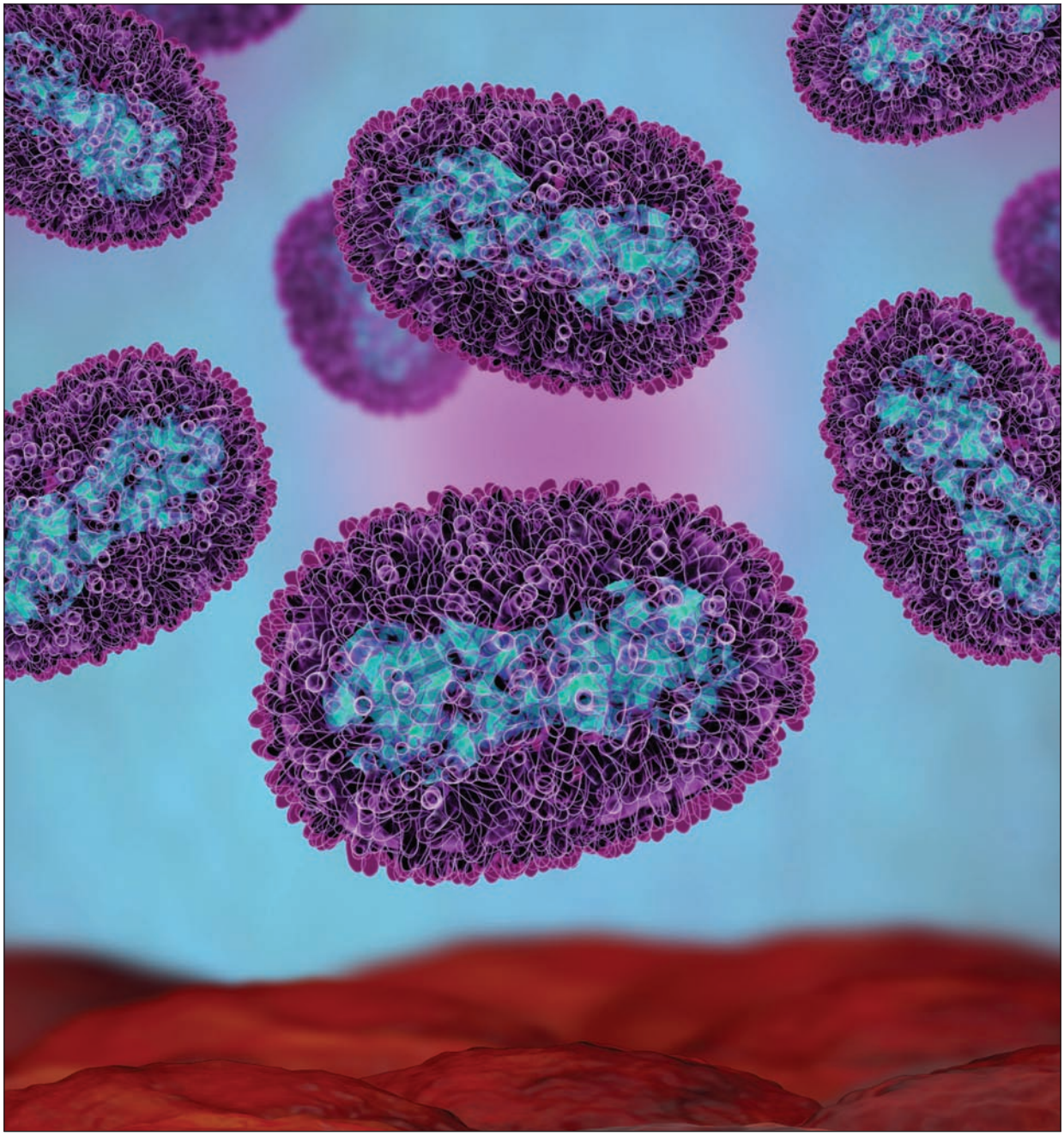

Meletios Verras

Mpox (monkeypox): Diagnosis, prevention, and management in adults

By Lynda Jarrell, DNP, APRN, FNP-BC, CNE and Kashiris Perryman, DNP, APRN, FNP-BC, CNE, LNC

Abstract: Mpox (formerly "monkeypox") is a viral zoonosis that presents similarly to smallpox but is less contagious and causes less severe disease. Mpox may be transmitted from infected animals to humans through direct contact or a scratch or bite. Human-to-human transmission occurs through direct contact, respiratory droplets, and fomites. Two vaccines, JYNNEOS® and ACAM2000®, are currently available for postexposure prophylaxis as well as for prevention in certain populations at high risk for mpox. Most cases of mpox are self-limited; however, tecovirimat, brincidofovir, and cidofovir are available as treatments for at-risk populations.

