

Mpox

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Module 2: [Self-Study Lessons](#)

Lesson 9: [Mpox](#)

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Introduction

Mpox is an infection caused by monkeypox virus, an orthopox virus previously associated with sporadic cases in Africa that usually involved contact with an animal reservoir ([Figure 1](#)).^[1] In May 2022, an mpox outbreak characterized by human-to-human transmission via primarily close physical contact spread throughout more than 100 countries not typically affected by endemic circulation.^[2] Clinical episodes in the context of this 2022 outbreak most frequently involved sexual transmission of mpox among men who have sex with men (MSM).^[2,3,4] Polymerase chain reaction (PCR) testing on samples obtained from mpox lesions is available for diagnosis and should be used in populations and circumstances with clinical suspicion of mpox. Vaccination as prevention should be prioritized for vulnerable groups. Although most patients improve with supportive care, multiple investigational therapies have been made available for treatment, especially in persons who are severely immunocompromised.

Epidemiology

Global Mpox Epidemiology

Monkeypox virus was first identified as a cause of human disease in the 1970s in West and Central Africa, primarily associated with exposure to animal hosts in which the virus circulates. Since then, increased rates of cases across that region have been seen, and mpox was reported as endemic in multiple African countries, with most cases occurring in the Democratic Republic of the Congo (DRC).[5,6] Two clades of the virus have emerged in this context based on geography in Africa; clade I has been historically associated with more severe disease than clade II.[7] Previously, outbreaks in the United States have occurred primarily as spillover events from imported mammals from West Africa or as travel-associated cases without associated transmission.[8,9]

- **Clade II Global Outbreak:** In 2022, a global outbreak of clade II mpox occurred, with cases identified in non-endemic countries, including across Europe and the United States.[2,3,10] Since January 2022, there have been more than 100,000 confirmed cases of clade II mpox globally, with more than 100 reported deaths.[11] After the clade II case peaked in the summer of 2022, ongoing transmission and cases have continued to occur at lower rates.[11]
- **Clade I Outbreak in Central and Eastern Africa:** Since January 2024, more than 21,000 suspected cases of clade I mpox have been reported in the Democratic Republic of the Congo and several bordering countries; other countries, including the United States, have reported travel-associated clade I mpox.[12] Clade I mpox has previously been observed to be more transmissible and to cause more severe infections than has been observed with clade II infections. During this outbreak, a cluster of clade I infections was associated with sexual contact, the first such description of clade I mpox spread via sexual contact.[13] For patients with a clinical illness who report recent (within 21 days of the illness onset) travel to a country with an active mpox outbreak, the Centers for Disease Control and Prevention (CDC) recommends clinicians pursue monkeypox virus clade-specific testing.[14,15]

Mpox in the United States

In the United States, from January 2022 through January 11, 2024, the CDC reported more than 31,000 mpox (clade II) cases, with 56 mpox-associated deaths (Figure 2).[16,17] Cases in the 2022 outbreak disproportionately affected men who have sex with men.[3,18] Approximately 40% of those diagnosed with mpox also had HIV, and another 40% had been diagnosed with a reportable sexually transmitted infection (STI) in the previous year.[19] Among cases reported at the height of the outbreak, more than 90% were among men, and the highest number of cases were reported in persons 31 to 35 years of age.[4,16] Among all age groups, Hispanic/Latino and Black persons had higher case numbers, accounting for more than 60% of the total cases, despite representing only about one-third of the United States general population.[4,16] As of February 18, 2025, there have been four reported cases of Clade I mpox infection in the United States; all cases involved recent travel from an area of the world experiencing clade I mpox transmission.[12][Q] Mpox Epidemiology

Virology, Pathogenesis, and Transmission

Virus Classification and Structure

The monkeypox virus, the causative agent of mpox disease, is a member of the *Orthopoxvirus* genus in the family *Poxviridae*.[\[20,21,22\]](#) Orthopoxviruses are characterized by an ovoid brick-shaped morphology as seen on cryo-electron tomography. Monkeypox virus is 360 x 270 x 250 nm in size and contains linear double-stranded DNA of approximately 197 kilobases (kb). This genome encodes more than 200 proteins that are essential for the virus life cycle, virus assembly, and evasion of host immune defenses. Infectious monkeypox virus can exist in two distinct forms: extracellular enveloped virus (EEV, also abbreviated as EV) and intracellular mature virus (IMV, also abbreviated as MV) ([Figure 3](#)).[\[20,21,23\]](#) [Q] Mpox Virology

Life Cycle

Monkeypox virus infects and replicates within host cells as follows ([Figure 4](#)):[\[20,21,23\]](#)

1. **Virion Entry:** Monkeypox virus can attach to and enter a host cell in the form of an extracellular enveloped virus (EEV) or a mature virus (MV). The entry and fusion of the MV envelope with the plasma or endocytic membrane involves multiple viral proteins.
2. **Early Transcription and Translation:** Some monkeypox DNA is immediately transcribed and translated to produce early proteins, including growth factors, immune response modulators, and factors needed for DNA replication. This early step occurs in the host cell cytoplasm.
3. **Uncoating:** After cell entry, the uncoating of the viral core occurs, with shedding of the outer membranes and release of the core into the cytoplasm. The uncoating of the core facilitates DNA replication.
4. **DNA Replication:** Most of the monkeypox DNA replicates to form concatemeric DNA (long continuous DNA molecules that contain the same DNA sequence linked in series). This process occurs in a localized cytoplasmic region denoted as the viral factory.
5. **Intermediate Gene Transcription and Translation:** Within the viral factory region, the newly replicated (progeny) monkeypox viral DNA can undergo intermediate transcription and translation, generating intermediate proteins that include transcription factors required for late transcription. In addition, late proteins are generated, with some contributing to the viral structure and others playing a role in early transcription and translation.
6. **Late Gene Transcription and Translation:** Also, within the viral factory region, the progeny monkeypox viral DNA can undergo late transcription and translation, which produces late proteins, including some that contribute to the viral assembly process.
7. **Assembly:** The monkeypox DNA is resolved into a single genome and packaged into the core along with proteins necessary for early transcription.
8. **Morphogenesis:** The assembled core is moved out of the viral factory region, where it obtains an outer membrane and becomes a mature virus (MV). The MV generally remains trapped within the cell, except in the rare event of cell lysis.
9. **Wrapping:** Some portion of the total virus particles produced is further wrapped by trans-Golgi/late endosomal double membranes to form the intracellular enveloped virus (IEV). During this process, the viral p37 protein interacts with the cellular proteins Rab9 GTPase and TIP47, which together stimulate the wrapping of the MV to form the IEV.
10. **Exocytosis:** The IEV migrates to the cell periphery on microtubules and is released by exocytosis to become cell-associated enveloped virus (CEV). The CEV can infect neighboring cells. Approximately 1% of CEV are released into the extracellular space via motile actin tail formation to become extracellular enveloped virus (EEV). EEV are responsible for long-range dissemination of the virus.

Transmission

Most mpox infections in the 2022-2023 outbreak occurred through close physical contact, most during

sex.[16] Transmission has also occurred among household members and through needlestick exposures.[24,25,26,27,28,29] Person-to-person transmission of monkeypox virus occurs primarily through direct contact with an active lesion or sore (skin), contact with mucosal surfaces (e.g., throat, anus, or rectum), or through body fluids.[3,28,30] Cases of mpox have been reported after sexual contact with a presymptomatic or asymptomatic partner.[31,32,33] Monkeypox virus has been detected in human samples of skin, saliva/oropharyngeal isolates, anorectum, semen, urine/urethra, and conjunctival/ocular fluid, blood/plasma/serum, lower respiratory tract isolates, feces, and vaginal isolates.[30] Monkeypox virus has been detected in the upper respiratory tract and environmental samples, demonstrating that airborne viral transmission is possible, including potentially through air travel, but available data suggest the risk of person-to-person respiratory transmission appears to be low.[34,35] Though not felt to be a predominant source of transmission, contact with contaminated surfaces or objects, particularly soft, porous items, such as sheets and linens (without appropriate personal protective equipment), can result in infection.[36,37,38,39,40]

Clinical Manifestations

Mpox can cause a range of clinical syndromes in adults, both systemic and local. Characteristic lesions of mpox frequently start at the presumed site of inoculation, resulting in rash, proctitis, urethritis, and/or pharyngitis. In persons who develop symptomatic infection, the incubation period for mpox infection is anywhere from 4 days to up to 3 weeks, with symptoms typically lasting 2 to 4 weeks.[3,28,41,42,43] Mpox disease is self-limited in most patients, though it can be severe and life-threatening in immunocompromised persons.[44]

Systemic Symptoms

Systemic symptoms frequently occur early on in illness and include fever, malaise, chills, lymphadenopathy, headache, abdominal pain, and myalgias.[3,4,28,45,46]

Rash

Rash is the most common manifestation of mpox in various series and can occur with or without systemic symptoms. Lesions can appear anywhere on the body. Among cases reported in the 2022 mpox outbreak, lesions most frequently involved the anogenital region but were also commonly found on the mouth, hands, face, feet, or chest.[3,4,46] Sometimes, lesions first form on the tongue and in the mouth, known as enanthem.[47] Lesions typically progress through six stages over 2 to 4 weeks, though lesions may be present at different stages of development at the same time (Figure 5).[47] Although the rash eventually resolves, even without treatment, larger and deeper lesions may result in scarring and an unwanted cosmetic effect.[48,49]

Anorectal Symptoms

Many patients in the 2022 outbreak reported rectal symptoms, including rectal pain, rectal bleeding, tenesmus, pus/blood in stool, and proctitis.[3,4,50] These may or may not be associated with visible lesions in the anogenital area.[51] Pain is often the most prominent manifestation of anorectal involvement and can require hospitalization for pain management.

