Centers for Disease Control and Prevention

Clinical Considerations for Treatment and Prophylaxis of Monkeypox Virus Infection in People with HIV

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Who this is for: Healthcare professionals providing care for people with HIV.

What this is for: Considerations for the care of people with HIV, including prevention and treatment of monkeypox virus infection.

How to use: This information is intended as an aid for healthcare facilities and healthcare professionals developing plans for monkeypox virus infection treatment and prophylaxis for people with HIV.

Key Points

- People with advanced HIV or who are not virologically suppressed with antiretroviral therapy can be at increased risk of severe disease related to monkeypox virus infection.
- Post-exposure prophylaxis is available for people exposed to monkeypox.
- Antiviral treatments are available for people with a monkeypox infection.
- Vaccination with JYNNEOS is considered safe for people with HIV, and antiviral treatments have few interactions with antiretroviral medications.

These considerations are based upon limited evidence available to date about monkeypox virus infection in patients with HIV. The approaches outlined below are intentionally cautious until additional data become available.

Monkeypox in people with HIV

Available summary surveillance data from the European Union,[1] as well as separate reports from Portugal,[2] Spain,[3] and England,[4] report that 30% to 51% of patients with monkeypox for whom HIV status is known have HIV.

Regarding infection risk, it is currently unknown whether HIV alters (e.g., increases) a person's risk of acquiring monkeypox disease after exposure.

Regarding illness after infection, the available data indicate that people with advanced and uncontrolled HIV can be at a higher risk of severe or prolonged disease. In a 2017–18 case series of 122 Nigerian patients with monkeypox, 4 of the 7 deaths occurred among persons with untreated advanced HIV; however, information was absent about the overall proportion of patients who had HIV to determine if this mortality was disproportionally large.[5] A second 2017–18 case series, also from Nigeria, included 9 people with HIV for whom clinical data relevant to HIV status were provided: CD4 cell counts ranged from 20–357 cells/mm^3 and most had either failed antiretroviral therapy (ART) or were newly diagnosed, suggesting a lack of viral suppression. Compared with other patients, those with HIV had higher rates of secondary bacterial infection, more prolonged illness (and thereby also longer period of infectiousness), as well as a greater likelihood of a confluent or partially confluent rash rather than discrete lesions.[6] In contrast, reports from European countries where most patients are on effective ART have noted no deaths or evident excess in hospitalizations thus far among people with HIV and monkeypox.[2-4] Additionally, the WHO has stated that "people with HIV…who take antiretroviral therapy and have a robust immune system have not reported a more severe course of disease."[7]

Signs and Symptoms

The signs and symptoms of monkeypox virus infection are similar in people with or without HIV, including characteristic rash, fever, and lymphadenopathy. For immunocompromised people, monkeypox virus infection may present with atypical manifestations or more severe illness (e.g., sepsis, disseminated rash).

Monkeypox disease is characterized by an incubation period, prodrome, and rash. For full details, please see Clinical Recognition.

Incubation and prodrome

It is not known if people with HIV have different characteristics regarding the incubation or prodromal phase of illness.

Illness

Immunocompromised persons, including persons with advanced HIV or untreated HIV, may present with an atypical rash, including a disseminated rash, which may make diagnosis more challenging. In one study, people with poorly controlled HIV were more likely to have genital lesions and a confluent or partially confluent rash, as opposed to discrete lesions.[6] Additionally, people in this study with poorly controlled HIV were more likely to have prolonged illness.

Differential diagnosis

Monkeypox virus infection should also be considered when evaluating for other causes of rash, including herpes zoster (shingles), scabies, molluscum contagiosum, herpes, syphilis, chancroid, lymphogranuloma venereum, allergic skin rashes, and drug eruptions. Monkeypox can be confused with disseminated herpes zoster or herpes simplex virus infections. These herpesvirus infections more commonly affect persons with immunocompromising conditions, especially disseminated herpes zoster. Therefore, to establish a diagnosis for immunocompromised persons who present with a rash, clinicians should conduct a thorough history to assess for possible monkeypox exposures or epidemiologic risk factors, perform a complete physical examination, and order lab testing. Co-infections with monkeypox and sexually transmitted infections (STI) have been reported, therefore a broad approach to testing is recommended, including STI testing.[8]

For additional recommendations regarding case finding and clinical presentation, please see Updated Case-finding Guidance: Monkeypox Outbreak—United States, 2022.

