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Prevention and Treatment of Monkeypox

Revised 9/6/22: In the Prevention section, "smallpox" was removed in the first paragraph, last sentence of The Vaccines section when describing the vaccinia virus; it was also removed in Table 2, 3rd column of Vaccine virus.
Revised 12/2/22: On December 2, 2022, the CDC adopted the use of mpox to refer to monkeypox disease.

An outbreak of monkeypox has recently spread around the globe and across the US.[1] Updated information about the current outbreak is available from the CDC.[2]

MONKEYPOX — Monkeypox is caused by infection with an orthopoxvirus historically transmitted by wild animals such as rodents and primates. Unlike previous outbreaks, human-to-human transmission is responsible for the current outbreak; most cases have occurred in men who have sex with men.Clinical manifestations of monkeypox infection are similar to but generally milder than those of smallpox; they include fever, headache, myalgia, chills, fatigue, lymphadenopathy, and characteristic skin lesions. Skin lesions can be present without systemic symptoms.

PREVENTION — The CDC recommends pre-exposure prophylaxis for persons at high risk of infection and post-exposure prophylaxis for recently exposed persons to prevent monkeypox infection or reduce its severity. Two vaccines, *ACAM2000* and *Jynneos*, are authorized in the US for such use. Persons at risk for occupational exposure to an orthopoxvirus should receive **pre-exposure** prophylaxis with either *Jynneos* or *ACAM2000*.[3] During the current outbreak, the CDC also recommends that either vaccine be given for **post-exposure** prophylaxis within 4 days after a known or presumed exposure (see Table 1). If the vaccine is given 4-14 days after the date of exposure, vaccination may reduce symptoms of the disease, but may not prevent infection.[4]

The Vaccines – *ACAM2000* has been licensed in the US for years for prevention of smallpox and is now available for prevention of monkeypox infection under an expanded-access investigational new drug (IND) protocol. It contains a live, replication-competent vaccinia virus that can be transmitted to close contacts of the vaccinee.[4]

Jynneos, a two-dose ortho-poxvirus vaccine, was licensed by the FDA in 2019 for prevention of smallpox or monkeypox infection in adults who are at high risk for infection.[4] *Jynneos* contains a live, replication-deficient modified form of the vaccinia virus Ankara (modified vaccinia Ankara [MVA]), which is closely related to the variola and monkeypox viruses; MVA does not cause disease in humans. Immunocompromised persons, including those receiving immunosuppressive therapy, may have a diminished response to the vaccine. At the time of publication, *Jynneos* was in short supply in the US.

Table 1. Recommendations for Monkeypox Vaccination[1]

- Persons at risk for occupational exposure to an orthopoxvirus (research or clinical laboratory personnel performing diagnostic testing for orthopoxviruses, designated response team members, and healthcare personnel who administer *ACAM2000* or care for patients infected with an orthopoxvirus)
- Persons with a known exposure to monkeypox[2]
- Persons with a sex partner who was diagnosed with monkeypox within the past 14 days
- Persons who had any of the following within the past 14 days: multiple sex partners, group sex, sex at a commercial sex venue, or sex in an area where monkeypox transmission is occurring

1. CDC. Vaccination strategies. August 9, 2022. Available at: https://bit.ly/3dcObpq. Accessed August 18, 2022.
2. Within 4 days following exposure. If the vaccine is given 4-14 days after the date of exposure, vaccination may reduce symptoms of the disease, but may not prevent infection.

Clinical Studies — No data are available on the effectiveness of *Jynneos* or *ACAM2000* in the current outbreak.

FDA licensure of *Jynneos* was based on the results of a noninferiority clinical trial in 433 healthy adults 18-42 years old that compared immune responses with two subcutaneous doses of *Jynneos* to one dose of *ACAM2000*; none of the participants had been previously vaccinated against smallpox. *Jynneos* was noninferior to *ACAM2000* in producing a neutralizing antibody response against vaccinia virus (geometric mean titer of neutralizing antibodies was 153.5 at week 6 with *Jynneos* and 79.3 at week 4 with *ACAM2000*).[5] Vaccine effectiveness for prevention of monkeypox was inferred from comparable antibody responses to *ACAM2000* in healthy persons and from animal studies that showed prior vaccination with *Jynneos* protected nonhuman primates that were exposed to monkeypox virus.

Table 2. *Jynneos* vs *ACAM2000*

	Jynneos (Bavarian Nordic A/S)	*ACAM2000* (Emergent Biosolutions)
FDA-licensed indication	Prevention of smallpox and monkeypox in adults; available under an Emergency Use Authorization (EUA) for patients <18 years old	Prevention of smallpox in patients ≥1 year old; available under an expanded-access Investigational New Drug (IND) protocol for monkeypox
Vaccine virus	Replication-deficient modified vaccinia Ankara	Replication-competent vaccinia virus
Administration	Two 0.5-mL doses administered subcutaneously or two 0.1-mL doses administered intradermally[1] 28 days apart	Percutaneously with a bifurcated needle; single dose that requires 15 punctures
Presence of postvaccination lesion (marker of successful vaccination)	No	Yes (at the vaccination site; can take ≥6 weeks to heal)
Immune response	2 weeks after 2nd dose for maximal effect	Up to 4 weeks after single dose for maximal effect
Booster frequency (ACIP recommendations)	Every 2 years after 2-dose primary series for ongoing risk of occupational exposure to variola virus or monkeypox virus and at least every 10 years for exposure to less virulent orthopoxviruses	Every 3 years for ongoing risk of occupational exposure to variola virus or monkeypox virus and at least every 10 years for exposure to less virulent orthopoxviruses
Common adverse effects	Pain, redness, swelling, induration, and itching at the injection site, myalgia, headache, fatigue, nausea, and chills (in smallpox-naive healthy adults)	Pain, redness, swelling, and itching at the injection site, fatigue, malaise, chills, headache, and fever (in vaccine-naive or previously vaccinated persons); myocarditis and pericarditis can occur
Pregnancy	Not associated with adverse outcomes in the offspring of animals who received the vaccine	Can cause fetal harm
Contraindications (per ACIP)	Severe allergy to egg protein, ciprofloxacin, or gentamicin	Atopic dermatitis, other active exfoliative skin disorders, immunosuppression, pregnancy or breastfeeding, age <1 year, cardiac disease or ≥3 cardiac risk factors[2]; according to the label, patients with eye disease treated with topical corticosteroids should not receive the vaccine