Oropharyngeal Symptoms

Oropharyngeal symptoms reported include pharyngitis, odynophagia, epiglottitis, and oral or tonsillar lesions. Pain and difficulty with swallowing may limit oral intake and thus may be another indication for hospital admission.[28,46]

Ocular Manifestations

Ocular manifestations include conjunctivitis, keratitis, periorbital cellulitis, and blepharitis; these may be the result of autoinoculation from an infected peripheral lesion.[3,4,28,46] Ocular manifestations can be vision-threatening.[Q] Mpox Clinical Manifestations

Other Complications

- **Pain:** Significant pain has been noted to be a complication among the listed presentations above, especially in those with anorectal and penile involvement. Pain management (described below) is a cornerstone of therapy.[3,4,46,52]
- **Secondary Bacterial Infections:** Secondary skin and soft tissue infections, including cellulitis and balanitis, have been reported, though not in most cases.[3,53,54] Given the overlap between mpox lesions and systemic symptoms and symptoms concerning secondary bacterial infection, it can be

difficult to differentiate between the two.

- **Concomitant Sexually Transmitted Infections (STIs):** In a large global case series, concomitant STIs (gonorrhea, chlamydia, and syphilis) were found in nearly one-third of those who were tested.[\[3\]](#)
- **Severe Complications:** Among those with significant immunocompromise or advanced HIV, severe complications have been noted. These include bowel obstruction secondary to tissue edema, rectal wall perforation in severe proctitis, urethritis, paraphimosis, necrotizing lymphadenopathy, myopericarditis, and others.[\[55,56,57,58,59\]](#)
- **Severe Necrotizing Mpox in Advanced HIV:** In people with advanced HIV (CD4 counts less than 200 cells/mm³), a severe necrotizing form of mpox has been characterized by significant fulminant manifestations, including necrotizing skin lesions, visceral involvement (including lung and gastrointestinal tract), secondary infections, sepsis, and a high mortality rate (25% among those hospitalized in a global case series).[\[22,60,61,62\]](#)

Laboratory Diagnosis

Primary confirmation of an mpox diagnosis is done by PCR analysis on samples taken from active lesions and/or infected areas of the body. Serologic tests are not useful for diagnosing active infection and are mostly used for research purposes. In addition, the serologic tests often have cross-reactivity with other orthopoxviruses. Prior to collecting the sample, it is important to check with the local laboratory that will be processing the sample to confirm the specific requirements for swabs and transport media, as this may vary. Appropriate personal protective equipment (PPE), as described below in infection prevention and control, should be worn. Collection methods for samples are outlined as follows ([Figure 6](#)).

- Swabs of intact skin lesions, as well as samples of lesion crusts, are best. Intact lesions should not be unroofed prior to swabbing. Samples should ideally be collected from two different lesions in different body parts that are in different stages.
 - Swabs made of synthetic materials, like nylon or Dacron, may be sent either dry or in viral transport media. Two swabs should be sent for each lesion.
 - The swabs should be pressed firmly against the lesion and vigorously rubbed back and forth on the lesion 3 times; rotate the swab 180° so that the other side of the swab is in contact with the skin and repeat rubbing back and forth on the same lesion 3 more times.
 - Place the swab in an appropriate container with appropriate transport media.
 - If a patient has no skin lesions but mpox is still suspected, the virus may be detected in other areas like the throat, rectum, or urine, although testing at these sites is not FDA-approved and may not be available from commercial labs.[\[63\]](#) Testing these additional sites along with skin lesions does not increase the chances of making a diagnosis when visible lesions are present.[\[64,65\]](#) The Cepheid Xpert Mpox assay has emergency use authorization (EUA) from the FDA and when evaluated at anorectal and oropharyngeal mucocutaneous sites, this assay demonstrated high sensitivity.[\[66\]](#) [Q]
- Laboratory Diagnosis of Mpox

Treatment

Most patients with mpox recover completely, regardless of whether they receive treatment. Although the FDA has not approved any specific therapies for mpox, supportive care measures are commonly used to manage pain. Some medications originally developed for treating smallpox have been repurposed as medical countermeasures and are used for mpox. These medications may be helpful for patients who are at higher risk of developing severe disease, such as those with compromised immune systems, severe symptoms, or lesions in critical areas. It is important to note that none of these medications have been definitively proven to have a clinical benefit. There is no difference in management and/or treatment options for infection with clade I or clade II monkeypox virus.

Supportive Measures

Supportive care recommendations are primarily based on expert consensus and are targeted to symptoms. For proctitis, using stool softeners can help alleviate pain during bowel movements, and additional comfort can be provided using topical treatments like sitz baths and lidocaine gels. It is important to exercise caution when using topical steroids as they can suppress the local immune response. Over-the-counter pain relievers such as nonsteroidal anti-inflammatory drugs (NSAIDs) or acetaminophen are often sufficient for managing pain, although some patients with severe pain may require prescription pain relief with gabapentin or opioids. For individuals with pharyngeal disease, viscous lidocaine and saltwater gargles are commonly trialed.[67]

Medications Used for the Treatment of Mpox

Tecovirimat

Tecovirimat, an antiviral medicine initially developed to treat variola virus, targets and inhibits the activity of p37, a viral envelope-wrapping protein found in monkeypox virus (and other orthopoxviruses), and this inhibition prevents the formation of the enveloped virions (Figure 7).[68,69,70,71] For selected patients requiring treatment, tecovirimat has been available through the CDC's expanded access investigational new drug (e-IND) protocol.[72] More than 7,000 courses of tecovirimat for mpox treatment have been distributed in the United States, and severe adverse effects were rarely reported.[73,74,75] Use of tecovirimat through the Expanded Access-Investigational New Drug (EA-IND) application is now limited and restricted to those with severe disease or at risk for severe disease, which includes individuals who are severely immunocompromised, persons with atopic dermatitis, children, or pregnant women.[72,76]

- **Tecovirimat Resistance:** Several reports have documented monkeypox virus resistance to tecovirimat. Epidemiological surveillance in Los Angeles, California, identified six cases that did not improve on tecovirimat therapy and found a wide range of tecovirimat resistance levels in patients with HIV who had a CD4 count of less than 200 cells/mm³, suggesting selection for resistance.[77]. Furthermore, the CDC identified 50 isolates from 26 patients with a monkeypox virus tecovirimat-resistant phenotype, all of whom received treatment with tecovirimat.[78] Transmission of tecovirimat-resistant monkeypox virus has also been reported, with community spread; in this report, cases of drug-resistant monkeypox virus were documented among individuals who had not been exposed to tecovirimat.[79]
- **Tecovirimat Efficacy:** Two randomized clinical trials have shown that tecovirimat lacks clinical efficacy. The PALM007 study in the DRC found tecovirimat to be safe but ineffective in accelerating clade I mpox resolution.[80] The International Study of Tecovirimat for Mpox (STOMP) similarly demonstrated its safety but no improvement in clade II mpox resolution or pain relief. Further research is needed to clarify its role in individuals with advanced immunosuppression or as part of combination therapy.[72]
- **Oral Tecovirimat Therapy:** Oral tecovirimat is available in a 200 mg capsule formulation and in a liquid formulation.[55,76,81] The absorption of tecovirimat is contingent on coadministration with a moderate- or high-fat meal.[76] Adverse events are primarily limited to headache, nausea, and

vomiting.[76] The dosing of tecovirimat is weight-based.[81] The standard treatment duration is 14 days, though, in certain cases of severe disease and immunocompromised individuals, the course may be extended in discussion with an expert.