For additional recommendations on specimen collection for clinicians, please see Preparation and Collection of Specimens.

Treatment

Managing monkeypox in people with HIV

People with HIV may be at increased risk of severe disease and prolonged infectiousness. Therefore, prophylaxis (e.g., vaccination), medical treatment and close monitoring are a priority for this population. Providers should consider both viral suppression and CD4 count in weighing the risk of severe outcomes for any patient with HIV. As noted earlier, severe outcomes have been observed in people with inadequately treated HIV who have CD4 counts ≤ 350/mm^3 and are likely not virologically suppressed; however, the available data are presently insufficient to define actionable thresholds. Until more is known, clinicians should exercise clinical judgement to assess the extent of immunosuppression (from HIV or any other sources) and the risk for severe monkeypox illness. The patient's clinical team is best positioned to determine the degree of immune compromise and, with the input of public health practitioners, the need for prophylaxis (including vaccination) and treatment. The decision to treat and monitor an immunocompromised person in their home or an inpatient setting should likewise be individualized.

Managing HIV in people with monkeypox

ART and opportunistic infection prophylaxis should be continued in all people with HIV who develop monkeypox. Treatment interruption may lead to rebound viremia that could complicate the management of monkeypox virus infection (e.g., worsen the severity of illness). People taking antiretrovirals for HIV pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis

the severity of illness). People taking antiretrovirals for HIV pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP) should likewise continue taking these medications.

For persons with HIV diagnosed coincident with monkeypox or who are not taking ART, CDC recommends starting ART as soon as possible, and in consultation with an expert in HIV medicine if needed.

Clinicians using antivirals for monkeypox need to be alert for drug-drug interactions with any antiretrovirals used to treat[9] or prevent[10, 11] HIV infection as well as with any other medications used to prevent or treat HIV-related opportunistic infections.[12] Key critical interactions are discussed below for each monkeypox antiviral. Any potential drug-drug interactions not noted below can be assessed using the University of Liverpool HIV Drug Interactions database, an interactive online tool found at https://www.hiv-druginteractions.org/checker .

Treatment options

Tecovirimat (a.k.a. TPOXX, ST-246)

Tecovirimat is an antiviral medication available as a pill or as an injection for intravenous (IV) administration. It is approved by the FDA for treatment of smallpox in adults and children but not for monkeypox because data are not available on the effectiveness of tecovirimat in treating monkeypox in humans.

Tecovirimat can be administered under an expanded access Investigational New Drug (EA-IND) protocol and is available from the Strategic National Stockpile (SNS).

Studies using a variety of animal species have shown that tecovirimat is effective in treating orthopoxvirus-induced disease.[13] Human clinical trials indicated the drug was safe and tolerable with only minor side effects.[14] A case report from the UK suggested that tecovirimat may shorten the duration of illness and viral shedding.[15]

Cidofovir and Brincidofovir

Cidofovir is approved by the FDA for treatment of cytomegalovirus (CMV) retinitis in patients with advanced HIV. It is administered as an intravenous infusion. Brincidofovir is approved by the FDA for the treatment of human smallpox disease in adult and pediatric patients, including neonates. It is administered orally as a tablet or oral suspension. Currently, only cidofovir is available, either commercially or from the SNS.

Data are not available on the effectiveness of cidofovir and brincidofovir in treating human cases of monkeypox. However, both have proven activity against poxviruses in *in vitro* and animal studies. At this time, it is unknown if a person with severe monkeypox virus infection will benefit from treatment with either antiviral, although their use may be considered in such instances.

Vaccinia Immune Globulin Intravenous (VIGIV)

Data are not available on the effectiveness of VIGIV in treatment of monkeypox virus infection. VIGIV for the treatment of monkeypox is administered under an EA-IND and it is unknown whether a person with severe monkeypox virus infection will benefit from treatment with VIGIV. However, healthcare providers may consider its use in severe cases.

For further details regarding therapeutic recommendations and clinical guidance for the treatment on monkeypox, see Treatment and Clinician FAQs.

