



Emerging Treatment Update: Monkeypox

Potential Pre- and Post-Exposure Therapies

June 30, 2022

Background

Monkeypox is a rare disease caused by infection with the monkeypox virus. Monkeypox virus is an enveloped double-stranded DNA virus belonging to the Orthopoxvirus genus in the family Poxviridae. The Orthopoxvirus genus also includes variola virus (which causes smallpox), vaccinia virus (used in the smallpox vaccine), and cowpox virus. Monkeypox is not related to chickenpox. The Centers for Disease Control and Prevention (CDC) are tracking multiple cases of monkeypox that have been reported in several countries that don't normally report monkeypox including the United States. It's not clear how the people were exposed to monkeypox, but early data suggest that gay, bisexual, and other men who have sex with men make up a high number of cases. However, anyone who has been in close contact with someone who has monkeypox is at risk. Monkeypox is rare and does not spread easily between people without close contact. **The threat of monkeypox to the general U.S. population remains LOW.** CDC is urging healthcare providers in the U.S. to be alert for patients who have rash illnesses consistent with monkeypox.

Transmission

Monkeypox was first discovered in 1958 from two outbreaks among colonies of monkeys kept for research.^[1] The first known human case of monkeypox occurred in 1970 in the Democratic Republic of the Congo.^[2] The monkeypox virus can spread from animals to humans by being scratched or bitten by the animal or by preparing or eating meat or using products from an infected animal. The monkeypox virus can spread from person-to-person through:

- direct contact with the infectious rash, scabs, or body fluids
- respiratory secretions during prolonged face-to-face contact or during intimate physical contact such as kissing, cuddling, or sex
- touching items (such as clothing or linens) that previously touched the infectious rash or body fluids
- pregnant people can spread the virus to their fetus through the placenta

Signs and symptoms

Monkeypox symptoms are similar to smallpox symptoms, but milder; and monkeypox is rarely fatal. The time to onset of symptoms of monkeypox is usually from 6 to 13 days but can range from 5 to 21 days. Symptoms include a rash that can look like pimples or blisters that appears on the face, inside the mouth, and on other parts of the body, like the hands, feet, chest, genitals, or anus. The rash goes through different stages before healing completely. The illness typically lasts 2-4 weeks. Some people may only experience a rash while others may experience additional symptoms which can include fever, headache, muscle aches and backache, swollen lymph nodes, chills, and exhaustion.

Prevention (Pre-exposure prophylaxis)

Vaccines that are effective against orthopoxviruses (e.g., smallpox) are also effective against monkeypox. On November 3, 2021, the Advisory Committee and Immunization Practices (ACIP) voted to recommend vaccination for select persons at risk for occupational exposure to orthopoxviruses.^[3]

- Clinical laboratory personnel who perform testing to diagnose orthopoxviruses, including those who use polymerase chain reaction (PCR) assays for diagnosis of orthopoxviruses, including Monkeypox virus
- Research laboratory workers who directly handle cultures or animals contaminated or infected with orthopoxviruses that infect humans, including Monkeypox virus, replication-competent Vaccinia virus, or recombinant Vaccinia viruses derived from replication-competent Vaccinia virus strains
- Certain healthcare and public health response team members designated by public health authorities to be vaccinated for preparedness purposes

At this time, most clinicians in the United States and laboratorians not performing the orthopoxvirus generic test to diagnose orthopoxviruses, including monkeypox, are not advised to receive orthopoxvirus PrEP.

Vaccines available for the prevention of monkeypox:

JYNNEOS (Imvamune or Imvanex)	An attenuated live virus vaccine. Indicated for the prevention of smallpox and monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection. CDC is developing an Expanded Access Investigational New Drug Protocol to allow the use of JYNNEOS for monkeypox in pediatric populations.
ACAM2000 (replaced Dryvax)	A live vaccinia virus vaccine licensed by the FDA in August 2007. Indicated for active immunization against smallpox disease for persons determined to be at high risk for smallpox infection. CDC-held Emergency Access Investigational New Drug Protocol allows use for Non-Variola Orthopoxvirus Infection (e.g., monkeypox) during an outbreak. Safety: there is a risk of inadvertent inoculation and auto-inoculation and a risk of myopericarditis (5.7 cases per 1,000 primary vaccines) with the ACAM2000 vaccine.