Table 1. Tecovirimat Oral Dosing for the Treatment of Mpox in Adults

Table 1.		
Tecovirimat Recommended Oral Dosing for the Treatment of Mpox in Adults*		
Weight (kg)	Weight (lbs)	Oral Dosing (Capsules) ^{^+}
*Recommendations listed in this table are based on Expanded Access IND Protocol: Use of Tecovirimat (TPOXX®) for Treatment of Human Non-Variola Orthopoxvirus Infections in Adults and Children. IND No. 116,039 CDC IRB No. 6402 Version 6.3 Updated on January 31, 2025		
25 kg to <40 kg	55 lbs to <88 lbs	400 mg every 12 hours
40 kg to <120 kg	88 lbs to <264 lbs	600 mg every 12 hours
≥120 kg	≥264 lbs	600 mg every 8 hours
[^] Each tecovirimat capsule = 200 mg ⁺ Tecovirimat capsules should be taken within 30 minutes after a full meal containing moderate or high fat. Carefully open the required number of capsules and mix contents of capsule(s) with 30 mL of liquid (e.g., milk, chocolate milk, water) or soft food (e.g., apple sauce, yogurt). Administer the entire mixture within 30 minutes of preparation.		

Source:

- Centers for Disease Control and Prevention (CDC). Mpox. Tecovirimat (TPOXX) for Treatment of Mpox. Updated February 6, 2025 [[CDC](#)]

- Intravenous Tecovirimat Therapy:** Tecovirimat is also available as an intravenous formulation for those unable to tolerate the oral formulation or the fatty meal required for absorption. It is contraindicated in persons with severe renal dysfunction (creatinine clearance less than 30 mL/min) and should be used with caution even in those with mild-moderate impairment, due to the risk of accumulation of hydroxypropyl-β-cyclodextrin, an added ingredient in the intravenous preparation.[55,76,81] Adverse events are generally injection site-related, including pain, swelling, erythema, and extravasation.[76] Similar to oral dosing of tecovirimat, dosing of intravenous tecovirimat is weight-based. Once able to tolerate oral intake, those receiving IV tecovirimat should transition to the oral formulation to complete the standard 14-day course.

Table 2. Tecovirimat Intravenous Dosing for the Treatment of Mpox in Adults

Table 2.					
Tecovirimat Recommended Intravenous Dosing for the Treatment of Mpox in Adults*					
Weight (kg)	Weight (lbs)	Recommended Dose	Volume of IV Tecovirimat	Volume of Diluent	Total Volume for Infusion
*Recommendations listed in this table are based on Expanded Access IND Protocol: Use of Tecovirimat (TPOXX®) for Treatment of Human Non-Variola Orthopoxvirus Infections in Adults and Children. IND No. 116,039 CDC IRB No. 6402 Version 6.3 Updated on January 31, 2025					
<35 kg	<77 lbs	6 mg/kg every 12 hours by IV infusion over 6 hours	0.6 mg mL/kg	1.2 mL/kg	Varies by weight
35 kg to <120 kg	77 lbs to <264 lbs	200 mg every 12 hours by IV infusion over 6 hours	20 mL	40 mL	60 mL
≥120 kg	≥264 lbs	300 mg every 12 hours by IV	30 mL	60 mL	90 mL

Weight (kg)	Weight (lbs)	Recommended Dose	Volume of IV Tecovirimat	Volume of Diluent	Total Volume for Infusion
		infusion over 6 hours			

When clinical improvement has occurred, patients should be switched to tecovirimat oral capsules to complete the standard 14-day treatment course as soon as oral therapy can be tolerated.

Source:

- Centers for Disease Control and Prevention (CDC). Mpox. Tecovirimat (TPOXX) for Treatment of Mpox. Updated February 6, 2025 [CDC]

[Q] Tecovirimat

Brincidofovir

Brincidofovir is a lipid prodrug of cidofovir. Brincidofovir is an antiviral medication that works by inhibiting the activity of DNA polymerase (Figure 8). Oral brincidofovir is FDA-approved to treat smallpox. Brincidofovir is available through an FDA EA-IND for the treatment of mpox. Most patients who have received brincidofovir for mpox were severely immunocompromised and were concomitantly receiving tecovirimat.[72] Use of brincidofovir through the e-IND application is now limited and restricted to those with severe disease or at risk for severe disease, which includes individuals who are severely immunocompromised, persons with atopic dermatitis, children, or women who are pregnant.

- Brincidofovir Efficacy:** Animal studies suggest that the combination of tecovirimat and brincidofovir may act synergistically against monkeypox virus, and this pairing should be considered for patients with mpox who have severe immunosuppression or progressive mpox disease.[82] There are limited clinical data for the use of brincidofovir, with or without tecovirimat, for the treatment of mpox in humans.
- Oral Brincidofovir Therapy:** When oral brincidofovir is used to treat mpox in adults and in younger persons who weigh at least 46 kg, the recommended dose is 200 mg once weekly for 2 doses (given on days 1 and 8).[72] Major side effects associated with brincidofovir include diarrhea and hepatotoxicity. Most experts would use brincidofovir in combination with either tecovirimat or Vaccinia Immune Globulin Intravenous (VIGIV).[72]

Table 3. Brincidofovir Oral Dosing

Table 3.		
Brincidofovir Recommended Oral Dosing for the Treatment of Mpox*		
Weight (kg)	Weight (lbs)	Oral Tablet [^] Dosing
*Recommendations listed in this table are based on Brincidofovir (<i>Tembexa</i>) Prescribing Information		
<10 kg	<22 lbs	NA
10 kg to <48 kg	22 lbs to 106 lbs	NA
≥48 kg	≥106 lbs	200 mg once weekly for 2 doses
*Doses of brincidofovir are given on days 1 and 8		
[^] Each tablet of brincidofovir = 100 mg		

Source:

- Centers for Disease Control and Prevention (CDC). Mpox. Clinical Treatment of Mpox. Updated January 30, 2025 [CDC]

Cidofovir

Similar to brincidofovir, cidofovir works by inhibiting the activity of DNA polymerase. Cidofovir has been approved by the FDA for intravenous treatment of cytomegalovirus retinitis. Although animal studies have

shown potential effectiveness against orthopoxviruses, there is currently no human data confirming its efficacy for treating mpox. Due to the significant risk of nephrotoxicity associated with cidofovir, intravenous cidofovir for the treatment of mpox has rarely been used, and when used, it has primarily been reserved for individuals with severe disease and significant immunosuppression who cannot take oral brincidofovir. Case studies have suggested improvement after cidofovir administration.[83,84] For the treatment of mpox, cidofovir has also been administered as a topical cream applied directly to lesions and as a solution directly injected into a lesion.[85][Q] Cidofovir Toxicity

Vaccinia Immune Globulin Intravenous (VIGIV)

Vaccinia immune globulin intravenous (VIGIV) is a treatment for mpox that involves transferring antibodies against vaccinia virus, which is believed to provide some level of cross-protection against monkeypox virus.[72] The VIGIV treatment may be beneficial for immunocompromised individuals, who are unlikely to mount an antibody response, especially those with advanced HIV. Some case reports have shown improvement in patients with severe mpox who received VIGIV, suggesting that it should be considered for evaluation in individuals with advanced HIV and severe mpox.[86] The FDA has approved the use of VIGIV for complications due to vaccinia vaccination, but it is not approved for the treatment or prevention of mpox.[72] Requests to use VIGIV for severe mpox cases can be submitted to the CDC on a case-by-case basis.[72]

Trifluridine Eye Drops

Trifluridine eye drops are approved by the FDA for treating eye infections caused by the herpes simplex virus and are also thought to have activity against orthopoxviruses.[87,88,89,90] Therefore, they should be considered as a treatment option for patients with ocular disease from mpox.

Recommended Treatment of Mpox

Given the disappointing clinical trial findings, tecovirimat use should be guided by shared decision-making, carefully weighing the potential risks and benefits with individuals who meet EA-IND criteria. Consideration for use includes patients with active skin conditions that increase the risk of disseminated infection, women who are pregnant or lactating, and children. For individuals who are severely immunocompromised or present with protracted or life-threatening mpox, combination therapy with tecovirimat and brincidofovir should be considered, balancing the potential for improved outcomes against the risks of treatment. For severe cases involving patients who cannot take oral therapy, the combination of intravenous tecovirimat and intravenous cidofovir could be considered.

