient, transplant provider and transplant infectious disease specialist if there is a desire to procure and use an organ from a deceased donor within 21 days of reported high-risk monkeypox exposure.

After discussion with CDC, Tecovirimat (TPOXX) may be considered as an option for prophylaxis of a transplant recipient who was inadvertently transplanted with an organ from an infectious donor (e.g., when the diagnosis of monkeypox is confirmed after the allograft organ has been transplanted).

All cases of suspected transmission of monkeypox through organ transplantation should be reported to Disease Transmission Advisory Committee (DTAC) for review and monitoring.

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