Vaccine contraindications

Contraindication	ACAM2000 Primary Vaccinees	ACAM2000 Revaccinees	ACAM2000 Household Contacts	JYNNEOS
History or presence of atopic dermatitis	X	X	X	
Other active exfoliative skin conditions	X	X	X	
Conditions associated with immunosuppression	X	X	X	
Pregnancy	X	X	X	
Aged <1 year	X	X	X	
Breastfeeding	X	X		
Serious vaccine component allergy	X	X		X
Known underlying heart disease (e.g., coronary artery disease or cardiomyopathy)	X	X		
Three or more known major cardiac risk factors	X			

Note: an 'x' indicates a contraindication to vaccination

Treatment (Post-Exposure)

Many individuals infected with monkeypox virus have a mild, self-limiting disease course in the absence of specific therapy. The prognosis for monkeypox depends on multiple factors such as previous vaccination status, initial health status, and concurrent illnesses or comorbidities. Treatment for monkeypox should be considered following consultation with the CDC for:

- Persons who may be at high risk of severe disease:
 - People with immunocompromising conditions (e.g., HIV/AIDS, leukemia, lymphoma, generalized malignancy, etc.)
 - Pediatric populations, particularly patients younger than 8 years of age
 - Pregnant or breastfeeding women
 - People with a history or presence of atopic dermatitis, people with other active exfoliative skin conditions
 - People with one or more complication
- Persons with monkeypox virus aberrant infections that include its accidental implantation in eyes, mouth, or other anatomical areas where monkeypox virus infection might constitute a special hazard (e.g., the genitals or anus)

Interim clinical guidance for the treatment of monkeypox can be found on the [CDC Treatment Information for Healthcare Professionals website](#).

Medical countermeasures available for the treatment of monkeypox:

Tecovirimat (TPOXX or ST-246)	An antiviral medication that is approved by the FDA as oral or injectable formulation for the treatment of human smallpox disease in adults and pediatric patients weighing at least 13 kg. CDC-held Emergency Access Investigational New Drug Protocol allows use of Tecovirimat for Non-Variola Orthopoxvirus Infection (e.g., monkeypox)
Vaccinia Immune Globulin Intravenous (VIGIV)	Licensed by FDA for the treatment of complications due to vaccinia vaccination. CDC-held Emergency Access Investigational New Drug Protocol allows use of VIGIV for Non-Variola Orthopoxvirus Infection (e.g., monkeypox). Data are not available on the effectiveness of VIG in treatment of monkeypox virus infection. Use of VIG has no proven benefit in the treatment of monkeypox and it is unknown whether a person with severe monkeypox infection will benefit from treatment with VIG. However, healthcare providers may consider its use in severe cases. VIGIV can be considered for prophylactic use in an exposed person with severe immunodeficiency in T-cell function for which smallpox vaccination following exposure to monkeypox virus is contraindicated.
Cidofovir (Vistide)	An antiviral medication that is approved by the FDA for the treatment of cytomegalovirus (CMV) retinitis in patients with Acquired Immunodeficiency Syndrome (AIDS). CDC-held Emergency Access Investigational New Drug Protocol allows the use of Cidofovir for Non-Variola Orthopoxvirus Infection (e.g., monkeypox). It is unknown whether or not a person with severe monkeypox infection will benefit from treatment with Cidofovir, although its use may be considered in such instances. There is a risk of dose-dependent nephrotoxicity associated with cidofovir; initiation of therapy is contraindicated in patients with a serum creatinine >1.5mg/dL, a calculated creatinine clearance <55mL/min, a urine protein ≥100mg/dL, receiving agents with nephrotoxic potential, or a sulfa allergy.
Brincidofovir (CMX001 or Tembexa)	An antiviral medication that was approved by the FDA for the treatment of human smallpox disease in adult and pediatric patients, including neonates. Data is not available on the effectiveness of Brincidofovir in treating cases of monkeypox in people. However, it has shown to be effective against orthopoxviruses in in vitro and animal studies. CDC is currently developing an EA-IND to help facilitate use of Brincidofovir as a treatment for monkeypox. Persons exposed to monkeypox virus and who have not received the smallpox vaccine within the last 3 years, should consider getting vaccinated.
Vaccination	Smallpox and monkeypox vaccines may help prevent disease or make it less severe when given after exposure. The sooner an exposed person gets the vaccine, the better. CDC recommends that the vaccine be given within 4 days from the date of exposure in order to prevent onset of the disease. If given between 4–14 days after the date of exposure, vaccination may reduce the symptoms of disease, but may not prevent the disease.

Access to medications

Vaccines (JYNNEOS and ACAM2000) are licensed vaccines in the United States and are available from the US Strategic National Stockpile (SNS). Tecovirimat, vaccinia immune globulin intravenous, cidofovir, and brincidofovir are licensed by the FDA; these products, excluding brincidofovir) are available through the SNS.

To request medications for use in a patient with suspected, probable, or confirmed monkeypox, please contact your state/territorial health department or CDC through the CDC Emergency Operations Center (770-488-7100).

References:

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 - World Health Organization. (May 19, 2022). Monkeypox. <https://www.who.int/news-room/fact-sheets/detail/monkeypox> 
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