Infection Control in Health Care Settings

From an infection prevention and control standpoint, samples from clade I and II monkeypox virus are regulated as Category B infectious substances. In contrast, samples or clinical waste from cultures of clade 1 monkeypox virus are designated Category B infectious substances under hazardous materials regulations (select agents).[91] The following summarizes key recommendations regarding infection prevention and control in health care settings.[92]

- **Rooming:** Patients with suspected or confirmed mpox should be placed in a single-person room; special air handling (a negative pressure isolation room) is not necessary, except during intubation, extubation, and procedures that may spread oral secretions (e.g., induced sputum collection). Ideally, there should be a dedicated bathroom for mpox patient use. When a patient leaves the room, all exposed lesions should be covered, and the patient should wear a well-fitting medical mask.[92]
- **Personal Protective Equipment:** Prior to entering a patient's room with either suspected or confirmed mpox, health care providers should perform hygiene and then don PPE as follows: a fit-tested, NIOSH-approved respiratory mask (equipped with an N95 filter or higher), eye protection (with coverage of front and sides of face), gloves, and a gown ([Figure 9](#)).[92]
- **Cleaning:** Perform standard cleaning and disinfection with a recommended EPA-registered disinfectant. Soiled bedding, towels, and clothing should be handled while in PPE and subsequently contained; shaking or handling should be avoided so as not to aerosolize infectious particles. Avoid dry dusting, sweeping, vacuuming, or other cleaning methods. Soiled material may be disposed of in the same way as any other infectious medical waste. After cleaning the room, new patients may be placed in the same room. This guidance applies to the monkeypox virus clade associated with the 2022 mpox outbreak.[92]
- **Health Care Exposures:** Asymptomatic health care personnel not wearing full PPE who have an exposure to a patient with mpox should self-monitor symptoms for 21 days but can continue to work if they remain asymptomatic. Health care workers with higher risk exposures (i.e., unprotected contact with broken skin, mucous membranes, mpox skin lesions, or soiled material) may be recommended to receive postexposure prophylaxis JYNNEOS vaccination.[92][Q] Infection Control Measures

Prevention of Mpox Infection

Reducing Exposure

A key component of mpox infection prevention is avoidance of close contact, including intimate and sexual exposure, with people with mpox, as well as any objects and materials that a person with active mpox infection has used. In the context of the 2022 outbreak, men who have sex with men (MSM) adopted strategies for mpox prevention, including increased condom use, decreased number of sex partners, reduced number of one-time sex encounters, and decreased frequency of sex with partners met on dating apps, at sex venues, or at group sex parties.[93] Reducing exposure is an important bridge to primary prevention strategies like vaccination.

Mpox Vaccines Before Exposure to Mpox

Currently, there are two vaccines available for the prevention of mpox infection: modified vaccinia Ankara-Bavarian Nordic (MVA-BN, JYNNEOS) and ACAM2000. Vaccination with either JYNNEOS or ACAM2000 is expected to be protective against clade I and II monkeypox virus. The JYNNEOS vaccine is an attenuated, nonreplicating vaccinia virus vaccine that is FDA-approved for the prevention of mpox (and smallpox) disease in persons 18 years of age and older who are at high risk for monkeypox virus infection.[94,95] In the United States, JYNNEOS is the preferred mpox vaccine, and is recommended by the Advisory Committee for Immunization Practices (ACIP) for all people 18 years of age and older who are at risk for mpox infection.[96,97] The replication-competent smallpox vaccine (ACAM2000) is FDA-approved for the prevention of smallpox infection, and it has been made available in the United States for prevention of mpox under an Expanded Access Investigational New Drug Application (EA-IND).[98] The ACAM200 is not the recommended mpox vaccine in the United States, primarily because this vaccine contains replication-competent virus, which, in the first three weeks after vaccination, could risk autoinoculation of the vaccinia virus from the inoculation site to other body sites, as well as potential transmission to others.[99] In addition, ACAM2000 should not be used in persons with immune deficiencies, persons with HIV, during pregnancy, persons with active eczema (risk of eczema vaccinatum), and in persons with multiple major cardiac risk factors (risk of myocarditis and/or pericarditis).[100,101,102]

Mpox Vaccine Indications

The following summarizes CDC and ACIP recommendations for mpox vaccination.[96,97,98,103] Mpox vaccination is not recommended for persons who have previously been diagnosed with mpox, and it is not recommended for persons who have already received the recommended two doses of the JYNNEOS vaccine.[98,103] The JYNNEOS vaccine is recommended for any person 18 years of age and older who is at risk for mpox infection.[96,97,98,103] Mpox vaccination is recommended for the following indications:

- Persons who are gay, bisexual, and other MSM, or a person who has sex with gay, bisexual, or other MSM AND who in the past 6 months and has had any of the following:
 - A new diagnosis of at least 1 sexually transmitted disease
 - More than 1 sex partner
- Persons with any of the following in the past 6 months:
 - Sex at a commercial sex venue
 - Sex in association with a large public event in a geographic area where mpox transmission is occurring
- Persons who are sex partners of the persons described above
- Persons who anticipate experiencing any of the situations described above
- Persons traveling to a country with a clade I mpox outbreak and anticipate any of the following activities during travel:
 - Sex with a new partner
 - Sex at a commercial sex venue (e.g., a sex club or bathhouse)

- Sex in exchange for money, goods, drugs, or other trade
- Sex in association with a large public event (e.g., a rave, party, or festival)
- Persons at risk for occupational exposure to orthopoxviruses (e.g., certain people who work in a laboratory or a healthcare facility).

Mpox JYNNEOS Vaccine Dosing and Schedule

Vaccine Administration and Schedule

The FDA-approved immunization with JYNNEOS against mpox requires two vaccine doses given 28 days (4 weeks) apart, using a standard subcutaneous administration (0.5 mL per dose).^[98] The alternative administration is an intradermal dose of 0.1 mL per dose (approved under an Emergency Use Authorization) for persons 18 years of age and older ([Figure 10](#)). If vaccine shortages exist, intradermal administration may be preferred over subcutaneous vaccination, since only one-fifth the amount of the vaccine is required, and available data indicate equivalent immune responses to intradermal and subcutaneous dosing.^[104,105] With intradermal dosing, however, adverse cutaneous reactions occur more often and are more likely to be severe. If a patient has received one subcutaneous vaccination dose, the second dose can be administered as either a subcutaneous or intradermal injection, and vice versa. Patients with a history of developing keloid scars should be offered subcutaneous over intradermal administration to minimize the risk of scarring.^[Q] JYNNEOS Vaccine

Acceptable Intervals Between Doses

The recommended time between vaccine doses is 28 days ([Figure 11](#)). The second dose may be given up to 4 days early and up to 7 days late.^[98] There are, however, no recommendations to restart the vaccine series if the second dose is given earlier than day 24 or later than day 35.^[98]

Contraindications and Precautions

The JYNNEOS vaccine is produced using chicken embryo fibroblast cells to grow the vaccinia virus; the final vaccine product also contains small amounts of gentamicin and ciprofloxacin. JYNNEOS vaccine is contraindicated in persons who have experienced a severe allergic reaction after a previous dose of JYNNEOS.^[96] In addition, precaution is advised for persons with a history of severe allergic reaction (e.g., anaphylaxis) to any of the components in the vaccine, including chicken protein, egg protein, gentamicin, or ciprofloxacin.^[98]^[Q] JYNNEOS Precaution

Mpox Vaccine Special Considerations

- **Persons Who Previously Received Smallpox Vaccination:** Vaccination is recommended against mpox in eligible groups regardless of prior smallpox vaccination status, given the possibility of waning immunity.
- **Persons with HIV:** In persons with HIV, the MVA vaccine is both safe and effective. In studies, patients with HIV and CD4 counts greater than 350 cells/mm³ had similar antibody responses to those without HIV; total antibody titers were lower in people with more advanced disease (CD4 between 200 and 350 cells/mm³), though still present.^[106,107]
- **Vaccine Coadministration Considerations:** Vaccination with JYNNEOS may be administered at the same time as any other vaccines, though ideally in different limbs. Providers and patients may consider waiting 4 weeks after vaccination against COVID-19 vaccines because of the rare side effects of myocarditis or pericarditis associated with both those vaccines and ACAM2000, a live smallpox vaccine.^[101,108] Recent data suggests the risk of myocarditis associated with JYNNEOS is extremely low.^[109]
- **Persons with Prior Mpox:** For persons who have current or prior mpox clinical disease, there is no recommendation to receive any mpox vaccination.