The disease now known as mpox, updated from the former "monkeypox" (a name change recently advocated for and planned for stepwise adoption by the World Health Organization), is a viral zoonosis resulting from an enveloped double-stranded DNA virus belonging to the *Orthopoxvirus* genus of the *Poxviridae* family. Mpox is similar in presentation to smallpox but is less contagious and disease is less severe. Smallpox was eradicated in 1980, resulting in discontinuation of the vaccine and mpox's emergence as the most important orthopoxvirus in terms of public health. Mpox is primarily found in tropical rainforest regions of West and Central Africa but is now being reported in both endemic and nonendemic countries.[1]

Animal hosts include an assortment of rodents and nonhuman primates. The first established human case of mpox occurred in a 9-month-old male in 1970 in the Democratic Republic of the Congo. Since 1970, most cases have been reported in African countries. The first outbreak outside of Africa occurred in the US in 2003 and was tied to contact with pet prairie dogs carrying the disease. These animals were imported from Ghana.[1] In May 2022, numerous cases of the virus were found in several nonendemic countries, including the US.[1] On May 23, 2022, the CDC initiated an emergency response to mpox. This response encompasses education of clinicians and the public, an increase in lab testing, provision of a framework for prevention, and development of medical guidelines for treatment and postexposure prophylaxis.[2] As of March 2023, more than 30,000 cases of mpox had been reported in the US. At least one case has now been reported in all states and the District of Columbia. The CDC reports that mpox cases currently are declining but advises providers to remain vigilant.[3]

Pathobiology

DNA viruses such as poxviruses (including mpox) typically do not mutate as rapidly as RNA viruses. The mpox virus (MPV) is emerging and mutating faster than expected with genomes from the current outbreak sharing more than 40 mutations with one another. These mutations may be caused by the host fighting off the virus or by the virus's evolution to become more readily transmissible. Scientists need more information about how the virus communicates with the host.[4,5]

The CDC labs have identified two genetically distinct mpox strains in the US. Ten virus isolates have been sequenced by the CDC from the recent outbreaks. Three are distinct from the other seven; although these three vary from one another, they appear to have a common lineage.[5] These three emerged from Nigeria, West Africa, and either the Middle East or East Africa, respectively, implying that mpox outbreaks have been occurring outside endemic countries for longer than previously thought.[5,6]

Transmission and etiology

Human-to-human transmission can occur via direct contact of skin or mucosal surfaces to a viral lesion or body fluids, indirect contact with infected fomites, or respiratory droplets.[7] Additionally, mother-to-child transmission can occur through placental transfer and skin-to-skin contact during and after birth.[5] Though not classified as a sexually transmitted infection, mpox readily spreads during intimate and sexual contact.[5] Current data show that the principal mode of transmission is through close contact during intimate or sexual activity wherein an individual has one or more lesions in the mouth, anorectum, or vagina. The majority of infections have been among men who have sex with men (MSM).[5] A less

Keywords: ACAM2000®, brincidofovir, cidofovir, JYNNEOS®, monkeypox, mpox, orthopoxvirus, tecovirimat, zoonosis

common mode of transmission is through inanimate objects such as towels, bedding, and sex toys.[5,8] Transmission through needle-stick injury has been reported.[9,10] Mpox may also spread from animals to humans through a bite, scratch, or other contact—direct or indirect—with lesion content or other body fluids.[9,11,12]

Mpox mortality is projected between 1% and 11%.[1,13] Once infected, the incubation period is between 5 and 13 days but can be up to 21 days. Presentation usually entails fever, chills, fatigue, headache, muscle aches, sore throat, and lymphadenopathy. A rash appears on the skin and oral mucous membranes about 2 days after development of fever. Initially, there are macules, which progress to papules, vesicles, and pustules before finally becoming crusts that scab before healing. The initial lesions are typically at the site of inoculation.[8] The rash may cover the entire body in severe cases. Symptoms usually last 2 to 4 weeks.[1,8] Scars will ultimately appear after the vesicles have scabbed over and healed. The scars may last for years. Mpox is transmissible from the start of symptoms until the rash is healed and replaced with a new layer of skin.[13,14]