Considerations for use in people with HIV

Tecovirimat (a.k.a. TPOXX, ST-246)

Few interactions are expected with antiretroviral therapy for HIV. According to the Liverpool HIV drug interactions page , clinically relevant drug interactions that may require dose adjustment would be anticipated only between tecovirimat and the non-nucleoside reverse transcriptase inhibitors (NNRTIs) doravirine and rilpivirine, and the CCR5 antagonist maraviroc. Dose increases for doravirine, rilpivirine, and maraviroc should be considered when co-administered with tecovirimat and for two weeks after completion of tecovirimat therapy (see Liverpool website for details). When co-administering tecovirimat with

long-acting cabotegravir/rilpivirine, consider adding oral rilpivirine 25 mg once daily during treatment with tecovirimat and for approximately 2 weeks after the end of treatment as any reduction in rilpivirine exposure may persist for up to 14 days after stopping tecovirimat. Alternatively, if unable to obtain oral rilpivirine, then consider adding the oral ART regimen the patient was taking prior to initiation of long-acting cabotegravir/rilpivirine and continue that oral regimen for 2 weeks after completing tecovirimat.

Cidofovir and Brincidofovir

Cidofovir is contraindicated in patients with serum creatinine >1.5 mg/dL because of the nephrotoxicity associated with these medications. Therefore, co-administration of cidofovir with tenofovir disoproxil fumarate (TDF) is not recommended. If concomitant use of TDF and nephrotoxic agents is unavoidable, renal function should be monitored closely. Cidofovir is typically co-administered with probenecid both to reduce nephrotoxicity and boost its effectiveness. Probenecid substantially increases zidovudine plasma levels; if co-administered, zidovudine should either be temporarily discontinued or decreased by 50% on the day of cidofovir-probenecid administration to avoid zidovudine-induced hematological toxicity.

Brincidofovir has clinically relevant drug interaction with protease inhibitors (PIs), cobicistat, and fostemsavir that may require modification of therapy. If PIs or fostemsavir are co-administered with brincidofovir, clinicians should monitor closely for adverse reactions (e.g., elevations in transaminase levels) and dosing of antiretroviral therapy should be delayed for at least 3 hours after brincidofovir administration.

Both cidofovir and brincidofovir have interactions (including contraindications for use) with other medications that should be assessed by the clinical team. Currently, only cidofovir is available, either commercially or from the SNS.

Vaccinia Immune Globulin Intravenous (VIGIV)

There are no specific contraindications for use of VIGIV among people with HIV, and no known or anticipated interactions with antiretroviral therapy.

Monkeypox can cause keratitis. Caution should be exercised when using VIGIV in the treatment of persons with active keratitis, as increased corneal scarring was observed in an animal model of vaccinia keratitis.

VIGIV is contraindicated in individuals with a history of anaphylaxis or prior severe systemic reaction association with the parenteral administration of this or other human immune globulin preparations. VIGIV is contraindicated in IgA-deficient patients with antibodies against IgA and a history of IgA hypersensitivity.

Vaccination with live virus vaccines (e.g., varicella, measles, mumps, and rubella) should be deferred for 3 months after use of VIGIV.

For additional details regarding therapeutic recommendations, see Treatment.

Pre- and Post-Exposure Prophylaxis

Preexposure prophylaxis

Preexposure prophylaxis should be offered to people with HIV if indicated. At this time, the only form of preexposure prophylaxis available or authorized for monkeypox is vaccination. The risks and benefits of preexposure prophylaxis by vaccination should be discussed with the patient using shared decision-making.

When preexposure prophylaxis by vaccination is chosen, JYNNEOS should be used for people with HIV. Given limited supply of JYNNEOS vaccine, the national vaccine strategy for monkeypox is implementing a phased approach. During the initial phases, priority should be given to postexposure prophylaxis. In later phases, vaccine supply will increase and will make preexposure prophylaxis more feasible. Based on available guidance from ACIP, ACAM2000 should not be used due to the risk of adverse effects from the spread of vaccinia virus.

Postexposure prophylaxis

Postexposure prophylaxis by vaccination should be offered to people with HIV if indicated. The risks and benefits of postexposure prophylaxis by vaccination should be discussed with the patient using shared decision-making. Other therapies, including the antiviral medication tecovirimat and vaccinia immune globulin, may be considered for monkeypox PEP on an individual case-by-case basis depending on the known high-risk exposure to a confirmed or probable case of infection and clinical conditions that necessitate an alternative option to PEP vaccination. The efficacy of these therapies as monkeypox PEP is unknown.

While the use of smallpox vaccines for post-exposure prophylaxis has not been studied, early use of vaccination (within 4 days from exposure) could prevent monkeypox virus infection and later use (5 days or more after exposure) may decrease the severity of monkeypox disease if infection occurs.

When postexposure prophylaxis by vaccination is chosen, JYNNEOS should be used for people with HIV.