Mpox Vaccine Efficacy

Available data suggest two doses of the JYNNEOS vaccine has an efficacy that has ranged from 66-89% protection against mpox disease.[\[105,110,111,112\]](#) A comparison of mpox incidence from July to September 2022 demonstrated mpox incidence 14 times higher in a group of vaccine-eligible but unvaccinated men as compared to those who had received at least one dose of JYNNEOS; later data extending to 43 United States jurisdictions demonstrated additional risk reduction among those who had received two JYNNEOS doses versus one.[\[111,112\]](#) A study from the United Kingdom that took place in 2023 estimated JYNNEOS effectiveness at 80% following the two-dose primary series; cases were evaluated throughout 2023, and most participants in this study were vaccinated between July 2022 and March 2023.[\[110\]](#).[\[111\]](#)

Booster Doses of Mpox Vaccines

Booster doses of the JYNNEOS vaccine are not currently recommended for the general public, as evidence, including immunogenicity data, indicates that the standard two-dose regimen provides durable and substantial protection against mpox.[\[103\]](#) Epidemiologic data from the 2022–2023 outbreak found that breakthrough infections among fully vaccinated individuals were rare (less than 1%) and occurred at varying intervals after vaccination, with no pattern indicative of waning immunity. When breakthrough cases did occur, they were associated with milder disease, further supporting the effectiveness of the two-dose schedule.[\[113,114,115\]](#) There is no established threshold of antibody titers required for protection, and protection against mpox is mediated by multiple immune components, including cell-mediated and innate immunity, which do not directly correlate with circulating antibody levels. These data, taken together, reinforce that protection after the two-dose JYNNEOS series remains strong for at least five years, negating the need for booster doses in the general population. In contrast, note that booster doses are recommended for individuals at occupational risk of exposure to high inoculum or orthopoxviruses, such as certain research laboratory workers.[\[103\]](#)

Vaccination as Mpox Postexposure Prophylaxis (PEP)

The JYNNEOS vaccine is indicated for persons who have recently had close contact with someone with mpox. To prevent infection, those receiving mpox PEP should ideally receive JYNNEOS vaccination within 4 days of a known exposure to mpox. If more than 4 days have elapsed since the exposure, PEP vaccination can be considered if the exposure was within 14 days, but vaccination after day 4 is less likely to be effective than if given within 4 days of the exposure and at best is likely to lessen the severity of the disease.[\[116,117\]](#)[\[Q\]](#)
JYNNEOS Postexposure Prophylaxis

Counseling and Education

Counseling for Patients Awaiting Test Results

The following counseling recommendations are for those individuals who have been evaluated for mpox and are awaiting test results.

- Patients with possible mpox should stay isolated if possible. This means staying at home and separated from others without attending work, school, or other public settings.
- Patients should be counseled to avoid public or other group transportation, if possible. If use of public transportation is unavoidable, they should wear a mask, ensure all lesions are covered, and avoid any physical contact with others.
- Persons awaiting test results who need further medical care should inform their medical provider that they have been tested for mpox. If there is an unavoidable need to seek medical care (for example, for further medical testing or treatment), the patient should ensure the rash is fully covered and wear a mask during the entire medical visit.
- If possible, consider isolation from pets such as dogs, as human-to-dog transmission has been documented.[[118](#),[119](#)]

Counseling for Patients With Positive Mpox Test Results

The following counseling recommendations are for those individuals who have been evaluated for mpox and have positive test results:

- Persons with mpox should follow isolation instructions as described above for patients awaiting test results.
- If someone with mpox cannot fully separate from others in the household, they should wear a face mask, avoid physical contact, and cover any lesions when in shared spaces. They should try to use a separate bathroom if available. Utensils, clothing, towels, bedding, and other similar items should not be shared.
- Patients should wash their hands often with soap and water, or use an alcohol-based hand sanitizer. Any item that has been touched should be cleaned; clothing items should ideally be machine washed.
- Patients should stay isolated until any rash is fully resolved, all scabs have fallen off, and new skin is forming underneath. This usually takes 2-4 weeks. If they did not have a rash, they should be counseled to stay isolated until all symptoms (e.g., rectal pain, urethral pain) have fully resolved.
- There is limited data to inform counseling on the time period after infection in which resuming sexual activity is safe. The World Health Organization has recommended condom use for up to 12 weeks after infection; CDC has no formal recommendation. Available data suggest detection of monkeypox virus occurs for a shorter duration in semen specimens than in perianal skin.[[120](#),[121](#)]

Summary Points

- In 2022, a mpox outbreak occurred in non-endemic countries, including the United States and multiple countries in Europe. This outbreak was associated with close contact, including sexual contact.
- Person-to-person transmission of mpox occurs primarily through direct contact with an active lesion or sore, or contact with mucosal surfaces or bodily fluids.
- Mpox can cause a wide array of symptoms, including systemic symptoms, a characteristic rash, as well as anorectal, oropharyngeal, and ocular manifestations. Serious complications, including severe pain, stricturing, and others, may occur, especially in those with significant immunocompromise, including advanced HIV disease.
- The diagnosis of mpox is confirmed by PCR testing of samples taken from active lesions or infected areas.
- Primary treatment cornerstones are supportive care; several antiviral options exist with emerging data, including tecovirimat, brincidofovir, cidofovir, and vaccinia immune globulin intravenous. Monotherapy with tecovirimat has been safe, but not effective.
- In the United States, the JYNNEOS vaccine is the preferred and recommended vaccine for the prevention of mpox disease. This vaccine has demonstrated high efficacy.
- To prevent the spread of mpox to others, patients with active mpox should stay isolated and keep lesions covered until full resolution of the lesions has occurred.

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(Smallpox and Monkeypox Vaccine, Live, Non-Replicating) for Prevention of Monkeypox Disease in Individuals Determined to be at High Risk for Monkeypox Infection

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Figures

Figure 1 Monkeypox Virus

Illustration: Cognition Studio, Inc. and David H. Spach, MD

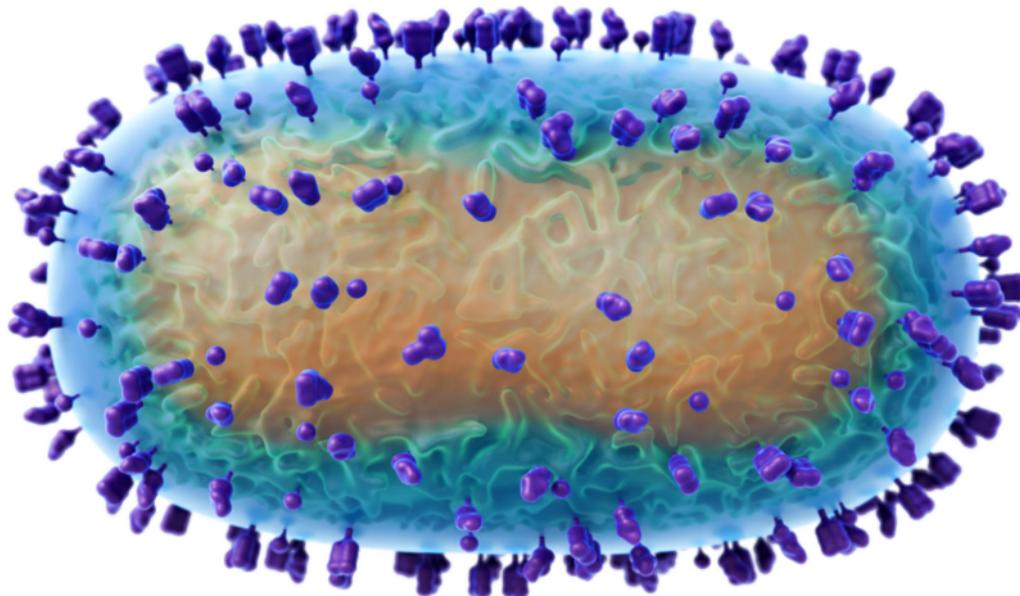


Figure 2 Mpox Epidemiology in United States, 2022-2024

Source: Centers for Disease Control and Prevention (CDC). Mpox. 2022-2023 Outbreak Cases and Data. January 11, 2024.

This is a dynamic visualization. Please visit our website to experience this dynamic content.
 The greatest number of mpox cases have occurred among persons who were 31 to 35 years of age.

