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Monkeypox (hMPXV Infection): A Practical Review

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ABSTRACT

Monkeypox, a neglected disease previously confined to Africa, is causing a worldwide outbreak affecting predominantly males who have sex with males, especially those who are infected with HIV. The clinical presentation during the current outbreak differs from endemic cases. Treatment with tecovirimat and other antivirals is available. Immunization may be used as preexposure and postexposure prophylaxis.
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Monkeypox, previously considered an exotic disease confined to Africa, is causing a worldwide outbreak with cases reported predominantly among males who have sex with males. This article provides a practical review of the disease.

In accordance with the recommendation by numerous scientists to avoid using discriminatory and misleading terminology, we use hMPXV to refer to the virus.[1]

THE ORGANISM

hMPXV belongs to the family Poxviridae and the subfamily Cordopoxvirinae (poxviruses of vertebrates). Several genera of Cordopoxvirinae affect humans (as seen in Table 1), one of which is hMPXV.[2] hMPXV is a large (400 nm × 250 nm) brick-shaped virus containing double-stranded DNA. The poxviridae family has 90% genomic sequence homology among its members. Figure 1 describes the replication cycle of hMPXV (extrapolated from the vaccinia virus, used to manufacture smallpox vaccine) cycle.[3]

Since its discovery, hMPXV has been phylogenetically distinguished into 2 clades: the Central African or Congo Basin (Clade 1) and the West African (Clade 2). The pandemic virus isolated in 2022 is phylogenetically close to clade 2; however, there were enough differences to call it clade 3. In August 2022, a group of World Health Organization (WHO) experts established a new nomenclature: clade 1 became clade I, clade 2 became clade IIa, and clade 3 (the current circulating hMPXV) became clade IIb.[4] The phylogenetic evolution of hMPXV has been attributed to apolipoprotein B mRNA editing enzyme, catalytic polypeptide (APOBEC) enzymes. These deaminases convert cytidine to thymidine and guanosine to adenine. Although useful to modify foreign nucleic acid by inactivating its replication and transcription, APOBEC could accidentally render the viruses better fit to immune evasion or induce resistance to antiviral drugs.[5]

EPIDEMIOLOGY

hMPXV was discovered in 1958 during a smallpox-like outbreak in macaque monkeys at a Danish research center, hence, the "monkeypox" name; however, the animal reservoir is unknown. Small rodents harbor the virus in Africa.[6]

The first human case, resembling smallpox, was reported in 1970 in the Democratic Republic of Congo. Human disease is different according to the clade involved:

- Clade 1 hMPXV was reported in the Congo Basin: Cameroon, Congo, the Central African Republic, and Democratic Republic of Congo. Human-to-human transmission occurs. In those not vaccinated against smallpox, the fatality rate was 11% (and 15% in those younger than 4 years of age).[7]
- Clade 2 infection was reported in West Africa (Sierra Leone, Liberia, Ivory Coast, Ghana, and Nigeria). All cases were associated with contact with arboreal and nonarboreal rodents. Mortality was low.[8]

From the 1970s to the present, almost 30,000 cases of hMPXV infection, with a few hundred deaths, have been

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reported in the Congo Basin. In the 1980s, the source of infection was contact with animals (72%), and in the 1990s, contact with humans explained 78% of cases. Until the 1990s, 100% of deaths occurred in children younger than 10 years of age, and later, this group explained only 35% of the deaths. This change may be explained in part by weaning of the cross-protection provided by previous smallpox vaccination.[9]

Sporadic cases have been reported outside Africa, but in 2003 there was an outbreak of 47 cases of hMPXV infection in the US. These were acquired by contact with prairie dogs, which in turn became infected by being housed with rodents imported from Ghana. There were no fatalities, and no person-to-person transmission was documented. Genetic sequence analysis confirmed the isolates belonged to clade 2.[8]

Between 2017 and 2020 an outbreak of hMPXV infection was described in Nigeria, with similar modes of transmission as seen in the current epidemic. The surge of the disease was attributed to population growth and loss of smallpox immunity, but the international community paid little attention.[10]

In May 2022, an unusual outbreak of hMPXV infection was initially reported in the UK. Subsequently multiple cases appeared throughout the world. On July 23, WHO declared a Public Health Emergency of International Concern. As of October, more than 70,000 cases were reported worldwide, the majority in the United States. The outbreak affects disproportionately males who have sex with males, including many of those infected with HIV.[11] The epidemiological differences between the epidemic and the endemic forms of the disease are discussed in Table 2.