Vaccine Safety and Efficacy

JYNNEOS

JYNNEOS is a two-dose live virus vaccine that uses non-replicating modified vaccinia Ankara (MVA). [16] It is licensed by FDA for prevention of both smallpox and monkeypox disease in adults 18 years of age and older. The safety and immunogenicity of JYNNEOS has been specifically evaluated in people with HIV. In one study which enrolled people with HIV with CD4 counts between 200 and 750 cells/mm^3, the rates of adverse events did not differ between people with and without HIV.[17] In another study which enrolled people with HIV and CD4 counts >350 cells/mm^3 and people without HIV, vaccination was well tolerated and comparably immunogenic in terms of neutralizing antibody responses in both groups.[18] In another trial specifically enrolling persons with a prior diagnosis of AIDS who were virologically suppressed and had CD4 counts between 100 and 500, there were no serious safety concerns and the vaccine appeared efficacious based on immunogenicity at standard dosing.[19] Immunogenicity among persons with HIV who have CD4 counts below 100 cells/mm^3 or who are not virologically suppressed remains unknown.

For more information, please see Monkeypox and Smallpox Vaccine Guidance and Considerations for Monkeypox Vaccination.

ACAM2000

ACAM2000 is a single-dose live virus vaccine that uses replicating vaccinia. It is licensed by FDA for prevention of smallpox. ACAM2000 should not be given to people with HIV (regardless of immune status). Severe localized or systemic infection with vaccinia (progressive vaccinia) may occur in persons with weakened immune systems, including from HIV.

ACAM2000 vaccination should also be avoided if the vaccine recipient cannot sufficiently isolate from household contacts who have a history of atopic dermatitis or other active exfoliative skin condition, an immunocompromising condition, or who are pregnant or aged <1 year. Household contacts include persons with prolonged intimate contact with the potential vaccinee (e.g., sexual contacts) and others who might have direct contact with the vaccination site or with potentially contaminated materials (e.g., clothing or vaccination site dressings).

For more information, please see Monkeypox and Smallpox Vaccine Guidance and Considerations for Monkeypox Vaccination.

Vaccine adverse events

Adverse reactions should be reported to the Vaccine Adverse Event Reporting System (VAERS). Reports can be filed by healthcare providers or by vaccine recipients. To file an adverse reaction report, please visit www.vaers.hhs.gov or call 1-800-822-7967. VAERS is only for reporting reactions, and VAERS staff members do not give medical advice.

U.S. healthcare providers and health department staff with a complex monkeypox vaccine safety question about a specific patient residing in the U.S. or vaccine safety issue can contact the Clinical Immunization Safety Assessment (CISA) Project at CISAeval@cdc.gov to request a case consultation. In case of an emergent clinical vaccine safety inquiry, healthcare providers and health department staff can call the CDC Emergency Operations Center (EOC) Watch Desk at (770)-488-7100.

Patient Guidance

Prevention

People with HIV should follow the same guidance as anyone else to protect themselves from monkeypox.

- Avoid direct contact with rashes, sores, or scabs on a person with monkeypox, including during intimate contact such as sex. We believe this is currently the most common way that monkeypox is spreading in the U.S.
- Avoid contact with objects, fabrics (e.g., clothing, bedding, or towels), and surfaces that have been used by someone with monkeypox.
- Avoid contact with respiratory secretions, through kissing and other face-to-face contact from a person with monkeypox.

For more information, including guidance around sex, see Monkeypox Facts for People Who are Sexually Active.

Isolation and infection control

Infection control practices for the care of people with monkeypox are the same regardless of HIV status. Persons with monkeypox isolating at home should also follow precautions to protect others in the household.

A person is contagious until after all the scabs on the skin have fallen off and a fresh layer of intact skin has formed underneath. Based on limited evidence from Ogoina et al, this period of contagiousness may be prolonged due to a longer period of illness in people with HIV that are not virologically suppressed. Decisions regarding discontinuation of isolation precautions at a healthcare facility and at home should be made in consultation with the local or state health department.

References

1. Joint ECDC-WHO Regional Office for Europe Monkeypox Surveillance Bulletin, June 29 2022. Available at: https://cdn.who.int/media/docs/librariesprovider2/monkeypox/monkeypox_euro_ecdc_final_jointreport_2022-06-29_edited.pdf [1.33 MB, 30 pages] .