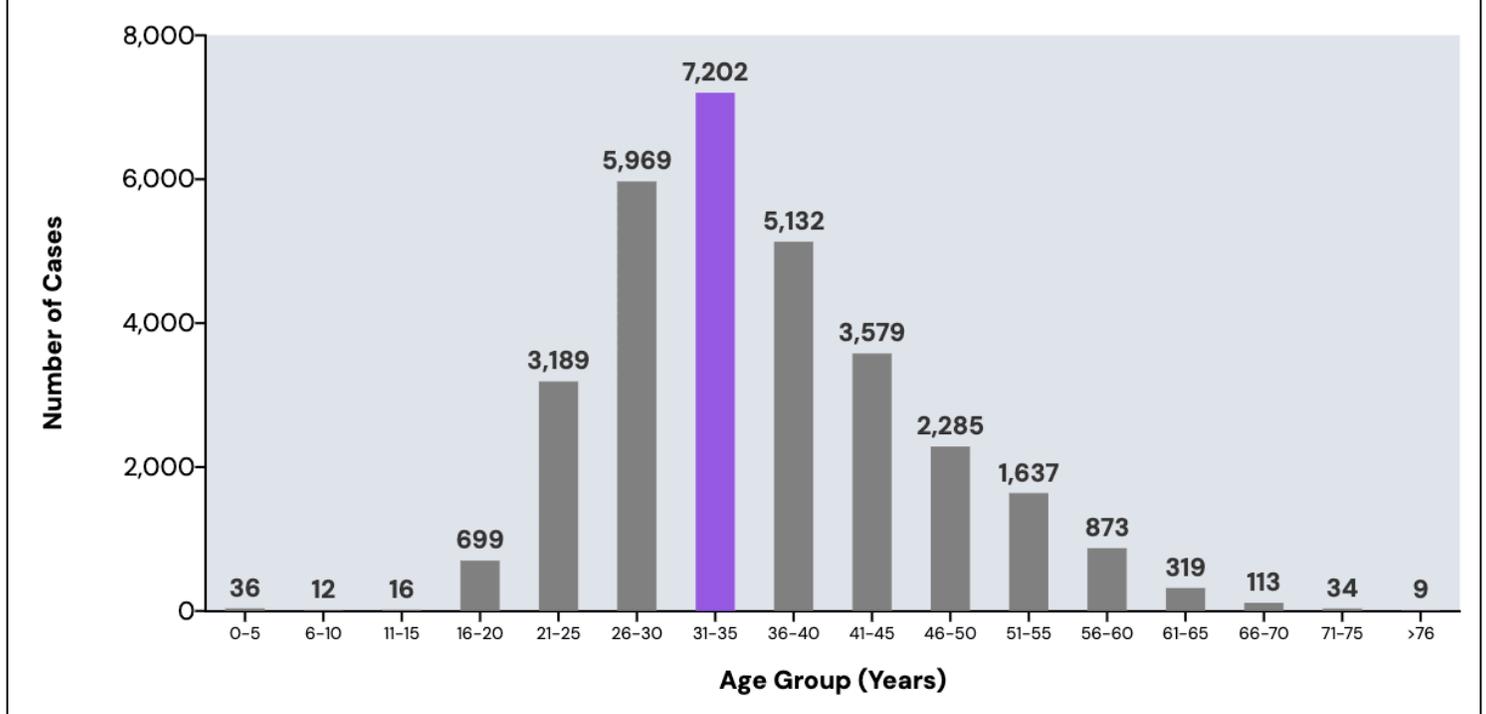
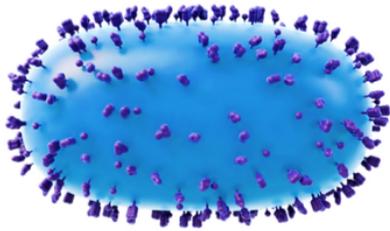


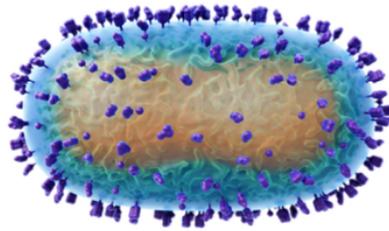
Figure 3 Monkeypox Virus Structure: Envelope and Mature Virus