Transmission of hMPXV from animals to humans occurs through direct contact with infected blood, bodily fluids, or mucosal or cutaneous lesions. Transmission from humans to humans occurs by contact with skin lesions or respiratory secretions, or by indirect contact with fomites. Airborne transmission has not been documented. In the current outbreak, the main means of transmission is close contact during sexual activity;[12] (however hMPXV is not considered a sexually transmitted infection because sexual activity is not the only means of transmission). In a survey of 45 infected patients, 98% identified themselves as homosexual or bisexual, 74% were HIV negative (out of which 91% were receiving HIV preexposure prophylaxis), 26% were HIV positive and were receiving appropriate treatment. A total of 64% had attended group sex events, 75% had new sexual partners, and 83% got dates via social apps.[13]

CLINICAL SIGNIFICANCE

- Monkeypox (hMPXV) infection is causing a pandemic (beyond its usual confinement in Africa).
- Transmission is via skin-to-skin contact, predominantly during sexual encounters.
- Males who have sex with males, especially those who are infected with HIV are most commonly affected.
- Pandemic cases have shorter incubation period, lesser number of lesions, and more circumscribed location of the lesions.
- Treatment is supportive, but specific antivirals are available.
- Vaccinations can be used for preexposure and postexposure prophylaxis.

CLINICAL MANIFESTATIONS

The clinical presentation of hMPXV infection in endemic countries differs from the manifestations seen during the current outbreak.[12,14,15]

In its classical presentation, hMPXV infection had an incubation period of 7-17 days. The disease started with fever, fatigue, and headache. Prominent maxillary, cervical, or inguinal lymphadenopathy preceding or concomitant with the rash was characteristic. The lymph nodes were described as firm and painful. The rash started in the face and disseminated centrifugally to the rest of the body. There were usually hundreds or thousands of lesions that progressed through 5 phases: macular, papular, vesicular, pustular, and desquamative. During the papular stage a typical central umbilication appeared. The lesions were in the same stage of progression at any given time (a helpful characteristic in differentiating the condition from chickenpox). The rate of complications was high (between 40% and 70%,

Table 1 Poxviridae Genuses Affecting Humans

Genus	Species	Hosts Other Than Humans
Moluscipox virus	Molluscum contagiosum virus	Dogs, birds, kangaroos, equids, primates
Orthopoxvirus	Cowpox virus	Alpacas, cats and large felids, cattle, elephants, mongooses, okapis, rhinoceros, rodents
	Monkeypox virus (hMPXV)	Squirrels, monkeys, great apes
	Vaccinia virus (virus in smallpox vaccine)	Buffalo, cattle, swine, rabbits
	Variola virus (smallpox virus)	None
Parapoxvirus	Bovine popular stomatitis virus	Cattle
	Orf virus	Sheep, goats
	Pseudocowpox virus	Cattle
Yatapoxvirus	Yabapox virus	Monkeys
	Tanapox virus	Monkeys