2. Perez Duque M, Ribeiro S, Martins JV, et al. Ongoing monkeypox virus outbreak, Portugal, 29 April to 23 May 2022. *Euro Surveill*. 2022;27(22):2200424. doi:10.2807/1560-7917.ES.2022.27.22.2200424

3. Iñigo Martínez J, Gil Montalbán E, Jiménez Bueno S, et al. Monkeypox outbreak predominantly affecting men who have sex with men, Madrid, Spain, 26 April to 16 June 2022. *Euro Surveill*. 2022 Jul;27(27). doi: 10.2807/1560-7917.ES.2022.27.27.2200471. PMID: 35801519.

4. UK Health Security Agency. Investigation into monkeypox outbreak in England, Technical Brief #3, updated July 8, 2022. Available at: https://www.gov.uk/government/publications/monkeypox-outbreak-technical-briefings .

5. Yinka-Ogunleye A, Aruna O, Dalhat M, et al. Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report. *Lancet Infect Dis*. 2019;19(8):872-879. doi:10.1016/S1473-3099(19)30294-4.

6. Ogoina D, Iroezindu M, James HI, et al. Clinical Course and Outcome of Human Monkeypox in Nigeria. *Clin Infect Dis*. 2020;71(8):e210-e214. doi:10.1093/cid/ciaa143.

7. World Health Organization. Multi-country monkeypox outbreak: situation update. June 4, 2022. Available at: https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON390 .

8. Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. *MMWR Recomm Rep*. 2021;70(4):1-187. Published 2021 Jul 23. doi:10.15585/mmwr.rr7004a1

9. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf [4 MB, 464 pages]

10. Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. Available at: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf [1.57 MB, 108 pages].

11. Centers for Disease Control and Prevention. Updated guidelines for antiretroviral postexposure prophylaxis after sexual, injection drug use, or other nonoccupational exposure to HIV—United States, 2016. Available at: https://stacks.cdc.gov/view/cdc/38856

12. Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Centers for Disease Control and Prevention, National Institutes for Health, the HIV Medicine Association, and the Infectious Disease Society of America. Available at: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/whats-new

13. Berhanu A, Prigge JT, Silvera PM, Honeychurch KM, Hruby DE, Grosenbach DW. Treatment with the smallpox antiviral tecovirimat (ST-246) alone or in combination with ACAM2000 vaccination is effective as a postsymptomatic therapy for monkeypox virus infection. *Antimicrob Agents Chemother*. 2015;59(7):4296-4300. doi:10.1128/AAC.00208-15

14. Grosenbach DW, Honeychurch K, Rose EA, et al. Oral Tecovirimat for the Treatment of Smallpox. *N Engl J Med*. 2018;379(1):44-53. doi:10.1056/NEJMoa1705688

15. Adler H, Gould S, Hine P, et al. Clinical features and management of human monkeypox: a retrospective observational study in the UK. *Lancet Infect Dis*. 2022;S1473-3099(22)00228-6. doi:10.1016/S1473-3099(22)00228-6

16. Rao AK, Petersen BW, Whitehill F, et al. Use of JYNNEOS (Smallpox and Monkeypox Vaccine, Live, Nonreplicating) for Preexposure Vaccination of Persons at Risk for Occupational Exposure to Orthopoxviruses: Recommendations of the Advisory Committee on Immunization Practices – United States, 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71(22):734-742. Published 2022 Jun 3. doi:10.15585/mmwr.mm7122e1

17. Overton ET, Stapleton J, Frank I, et al. Safety and Immunogenicity of Modified Vaccinia Ankara-Bavarian Nordic Smallpox Vaccine in Vaccinia-Naive and Experienced Human Immunodeficiency Virus-Infected Individuals: An Open-Label, Controlled Clinical Phase II Trial. *Open Forum Infect Dis*. 2015;2(2):ofv040. Published 2015 May 5. doi:10.1093/ofid/ofv040

18. Greenberg RN, Overton ET, Haas DW, et al. Safety, immunogenicity, and surrogate markers of clinical efficacy for modified vaccinia Ankara as a smallpox vaccine in HIV-infected subjects. *J Infect Dis*. 2013;207(5):749-758. doi:10.1093/infdis/jis753

19. Overton ET, Lawrence SJ, Stapleton JT, et al. A randomized phase II trial to compare safety and immunogenicity of the MVA-BN smallpox vaccine at various doses in adults with a history of AIDS. *Vaccine*. 2020;38(11):2600-2607. doi:10.1016/j.vaccine.2020.01.058

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