Illustration: Cognition Studio, Inc. and David H. Spach, MD

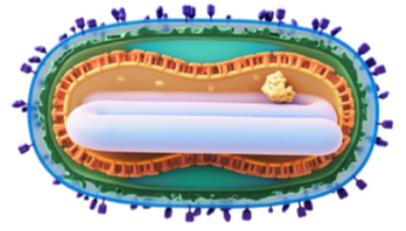
Enveloped Virus



Enveloped Virus Translucent



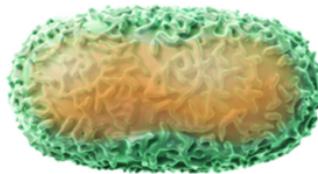
Enveloped Virus Hemisection



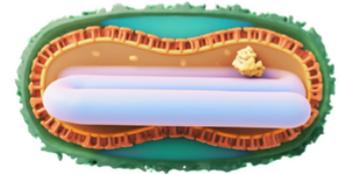
Mature Virus



Mature Virus Translucent



Mature Virus Hemisection



Enveloped Virus Hemisection with Labeling

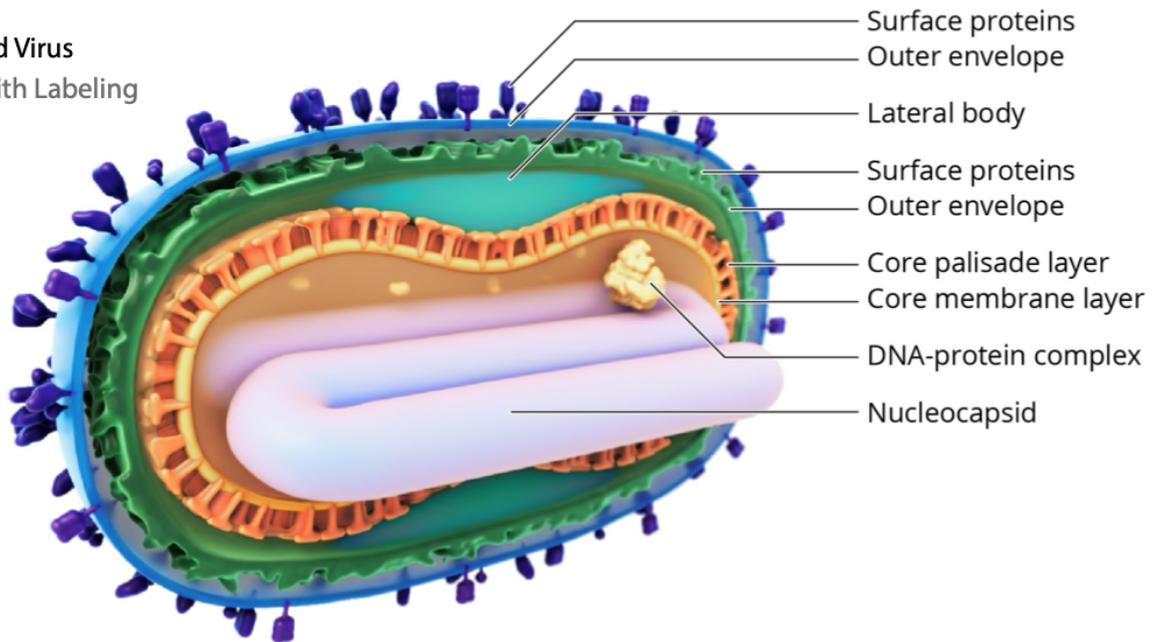


Figure 4 Monkeypox Virus Life Cycle

Illustration: Cognition Studio, Inc. and David H. Spach, MD

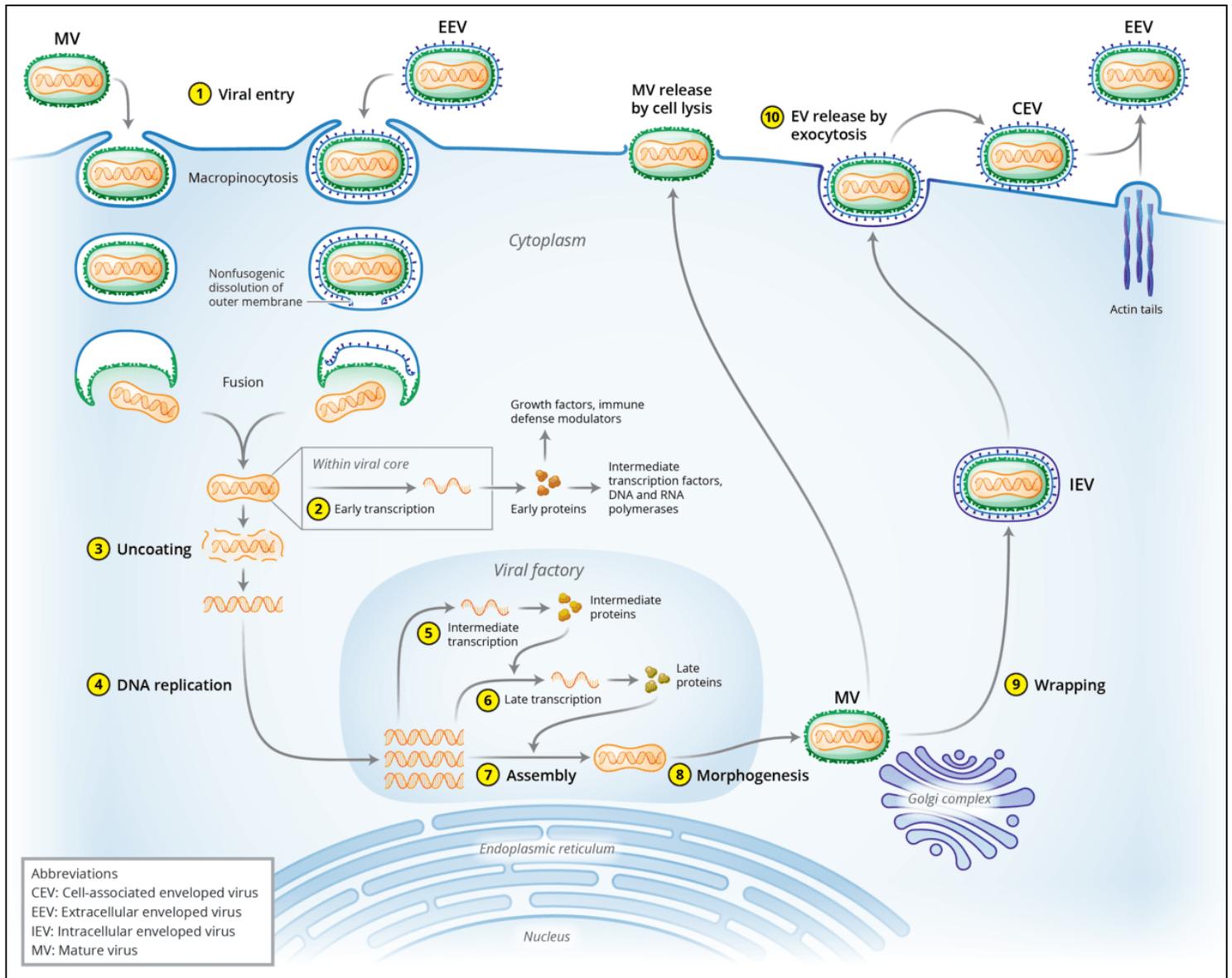
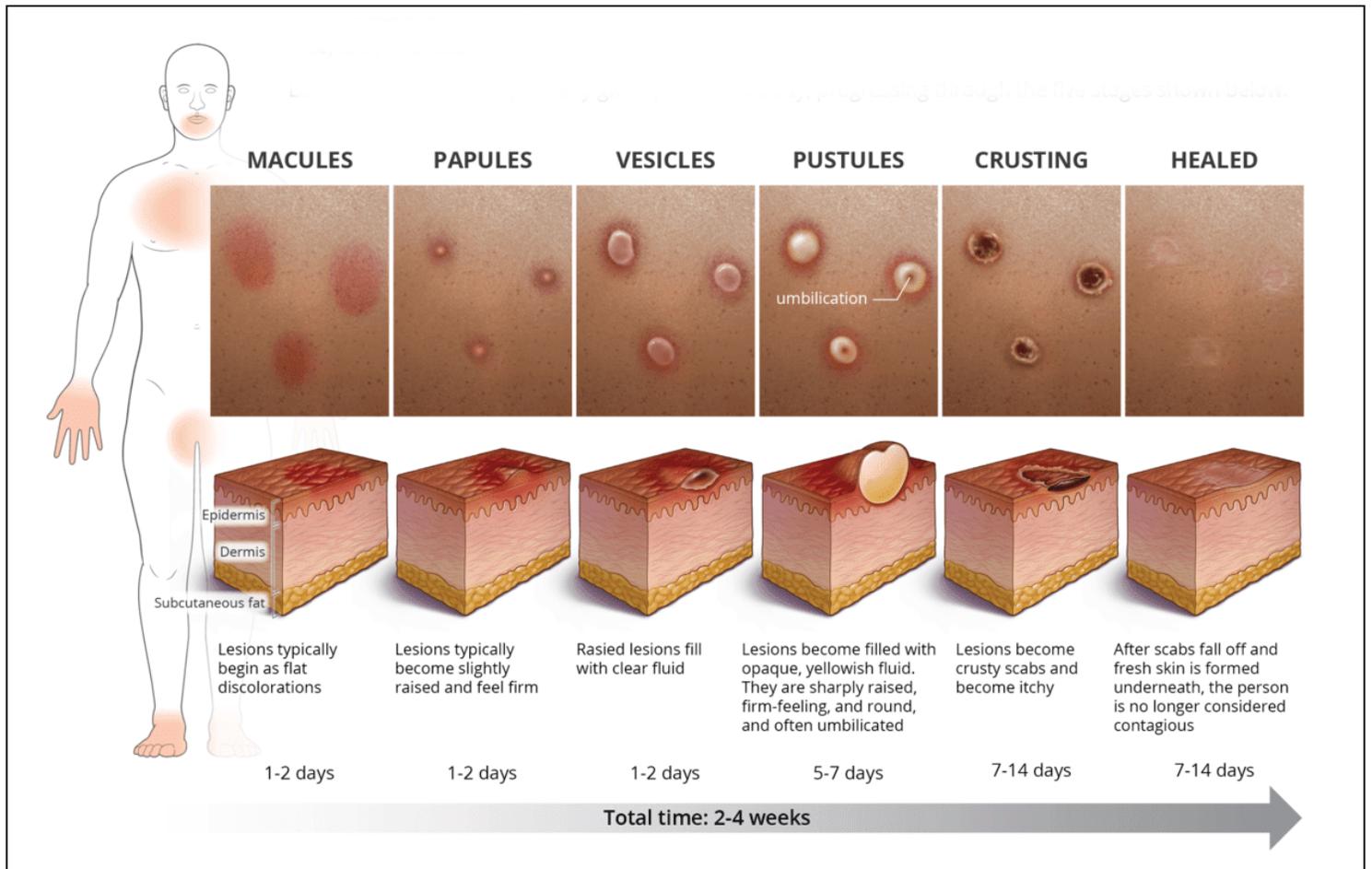


Figure 5 Mpox Cutaneous Lesions: Description and Progression

Illustration: Cognition Studio, Inc. and David H. Spach, MD



**Figure 6 (Image Series) - Obtaining Clinical Samples for Mpox Diagnosis (Image Series) - Figure 6 (Image Series) - Obtaining Clinical Samples for Mpox Diagnosis
Image 6A: Swab for Skin Lesion Sample**

Illustration: Cognition Studio, Inc. and David H. Spach, MD

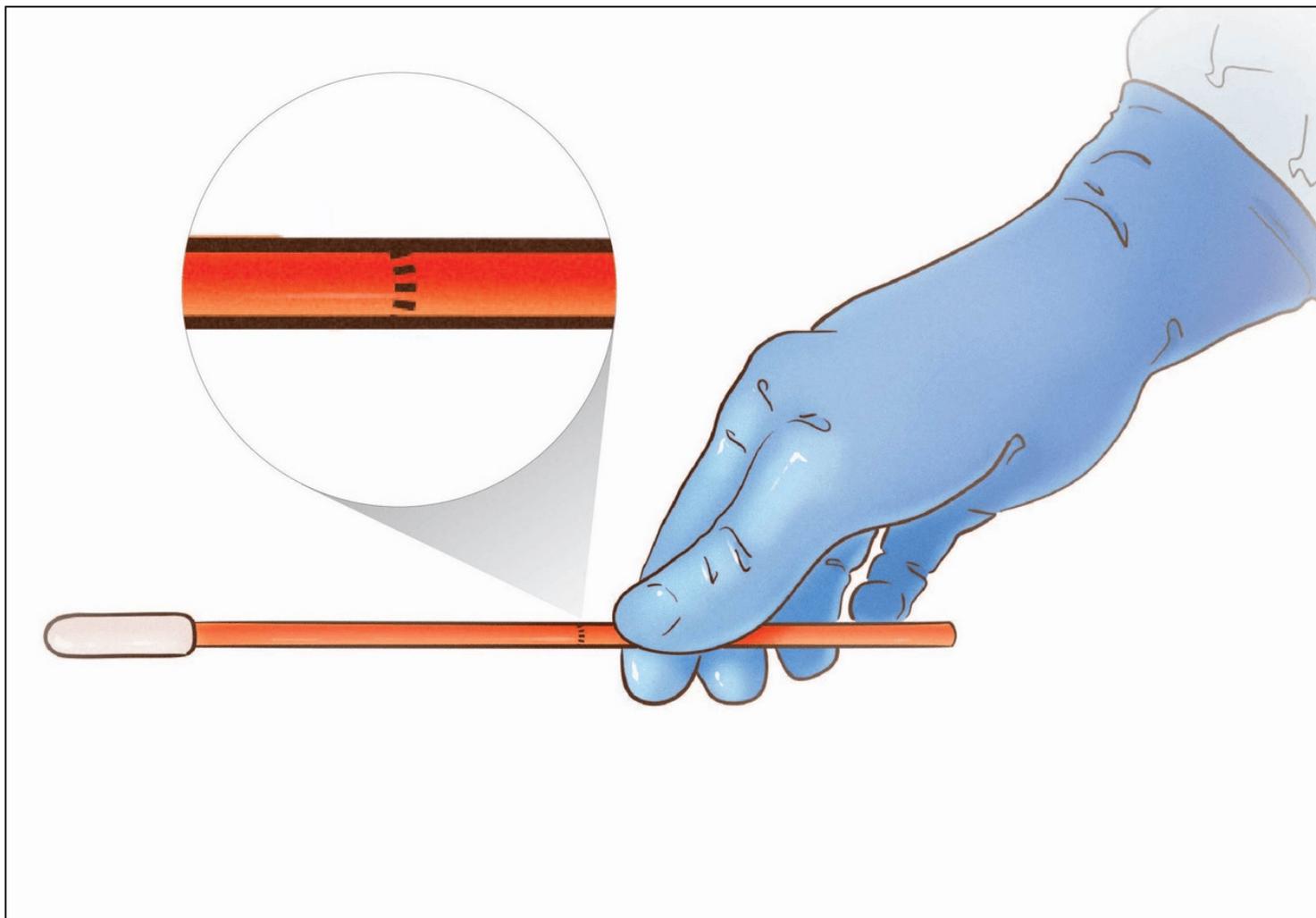


Figure 6 (Image Series) - Obtaining Clinical Samples for Mpox Diagnosis
Image 6B: Technique for Collection of Skin Sample