1. Lower dose permitted only for use in adults under an FDA emergency use authorization (EUA).
2. Hypertension, diabetes, hypercholesterolemia, heart disease at age ≤50 years in a first-degree relative, and smoking.

Emergency Use Authorization (EUA) of *Jynneos* for **intradermal** administration was based on the results of a trial that evaluated a two-dose series given intradermally compared to subcutaneously. The intradermal dose was one-fifth the subcutaneous dose. Immune responses were similar with both routes of administration.[6]

TREATMENT — Most patients with monkeypox have relatively mild, self-limiting disease. Treatment should be considered for patients with severe disease, those at risk of severe disease (immunocompromised persons, children [particularly those <8 years old], persons with atopic dermatitis or other active exfoliative skin disorders, pregnant or breastfeeding women, persons with one or more complications [e.g., secondary bacterial skin infection, gastroenteritis with severe nausea, vomiting, diarrhea, or dehydration]), and those with monkeypox infections that involve the eyes, mouth, genitals, or anus.

Tecovirimat *(TPOXX)* and brincidofovir *(Tembexa),* a prodrug of cidofovir (*Vistide*, and generics), are FDA-approved for treatment of smallpox; tecovirimat and cidofovir are available under an expanded-access protocol for treatment of monkeypox. No data are available on the effectiveness of these drugs in treating human cases of monkeypox, but they have been shown to be effective against orthopoxvirus infections in animal studies.[7] Intravenous vaccinia immune globulin (VIGIV) may also be considered for patients with severe monkeypox infection, but data on its efficacy for this indication are lacking.[8]

CONCLUSION — Vaccination against monkeypox with either *Jynneos* or *ACAM2000* is recommended by the CDC for all persons at risk for occupational exposure to orthopoxviruses. It is also recommended within 4 days after a known or presumed exposure to monkeypox. Use of *ACAM2000*, a live virus vaccine, should be limited to nonpregnant, nonimmunosuppressed persons; viral transmission to close contacts of the vaccinee can occur. Most patients with monkeypox have self-limiting disease, but treatment can be considered for persons with or at risk of severe disease. ■

Table 3: Drugs/Indications for Treatment of Monkeypox

Brincidofovir *(Tembexa)*

- FDA-approved for treatment of smallpox in children and adults
- CDC is currently developing an expanded-access investigational new drug (IND) application for treatment of monkeypox
- Not currently available from the strategic national stockpile

Tecovirimat *(TPOXX)*

- FDA-approved for treatment of smallpox in children and adults
- Available under an expanded-access protocol for treatment of monkeypox during an outbreak

Cidofovir *(Vistide)*

- FDA-approved for treatment of cytomegalovirus retinitis in patients with AIDS
- Available under an expanded-access protocol for treatment of orthopoxviruses, including monkeypox, during an outbreak

Vaccinia immune globulin intravenous (VIGIV)

- FDA-approved for treatment of complications due to vaccinia vaccination and aberrant infections induced by vaccinia virus (except in cases of isolated keratitis)
- Available under an expanded-access protocol for treatment of orthopoxviruses, including monkeypox, during an outbreak

1. CDC. 2022 Monkeypox outbreak global map. August 16, 2022. Available at: https://bit.ly/3OPNVtC. Accessed August 17, 2022.
2. CDC. Information for healthcare professionals. August 11, 2022. Available at: https://bit.ly/3zVackp. Accessed August 17, 2022.
3. AK Rao et al. Use of Jynneos (smallpox and monkeypox vaccine, live, nonreplicating) for preexposure vaccination of persons at risk for occupational exposure to orthopox-viruses: recommendations of the Advisory Committee on Immunization Practices – United States, 2022. MMWR Morb Mortal Wkly Rep 2022; 71:734.
4. CDC. Vaccination strategies. August 9, 2022. Available at: https://bit.ly/3dcObpq. Accessed August 17, 2022.
5. PR Pittman et al. Phase 3 efficacy trial of modified vaccinia Ankara as a vaccine against smallpox. N Engl J Med 2019; 381:1897.
6. FDA News Release. Monkeypox update: FDA authorizes emergency use of JYNNEOS vaccine to increase vaccine supply. August 9, 2022. https://bit.ly/3C85bYy. Accessed August 17, 2022.
7. A Sherwat et al. Tecovirimat and the treatment of Monkeypox - past, present, and future considerations. N Engl J Med 2022 August 3 (epub).
8. CDC. Interim clinical guidance for the treatment of monkeypox. July 28, 2022. Available at: https://bit.ly/3QaWXmz. Accessed August 17, 2022.

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