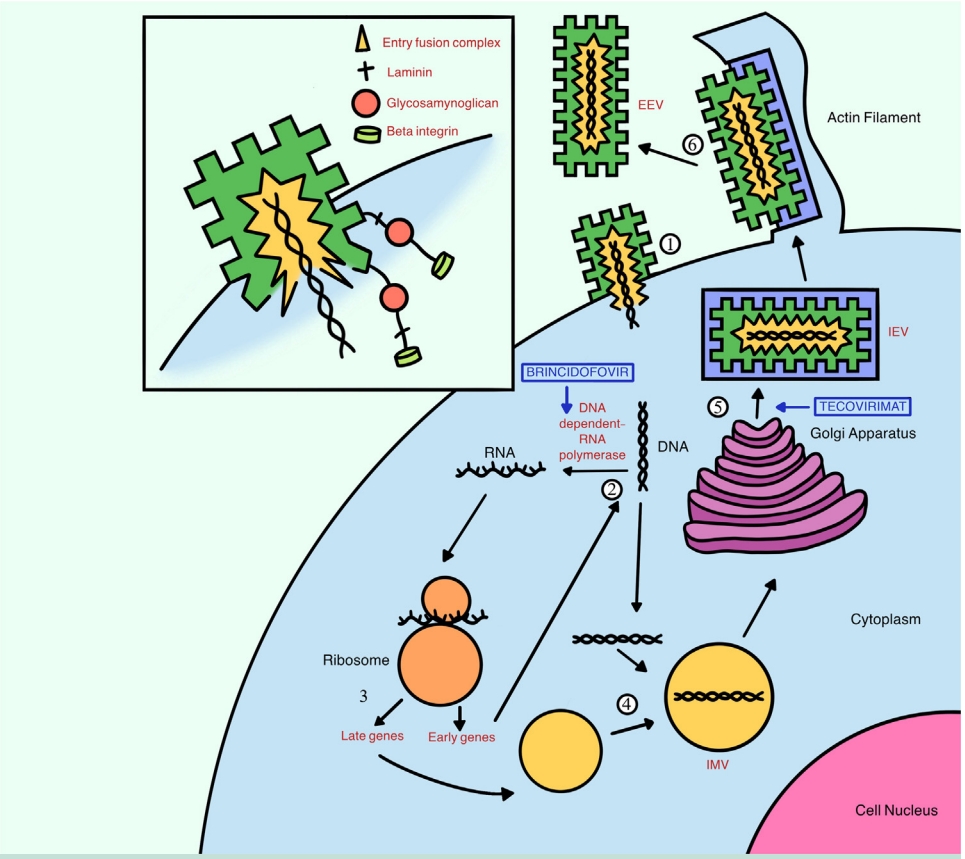

Figure 1 VACV is a large, enveloped, brick-shaped DNA virus that exists in three infectious forms: the intracellular mature virus (IMV), the intracellular triple-enveloped virus (IEV). and the extracellular double-enveloped virus (EEV).
1. To enter the cell, the EEV has an entry fusion complex (EFC) on the inner envelope. The outer envelope has proteins that interact with laminin and with the glycosaminoglycans (chondroitin sulfate and heparan sulfate, which facilitate interaction with other proteins, such as beta integrin or MARCO. They in turn allow disarming the outer envelope allowing entry of the virion.
2. The viral core that enters the cytoplasm contains the viral DNA as well as DNA-dependent RNA polymerase that allows for synthesis of RNA without the intervention of the cell nucleus.
3. The host cell ribosomes translate early and late genes from the viral mRNA. The early genes codify proteins that counteract host immune defenses and stimulate the replication of viral DNA. The late genes codify for proteins required for viral assembly.
4. Viral DNA and core proteins are assembled to become the IMV.
5. Between 5% and 10% IMV are wrapped by a Golgi cisterna or late endosome (LE) becoming 3-membrane wrapped virions (IEV). The F13L gene of the vaccinia virus encodes the membrane protein p37, which is pivotal in the fusion of the IMV membranes with the Golgi or LE. Tecovirimat binds specifically to the homologous F13L proteins (p37 and others), preventing the formation of IEV.
6. IEV surfs the actin filaments until the outermost membrane of the virion fuses with the extracellular membrane, releasing the two-membrane EEV into the extracellular.

depending on the smallpox vaccination status) and included dehydration, diarrhea, bronchopneumonia, ocular infections, and encephalitis. The mortality was high, particularly in children (up to 11%).[14]

Table 3 summarizes the contrasting clinical characteristics during the current outbreak: the incubation period is shorter, the number of lesions lesser, and the localization predominantly around the area of inoculation. Intense anal pain and mucosal compromise is common in the current epidemic.[12]

Figure 2 shows cutaneous lesions of hMPXV infection.

Other conditions can resemble hMPXV infection and should be considered in the differential diagnosis: smallpox, chickenpox, molluscum contagiosum, other poxvirus infections, rickettsial pox, and secondary syphilis.[16]

DIAGNOSIS

Confirmation of the diagnosis during the current outbreak requires obtaining samples from the skin or mucosal lesions for nucleic acid amplification.