Diagnosis

The differential diagnosis for mpox includes other poxviruses, herpes viruses, and sexually transmitted infections.[8] Diagnosis of MPV is gleaned from the patient's history, clinical presentation, and lab testing. The CDC recommends that two specimens be gathered from lesions in multiple stages of healing (for example, from vesicles to ulcerations and crusts).[16] Viral DNA should also be obtained from a variety of locations, such as the oropharynx, anus, and urethra. Potential specimen types may include swabs of lesion surface, exudate, or crusts. Labs vary on types of specimens accepted.[16]

Confirmation via diagnostic assays is essential to rule out other possible infections.[5,8] Diagnostic assays include polymerase chain reaction (PCR), enzyme-linked immunosorbent assay, western blot, and immunohistochemistry tests.[5,8] Viral DNA is used for the genome-specific real-time PCR test, which is the preferred test.[1,5] Positive tests are forwarded to the CDC to identify the specific variant of the virus.[8]

Prevention

Due to the stigma of mpox, people often avoid treatment, thus increasing the spread of the disease to others. Public health organizations should notify communities about possible spread of mpox among high-risk individuals including gay men, bisexual men, and other MSM and people who have multiple or new sex partners, as well as anyone who has had close contact with a symptomatic person. A person with symptoms suggestive of mpox should seek medical care and abstain from sexual activity or other activities involving close contact with others until resolution of the infection. Persons suspected of having mpox should be isolated from other patients, tested, and notified of results immediately. Contact tracing should be implemented for positive cases.[13]

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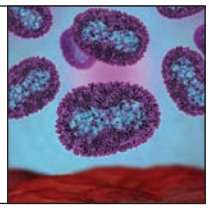

Prevention of mpox may be difficult in caregivers of persons with the infection. First-line prevention entails avoiding direct contact with skin lesions or objects used by persons with the infection. NPs and other healthcare providers caring for patients with lesions should don personal protective equipment (PPE) including gowns, gloves, eye protection, and fitted N95 masks.[8,17] A patient thought to have mpox should be placed in isolation in a single-person room.[17] If the patient is transported outside the room, they should be masked with lesions covered. An airborne infection isolation (negative-pressure) room should be used for procedures likely to spread oral secretions. Gloves, gowns, and masks should be used for handling dirty laundry to prevent contact with lesion material.[8,18]

Vaccines

There are two vaccines, originally intended for immunization against smallpox, that are now used in the US for mpox. These include JYNNEOS® (also known as Imvamune or Imvanex) and ACAM2000®. Vaccination plays a role in prevention of mpox and may also improve symptoms.

JYNNEOS. JYNNEOS is the main vaccine being used in the US during the current outbreak. It is a live vaccine made from the Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN) strain, an attenuated, nonreplicating orthopoxvirus.[19] It was initially approved in

2019 for prevention of smallpox and mpox disease via subcutaneous injection only for adults 18 years of age and older determined to be at high risk for smallpox or mpox infection. It was granted emergency use authorization (EUA) by the FDA in August 2022 for 1) immunization via intradermal injection for individuals 18 years of age and older found to be at high risk for contracting mpox and 2) subcutaneous administration for prevention of mpox in individuals younger than 18 years of age found to be at high risk for mpox infection.[20] Because the intradermal dose is only a fraction of the volume of a subcutaneous dose, this aspect of the EUA has the potential to increase the vaccine's availability by five times.[21] Historical data revealed that efficacy of smallpox vaccination with vaccinia virus against mpox is around 85%.[15]

The standard regimen for JYNNEOS is subcutaneous administration in two doses 28 days apart.[19,22] In the current outbreak, the alternative regimen of intradermal administration in two doses 28 days apart is preferred. However, those with a history of developing keloid scars are recommended to receive the vaccine subcutaneously. Unlike ACAM2000 (discussed below), vaccination with JYNNEOS does not entail a significant dermatologic reaction to indicate its success. Adverse reactions are rare but may include injection site irritation, fever and chills, headache, fatigue, and muscle aches. Primary immunogenicity peaks 2 weeks after completion of the two-dose series. Data on JYNNEOS administration in pregnant women is insufficient to inform vaccine-associated risks in pregnancy, and no evaluation of the effects of JYNNEOS in the breastfed infant or on milk production/excretion has been performed.[19] However, animal data do not show evidence of reproductive harm, and pregnancy and breastfeeding are not contraindications to receiving JYNNEOS. The decision to utilize JYNNEOS in pediatric patients should be made in consultation with the CDC.[22] The jurisdictional health department should be contacted prior to administration of the vaccine to individuals younger than 6 months of age.[22]