Table 2 Epidemiological Differences Between Endemic and Epidemic hMPXV Infection

Epidemiological Characteristic	Endemic Infection	Current Epidemic Infection
Geographic location	Rainforest of West and Central Africa	Worldwide
Areas affected	Small rural villages	Large urban areas
Clade causing infection	I, IIa	IIb
Age of infected	Younger than 15 years of age	Sexually active age
Comorbidities	Not reported	Sexually transmitted infections, including HIV HIV coinfection occurs in up to 40% of cases in the US
Transmission	Contact with animals (due to deforestation, hunting, migration) followed by secondary human-to-human transmission	Mainly human-to-human transmission during sexual contact
Mortality	High (between 3% and 10 % depending on the clade)	Very rare

Table 3 Clinical Characteristics of Endemic and Current Epidemic hMPXV Infection

Clinical Characteristic	Endemic Infection	Current Epidemic Infection
Incubation period (Guzzetta, 2022)	7-17 days	6-11 days
Prodromal symptoms	Fever, fatigue, and headache frequently present	Fever, fatigue, and headache occasionally present
Lymphadenopathy	Prominent and painful	May or may not be present
Number of lesions	Hundreds to thousands	Ten or less lesions, including solitary lesions
Rash distribution	Global	Localized, around site of inoculation
Stage of lesions	Usually, all lesions are at the same stage of evolution	Lesions may be at different stages of evolution
Disease without rash	Not reported	Rectal, pharyngeal, or mucosal lesions without rash have been reported
Complications	Dehydration, diarrhea, bronchopneumonia, ocular infections, and encephalitis	Anal pain, cellulitis, urinary signs, ocular infections, abscess, lymphangitis, and paronychia

Health care personnel should wear gowns, gloves, eye protection, and N-95 respirators while collecting samples. Samples should be obtained using sterile polyester or Dacron swabs (but not cotton) from the surface of the lesions or the exudate. Unroofing of lesions is not recommended, given risk of dissemination. Ideally two swabs from each site involved should be obtained. Testing from multiple sites improves sensitivity and reduces false-negative results. The swab should be transported in viral transport media. The sample should be labeled appropriately, and if not sent immediately, it can be refrigerated (2°C-8°C) or frozen (−10°C or lower) until processed.[17]

The Centers for Disease Control and Protection (CDC; via local public health departments) and several commercial laboratories (Aegis Science, Labcorp, Mayo Clinic Laboratories, Quest Diagnostics, and Sonic Healthcare) can process samples for polymerase chain reaction (PCR) testing, the preferred method of nucleic acid amplification. Some tests can identify hMPXV specifically, but others only recognize poxviruses in general. PCR tests are highly sensitive, are able to detect as little as 10 viral genomes, and are highly specific.[18,19]

There are tests other than PCR (summarized in Table 4) that could be used for diagnosis of hMPXV, but they do not provide fast enough results to be clinically relevant.[19]

Testing for gonococcus/chlamydia, syphilis, and HIV is pertinent in cases of hMPXV infections as they can coexist.

TREATMENT

Supportive Therapy

Most cases in the current epidemic are mild and do not require hospitalization. Supportive care is the standard (Table 5). Numerous recommendations are backed by experience in low-resource settings.[20] Other recommendations are more specific for the current outbreak; for example, rectal pain can be excruciating and may require hospitalization.

Antivirals

Use of systemic antivirals is only recommended in selected patients as summarized in Table 6. Topical trifluridine has been used in orthopoxvirus-associated corneal lesions, but there is no experience in hMPXV cases.

Tecovirimat (known also as ST-246 or TPOXX) is the antiviral of choice. This agent prevents the final maturation and release of virions by inhibiting the viral protein VP37. Tecovirimat was approved for the treatment of smallpox in adults and children weighing > 3 kg based in the "Animal Rule."[21] As smallpox was eradicated from Earth and studies were not feasible, the Food and Drug Administration (FDA) allowed the approval based on efficacy in animal models (survival in nonhuman primates infected with monkeypox virus and rabbits infected with rabbitpox virus) and safety

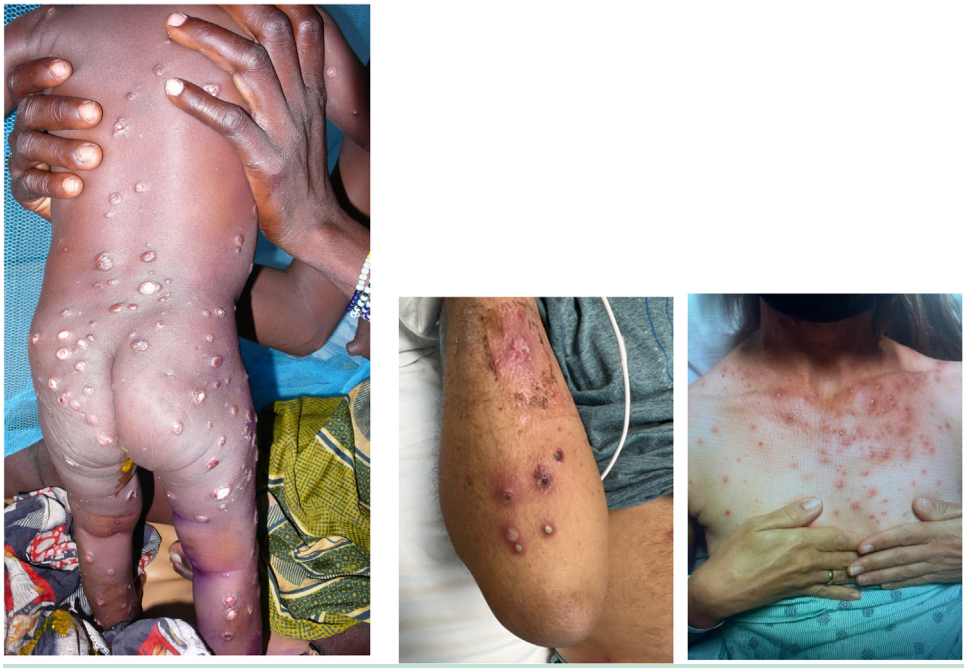

Figure 2 **(A)** A baby with "endemic" monkeypox virus in Africa. **(B)** A male with hMPXV infection following "fisting" (insertion of the hand into the rectum or vagina of someone as a means of sexual stimulation). **(C)** A female with hMPXV infection after performing cunnilingus and anilingus. Oral lesions not shown.

in human volunteers. Unfortunately, the few reports of human disease treated with the drug have not provided conclusive evidence of efficacy.[22] Ongoing clinical trials are testing the efficacy and safety of tecovirimat in human infection in Congo and the US.[23]

Tecovirimat is available in the US via selected local public health departments. Alternatively the CDC Emergency Operations Center can be contacted directly at 770-488-7100 for consultation. The CDC has established an expanded access for this Investigational New Drug (EA-IND). In practical terms, tecovirimat can be used immediately on receipt and required forms for the CDC institutional review board, such as informed consent, patient's intake form, and report of adverse events can be submitted after the vaccination has been administered.[24]

Table 4 Tests to Identify hMPXV (Other Than PCR)

Test	Comments
Restriction length fragment polymorphism	Detects nucleic acid material but requires viral culture and is time consuming
ELISA for detection of IgM and IgG in serum	May be false positive due to cross reactivity with other poxviruses Antibodies may appear several days after starting of clinical disease Testing of acute and convalescent titers may be necessary
Electron microscopy	Other poxviruses may look morphologically similar Sample preparation is complicated, and procedure is expensive
Immunochemistry and immunofluorescence	Requires biopsy and is not specific for monkeypox
Viral cultures	Time-consuming test

ELISA = enzyme-linked immunosorbent assay; IgG = immunoglobulin G; IgM = immunoglobulin M; PCR = polymerase chain reaction.