ACAM2000. ACAM2000 differs from JYNNEOS in that it is a replication-competent vaccinia virus rather than a replication-deficient modified vaccinia Ankara virus.[15] ACAM2000 was approved by the FDA in August 2007 for immunization against smallpox for people determined to be at high risk for smallpox infection.[15,23-25] ACAM2000 is available for use against mpox under expanded access Investigational New Drug (IND) protocol, which indicates ACAM2000 for utilization during an mpox outbreak only if for some reason JYNNEOS cannot be given or is in short supply.[22,23] Potential adult or pediatric use of ACAM2000 should be considered in consultation with the CDC.[22]

ACAM2000 is administered percutaneously using a bifurcated needle to prick the skin multiple times with a droplet of vaccine.[22] It has a boxed warning due to its potential for several serious adverse reactions. Clinicians must weigh risks versus benefits when considering its administration. ACAM2000 should be avoided in patients with congenital or acquired immunodeficiency disorders as well as those at increased risk for unrecognized HIV.[15,22] Successful vaccination with ACAM2000 should cause a significant cutaneous reaction at the injection site. The vaccinia virus is shed from the lesion at the vaccination site for several weeks, and therefore, there is a risk of unintended inoculation of others and unintended autoinoculation.[23] Adverse reactions worth noting include progressive vaccinia and eczema vaccinatum (EV). Progressive vaccinia, which can ultimately be fatal, can occur in individuals who are immunosuppressed; it involves severe localized or systemic infection with vaccinia, including progressive destruction of local areas of skin, subcutaneous tissue, and other underlying structures as well as distant cutaneous lesions.[26] Progressive vaccinia can also occur in contacts who are inadvertently infected by vaccinated individuals. EV is another adverse reaction of ACAM2000 vaccination that can develop in individuals with atopic dermatitis. EV, which is due to uncontrolled viral replication and can occur even among those whose atopic dermatitis is in remission, involves development of an extensive rash with systemic illness and is potentially fatal.[15,27] Vertical transmission can occur in pregnant or lactating females who receive the vaccine or are in close contact with someone who received the vaccine, resulting in fetal vaccinia that may lead to fetal or newborn death.[15,25] Other serious adverse reactions of ACAM2000 include myocarditis and/or pericarditis.[26,28]

ACAM2000 is contraindicated in infants younger than 1 year of age, and caution should be exercised relating to its use in anyone younger than 18 years of age. The vaccine is also contraindicated in patients with three or more of the following: hypertension, diabetes, hypercholesterolemia, heart

disease at age 50 years or younger in a first-degree relative, and smoking.[24] ACAM2000 should not be administered to anyone with a history of developing keloid scars.[22]

Preexposure prophylaxis. During the current mpox outbreak, the CDC recommends vaccination as preexposure prophylaxis for mpox for people with the highest risk of exposure, including MSM and transgender, nonbinary, and gender-diverse people who, in the past 6 months, have had a new diagnosis of a sexually transmitted infection or more than one sex partner; people who have had sex at a commercial sex venue or sex in association with a large public event in a geographic area where mpox transmission is occurring; sex partners of people with the aforementioned risks; and people who expect to experience the aforementioned risks.[22]

Occupational exposure. The Advisory Committee on Immunization Practices (ACIP) recommends preexposure vaccination for individuals with occupational exposure to MPV, such as research lab personnel working with orthopoxviruses.[8,23] In 2021, ACIP voted in favor of JYNNEOS as an alternative to ACAM2000 for primary vaccination and booster doses for these individuals. The ACIP recommends a booster dose of JYNNEOS every 2 years for individuals with risk for occupational exposure to more virulent strains of orthopoxviruses and every 10 years for risk for exposure to less virulent strains. Individuals who received ACAM2000 as their initial vaccine can receive booster doses of JYNNEOS in place of ACAM2000 booster doses.[24]

Postexposure prophylaxis. Brief interactions with individuals with mpox infection while using appropriate PPE do not pose high risk for infection, and mpox vaccination as postexposure prophylaxis (PEP) is therefore not recommended in these cases. Individuals who are known contacts of someone with mpox who are identified by public health authorities are eligible for PEP. Additionally, individuals with a sex partner within the last 14 days who was diagnosed with mpox as well as MSM and transgender, nonbinary, and gender-diverse people who, within the past 14 days, have had sex with multiple partners; group sex; sex at a commercial sex venue; or sex in association with an event or location where mpox transmission is occurring may also be eligible for PEP.[22]

The CDC recommends that individuals with high-degree exposure receive PEP vaccination, whereas benefits versus risks should be weighed prior to administering PEP in a patient with intermediate-degree exposure (see *Interim community exposure risk assessment and recommendations*).[22] Administration of the first vaccination within 4 days of exposure is recommended by the CDC to prevent disease. If vaccination occurs 4 to 14 days after the exposure date, the vaccine may not prevent disease onset but may reduce symptoms.[15] Recommendations for PEP for healthcare personnel can be found on the CDC website.[17]

Management

Most cases of mpox can be treated with supportive care. There are no FDA-approved treatments for mpox. Antivirals that can potentially be used to treat mpox include tecovirimat, brincidofovir, and cidofovir.[8,29] Antivirals should be considered in individuals with severe disease and/or for those with lesions involving the pharynx, penile foreskin, vulva, vagina, urethra, or anorectum. Treatment with antivirals should also be considered for people who are at high risk for severe disease including immunocompromised individuals; pediatric populations (especially those younger than 1 year); individuals who are pregnant or breastfeeding (although these drugs have not been studied in these populations); and individuals with certain dermatologic disorders.[22,30] In addition to antivirals, vaccinia immune globulin I.V. (VIGIV) may be authorized to treat mpox during an outbreak.[29,31]

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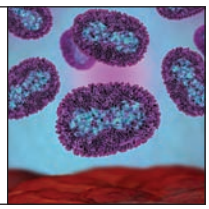


Tecovirimat. The FDA approved tecovirimat in 2018 for the treatment of smallpox in adults and children. It is manufactured in both I.V. and oral formulations.[31] Data regarding effectiveness for the treatment of mpox in humans are not yet available. Tecovirimat, however, has been shown to be effective in animal subjects with disease caused by orthopoxviruses and has an acceptable safety profile in healthy individuals. While randomized controlled trials (RCTs) are underway, the CDC and FDA have simplified the process for providing tecovirimat for mpox under an expanded

Interim community exposure risk assessment and recommendations

For monitoring and postexposure prophylaxis (PEP) in individuals exposed to mpox virus in a community setting

High degree of exposure

Exposure characteristics

- Contact between an exposed individual's broken skin or mucous membranes with the skin lesions or body fluids from a person with mpox **-OR-**
- Any sexual or intimate contact involving mucous membranes (for example, kissing, oral-genital, oral-anal, vaginal, or anal sex [insertive or receptive]) with a person with mpox **-OR-**
- Contact between an exposed individual's broken skin or mucous membranes with materials (for example, linens, clothing, objects, sex toys) that have contacted the skin lesions or body fluids of a person with mpox (for example, sharing food, handling or sharing of linens used by a person with mpox without having been disinfected† or laundered)

Recommendations

- Monitoring: Yes
- PEP¶: Recommended

Intermediate degree of exposure

Exposure characteristics

- Being within 6 feet for a total of 3 hours or more (cumulative) of an unmasked person with mpox without wearing a surgical mask or respirator **-OR-**
- Contact between an exposed individual's intact skin with the skin lesions or body fluids from a person with mpox **-OR-**
- Contact between an exposed individual's intact skin with materials (for example, linens, clothing, sex toys) that have contacted the skin lesions or body fluids from a person with mpox without having been disinfected† or laundered **-OR-**
- Contact between an exposed individual's clothing with the person with mpox's skin lesions or body fluids, or their soiled linens or dressings (for example, during turning, bathing, or assisting with transfer)

Recommendations

- Monitoring: Yes
- PEP¶: Informed clinical decision-making recommended on an individual basis to determine if the benefits of PEP outweigh the risks

Lower degree of exposure

Exposure characteristics

- Entry into the living space of a person with mpox (regardless of whether the person with mpox is present), and in the absence of any exposures above