Tecovirimat capsules should be taken 30 minutes after a full meal with moderate to high fat content. If the patient is unable to swallow capsules, the capsule content can be mixed with water and administer as liquid. Alternatively, tecovirimat is available intravenously. Tecovirimat dosing is based on weight (Table 7). Treatment is administered for 14 days but can be shorter or longer (but not to exceed 90 days) depending on the patient's clinical condition. Tecovirimat has not been studied in pregnant or lactating mothers, the benefits may outweigh potential risks of use.[25]

Tecovirimat is a weak inducer of cytochrome P450 (CYP)3A and a weak inhibitor of CYP2C8 and CYP2C19. It may cause increased repaglinide levels (causing hypoglycemia) and decreased midazolam levels. Tecovirimat should not be used concomitantly with carbotegravir/rilpivirine. It may also interact with doravirine, rilpivirine, and maraviroc, but the effects are mild and dose adjustments may not be required. Tecovirimat has a low barrier to resistance and change in the VP37 protein may decrease the efficacy of the drug.[26]

Intravenous tecorivimat is contraindicated if the creatinine clearance is < 30 mL/min.[25]

Table 5 Supportive Care in Monkeypox Infection

Type of Care	Recommendations
Systemic care	Appropriate oral or intravenous hydration and adequate nutrition may accelerate recovery
Pain control	Antipyretics and analgesics may improve comfort
	Short-term use of gabapentin and opioids may be indicated after taking into consideration comorbidities and potential medication interactions
	Oropharyngeal pain can be treated with saltwater rinses, chlorhexidine mouthwash, topical viscous lidocaine, or prescription analgesic mouthwash (containing an antihistaminic and a topical anesthetic)
	Rectal pain can be treated with stool softeners (to prevent painful defecation), warm sitz baths, and topical lidocaine
	Genital pain can be treated with topical lidocaine; the use of topical steroids is controversial
Skin care	Frequent cleansing of the skin may prevent overimposed bacterial infections
	Judicious application of occlusive dressings in areas with dense rash or in the face, may promote healing and prevent scarring
	Keeping short nails, wearing mittens, and administering antihistamines may control pruritus and prevent further skin damage
	Incision and drainage of abscess and use of antibiotics is indicated in overimposed bacterial infections
Ocular care	Topical lubricants and antibiotics (prophylactically or therapeutically) may prevent progression of ocular damage (ranging from conjunctivitis to corneal ulcerations)
	Topical trifluridine has been used in ocular vaccinia and may be effective in monkeypox

Cidofovir is a viral DNA polymerase inhibitor approved for the treatment of cytomegalovirus-induced retinitis in patients infected with HIV. Cidofovir has in-vitro and in-vivo activity against hMPXV, but clinical data in humans is lacking.[27] Although available commercially and via IND from the CDC, it is not the medication of choice during this outbreak.

Brincidofovir (Tembexa) is a lipid conjugate of cidofovir also approved by the FDA for treatment of smallpox based in the "Animal Rule." The medication is not commercially available but can be accessed via IND from the manufacturer by inquiring at expandedaccess@chimerix.com. Brincidofovir is available in liquid formulation and in tablets. The dosage is 200 mg weekly for 2 weeks. Treatment duration longer than 2 weeks has been associated with excessive mortality (in patients infected with cytomegalovirus). Brincidofovir can cause diarrhea and other gastrointestinal side effects and requires monitoring of liver enzymes. The medication is potentially teratogenic and should not be used in pregnancy.[28]

Vaccinia immunoglobulin (VIG) was administered in the past intramuscularly, but in 2005 an intravenous formulation was approved. This formulation allows administration of higher doses without causing pain. VIG has been approved for the treatment of vaccinia vaccination complications (specially eczema vaccinatum). VIG has efficacy in multiple orthopoxvirus animal models, but information on human hMPXV infection is lacking. VIG can be obtained via IND from the CDC. VIG should be administered at a dose of 6000 U/kg, but doses of up to 24,000 U/kg have been administered to healthy volunteers. VIG is contraindicated in cases of preexistent anaphylaxis or hypersensitivity. Like with any blood-derived product transfusion side effects may occur. VIG can interfere with the efficacy of live vaccines. VIG niche in the treatment of hMPXV may be as adjuvant along with use of other antiviral agents in severe cases.[29]

PREVENTION

Infection Control at Home

Measures of infection control at home include isolation; containment and use of personal protective equipment; and hygiene, cleaning, and disinfection (Table 8).[30]