Recommendations

- Monitoring: Yes
- PEP¶: None

No risk of exposure

Exposure characteristics

- No contact with the person with mpox, their potentially infectious contaminated materials, nor entry into their living space

Recommendations

- Monitoring: No
- PEP¶: None

¶ JYNNEOS and ACAM2000 are available for PEP

† Disinfection using a disinfectant registered with the US Environmental Protection Agency (EPA), such as those with an emerging viral pathogens claim found on EPA's List Q: www.epa.gov/pesticide-registration/disinfectants-emerging-viral-pathogens-evps-list-q

Factors that may increase the risk of mpox transmission include (but are not limited to): the person with mpox had clothes that were soiled with body fluids or secretions (for example, discharge, skin lesion crusts or scabs on clothes) or was coughing while not wearing a mask or respirator, or the exposed individual is not previously vaccinated against smallpox or mpox. People who may be at increased risk for severe disease include (but are not limited to): young children (<1 year of age), individuals who are pregnant or immunocompromised, and individuals with a history of atopic dermatitis or eczema.

Source: CDC

This information is available on the CDC website for no charge: www.cdc.gov/poxvirus/monkeypox/clinicians/monitoring.html

Information up-to-date as of time article went to press. As recommendations are evolving, providers are encouraged to check CDC website (including page listed above) for most current recommendations and information.

access IND protocol by reducing the number of required forms and data collection as well as allowing the option of virtual visits for patients in place of in-person visits.[30,32]

Brincidofovir. Brincidofovir has also been FDA-approved for the treatment of adult and pediatric patients, including neonates, with smallpox. Brincidofovir is an oral formulation that is a prodrug of cidofovir. No data are available regarding brincidofovir's efficacy for treating mpox, but the drug has been shown to be effective *in vitro* and in animals against orthopoxviruses.[29] In order to use brincidofovir for mpox, providers must request and obtain an FDA-authorized single-patient emergency use IND. The FDA will consider requests for this drug for patients who experience disease progression while receiving tecovirimat, whose disease initially improves then worsens after receiving tecovirimat, or who are ineligible or have a contraindication for tecovirimat.[29] RCTs are also currently underway to test brincidofovir's efficacy in the treatment of mpox. Brincidofovir has a better safety profile than cidofovir (described below), but liver function tests need to be performed before and during treatment due to the risk of increases in serum transaminases and bilirubin.

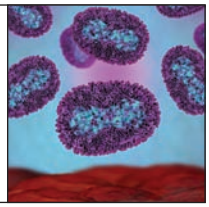
Cidofovir. Cidofovir is approved by the FDA for the treatment of cytomegalovirus retinitis in patients with AIDS.[29] Cidofovir is only available in I.V. formulation. Cidofovir has been shown to be effective for orthopoxviruses in *in vitro* and animal studies. Cidofovir should only be used if tecovirimat or brincidofovir have been ineffective or are contraindicated. Cidofovir has a boxed warning for nephrotoxicity and other possible adverse reactions.[8,23,31,33]

VIGIV. VIGIV is an immune globulin approved by the FDA for treatment of complications of vaccinia vaccination, including EV, progressive vaccinia, severe generalized vaccinia, vaccinia infections in individuals who have skin conditions, and certain aberrant infections induced by vaccinia virus. Data are limited on the effectiveness of VIGIV for mpox and smallpox. Use of VIGIV may be considered for certain immunocompromised individuals exposed to mpox for whom vaccination is contraindicated. Use of VIGIV as treatment for mpox is conducted via an expanded access IND.[8,29,31] The CDC reviews requests from providers for VIGIV for patients on a case-by-case basis.

Conclusion

Mpox is a contagious orthopoxvirus historically found in Africa but that has recently spread to nonendemic regions, including the US. Mpox cases currently are on the decline; however, the CDC warns against becoming overly optimistic. It is imperative that healthcare providers remain vigilant in diagnosing, preventing, and treating the disease to prevent long-term consequences. High-risk individuals and close contacts should be assessed for eligibility for vaccination with JYNNEOS. Treatment with certain antivirals—tecovirimat, brincidofovir, and cidofovir—should be considered for patients with severe cases. NPs and other clinicians, community leaders, and public health personnel must commit to coordinating efforts to control the current outbreak and ensure that affected individuals have access to appropriate treatment. NP

It is imperative that healthcare providers remain vigilant in diagnosing, preventing, and treating the disease to prevent long-term consequences.



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