Table 6 Indications for Antiviral Therapy in Monkeypox

Treatment Indications		Categories
Individuals at risk of complications	Certain females	Pregnant females, lactating females
	Patients with certain skin disorders	Atopic dermatitis, other exfoliative skin conditions
	Pediatric patients	Especially younger than 8 years
	Immunosuppressed patients	HIV infection, hematological malignancies, solid organ transplant, hematopoietic transplant, use of immunosuppressant agents
Individuals already having complications	Disease affecting areas that constitute a special hazard	Ocular and oral mucosa, genitalia and anus
	Severe disease	Monkeypox causing encephalitis or sepsis
	Comorbidities and complications	Associated bronchopneumonia, gastroenteritis, overimposed skin bacterial infection, other comorbidities

Table 7 Formulations and Dosing of Tecovirimat in Adults

Formulation	Weight	Dosing
Oral (200 mg capsules)	88 to < 244 lb	600 mg orally every 12 hours
	> 244 lbs	600 mg orally every 8 hours
Intravenous (10 mg/mL) (Should be diluted in twice as much 0.9 normal saline or 5% dextrose in water)	77 to < 244 lb	200 mg IV every 12 hours (infusion should last 6 hours)
	264 lb	300 mg IV every 12 hours (infusion should last 6 hours)

IV = intravenously.

Infection Control in the Hospital

If a patient with hMPXV infection is admitted to the hospital, infection prevention should be contacted immediately. Patients should be placed in a single-person room with private bathroom and the door should be kept closed. There is no need for a negative pressure room unless intubation or procedures that produce aerosols are required. Lesions should be covered with dressings or clothes. Patients should remain in isolation and with limited visitation until all skin lesions have crusted and a healthy layer of skin forms underneath the crust.[31]

Health care personnel should wash hands with soap and water or use waterless antiseptic agents frequently. When entering a patient's room, health care staff should wear gowns, gloves, eye protection, and a N-95 respirator. Cleaning and disinfection of the room and handling of soiled laundry should be done using standard procedure.[31]

Medical waste from patients in the current outbreak (clade IIB) should be managed as a Category A infectious substance ("an infectious substance capable of causing permanent disability or life-threatening disease"). Curiously medical waste from patients infected with clade I is considered Category B (not capable of causing such damage).[32]

In case of death, remains should be handled using contact, droplet, and airborne precautions. If an autopsy is performed, appropriate measures to prevent percutaneous injury are indicated. Samples should be taken from tissues demonstrating gross pathology. After the procedure, nonreusable items should be handled as medical waste and reusable equipment and surfaces should be cleaned or disinfected according to standard protocols.[33]

Vaccines

Smallpox vaccines can be used for prevention of hMPXV infection. Table 9 describes characteristics of smallpox vaccines; however, the remainder of this section only discusses vaccines currently used in the US for prevention of hMPXV infection.

The US National Monkeypox Vaccination Strategy has made available 2 preventative vaccines: JYNNEOS and ACAM2000. The vaccines can be obtained via local public health authorities.[34]

JYNNEOS, manufactured by Bavarian Nordic, is the preferred vaccination. This is a further attenuated Modified Vaccinia Ankara (MVA) strain grown in chicken embryos that cannot reproduce in mammal cells but confers immunity to smallpox. JYNNEOS has several advantages over ACAM2000: higher geometric mean titers and seroconversion rates; no cutaneous reactions (so called "take") that

Table 8 Infection Control Measures at Home

Measure	Activity
Isolation	Remain on separate room or space Avoid close contact with other people or pets Avoid sharing household items or utensils Use a separate bathroom if possible
Containment and use of personal protective equipment	Cover lesions with clothes or dressings Change own dressings if possible Wear a well-fitting mask Cover household surfaces that cannot be laundered with covers or blankets Noninfected household members should wear gloves and well-fitted mask at minimum if helping the sick
Hygiene, cleaning, and disinfection	Wash hands with soap and water or alcohol-based rub frequently Use an EPA-approved disinfectant on hard surfaces Contain soiled laundry until washed in a regular washing machine Dispose waste appropriately

EPA = Environmental Protection Agency.

Table 9 Characteristics of Vaccines Approved for Smallpox (and hMPXV)

Type	Generation (Examples)	Comments
Attenuated live virus replication-competent vaccines	First generation (Dryvax, Wetvax)	Used in initial eradication of smallpox; may be held in national reserves but do not meet current safety and manufacturing standards and are not recommended at this time
	Second generation (ACAM2000)	Contraindicated in immunosuppressed patients, pregnancy, atopic dermatitis, and others; risk of adverse events (eczema vaccinatum, generalized vaccinia, fatal progressive vaccinia); requires multiple percutaneous punctures with a bifurcated needle
Attenuated live virus replication-deficient vaccines	Third generation (Jynneos)	Uses more attenuated strain (Modified Vaccinia Ankara Bavarian Nordic strain or MVA-BN); administered subcutaneously with regular needle; fewer contraindications and fewer adverse events than lesser generations

cause a draining lesion with risk of autoinoculation; less risk of myopericarditis; and possibility to be used in immunosuppressed patients and people with eczema. JYNNEOS was licensed based on animal and clinical studies showing a comparable immune response to ACAM2000.[35]

To administer JYNNEOS, the provider is required to sign an agreement with the US Department of Health and Human Services to collect demographic and vaccine related information (product, dose number, lot, etc.) and to report serious adverse events.[36] The vaccine is administered in two doses (28 days apart) at 0.5 mL subcutaneously. Alternatively (to spare vaccine) 0.1 mL can be administered intradermally at the same interval.[37] Contraindications to the vaccine include history of anaphylaxis or severe allergic reaction to a previous dose of JYNNEOS, egg or chicken protein, gentamicin, or ciprofloxacin.[36]

ACAM2000 is a smallpox vaccine derived from a clone of Dryvax (the original vaccine used for eradication of smallpox) approved in 2015 for prevention of orthopoxviruses in laboratory and health care personnel at risk for occupational exposure. The vaccine is available (but not frequently used) via EA-IND. It requires a single dose, but it has several disadvantages including percutaneous administration using a bifurcated needle, more side effects (self-inoculation, myocarditis, pericarditis), and more contraindications (anaphylaxis to previous dose of ACAM2000 or excipients, immunosuppression, pregnancy, breastfeeding, prominent cardiac risk factors, eczema and other exfoliative skin conditions, cheloids, ocular infection treated with steroids, previous history of monkeypox) than JYNNEOS. Details about its administration can be found on the CDC website.[38]

Preexposure Prophylaxis

Vaccination before exposure is recommended in 2 groups:[34]

- Certain laboratory and health care workers who can be exposed to orthopoxviruses (a particular group at risk may be proctologists, especially those working with patients infected with HIV).
- Those with sexual risk in previous 6 months: Males who have sex with males who developed a sexually transmitted infections; people who engage in sex with commercial sex workers, or group sex, or participate in large sexual events in risky geographic areas; partners of people with risk factors.

Transmission risk among health care workers is possible but, in nonendemic areas, rare, with only 1 case identified in a review between 2000 and 2022.[39]

It must be noted that in certain geographic areas, such as New York, vaccine eligibility has expanded, and anyone who considers themselves to be at risk for hMPVX infection through sex or other intimate contact can receive the vaccine.[40]

Postexposure Prophylaxis

Vaccination after known exposure to hMPXV is indicated in those identified by the local public health authorities. In addition, expanded postexposure prophylaxis may be offered to those with a sex partner diagnosed with monkeypox within the last 14 days, or to those with sexual risk as described in the preexposure prophylaxis section.[34,40]

Vaccination is recommended within 4 days of the exposure for maximum efficacy. Vaccination between 4 and 14 days after contact provides lesser protection. Vaccination beyond 14 days may be even less effective but must be considered in immunosuppressed patients.[36]

VIG could be considered for postexposure prophylactics in those patients with severe T cell immunodeficiency who may be unable to mount an appropriate immune response with vaccination.[19]

One Health

Bushmeat hunting for human consumption and international demand of exotic pets may have fueled the emergence of monkeypox. One Health promotes alternatives to bushmeat, public awareness campaigns, education on hygienic handling of wild animals, routine vaccination of people at risk, and abolition of exotic pet trade. Although unlikely to curtail the current outbreak, it may help in preventing other zoonoses.[41]

Misinformation

Physicians and health care workers play an important role in preventing misinformation and stigmatization because it has occurred in other pandemics.[42]

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