Illustration: Cognition Studio, Inc. and David H. Spach, MD

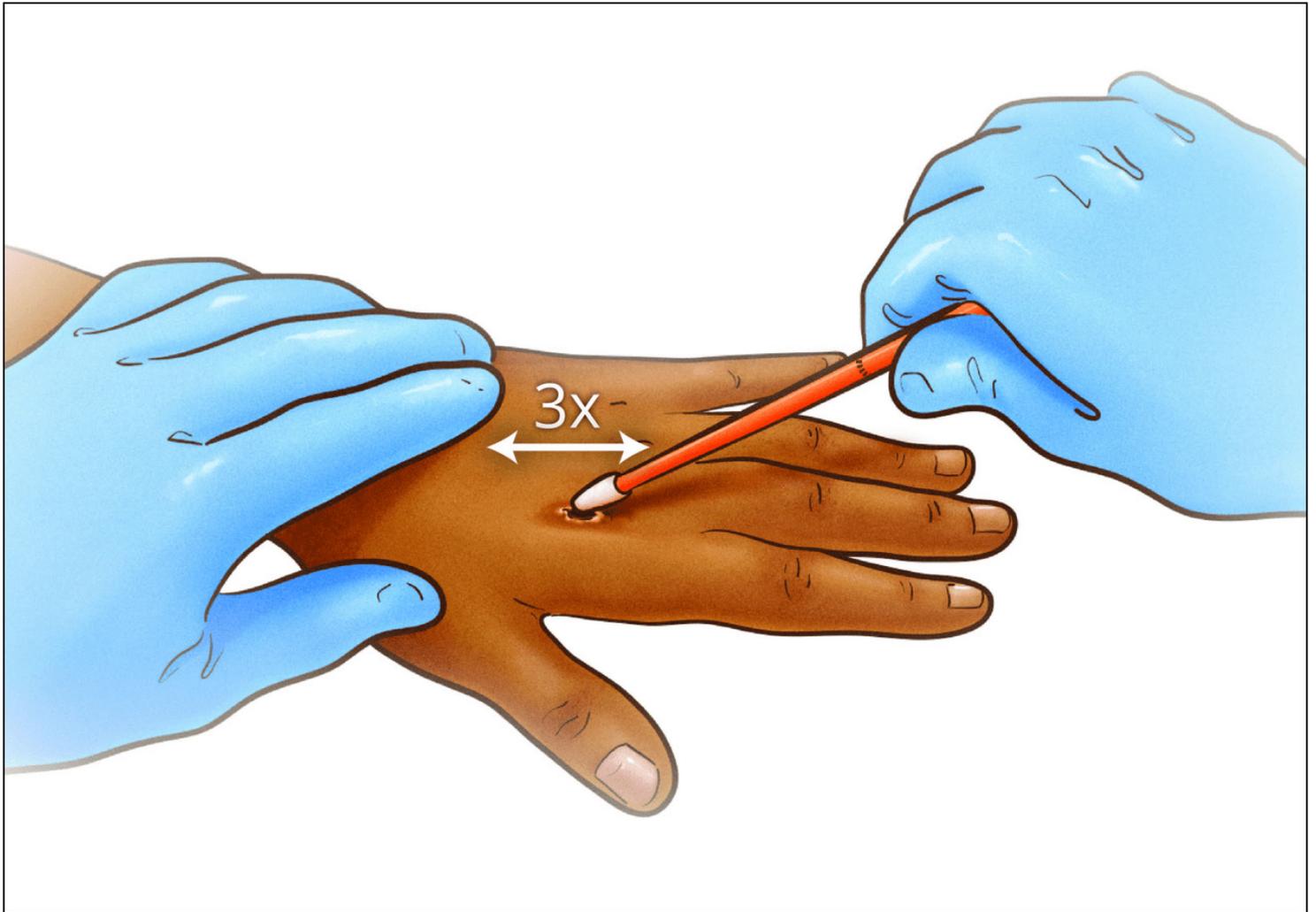


Figure 6 (Image Series) - Obtaining Clinical Samples for Mpox Diagnosis
Image 6C: Repeat Collection of Skin Sample with Same Swab

Illustration: Cognition Studio, Inc. and David H. Spach, MD

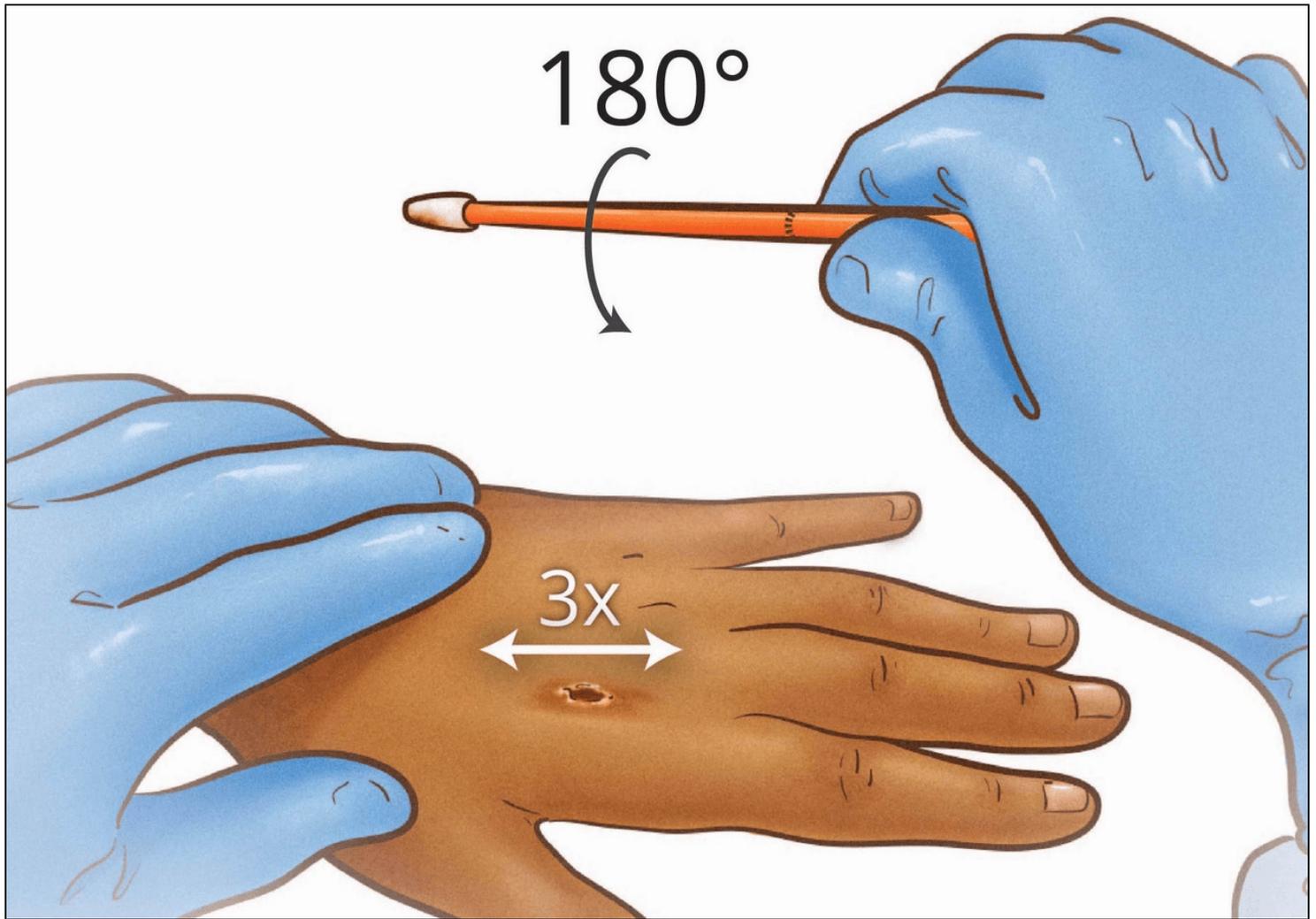


Figure 6 (Image Series) - Obtaining Clinical Samples for Mpox Diagnosis
Image 6D: Placing Swab in Appropriate Container

Illustration: Cognition Studio, Inc. and David H. Spach, MD



Figure 7 Tecovirimat Mechanism of Action Against Monkeypox Virus

Illustration: Cognition Studio, Inc., and David H. Spach, MD

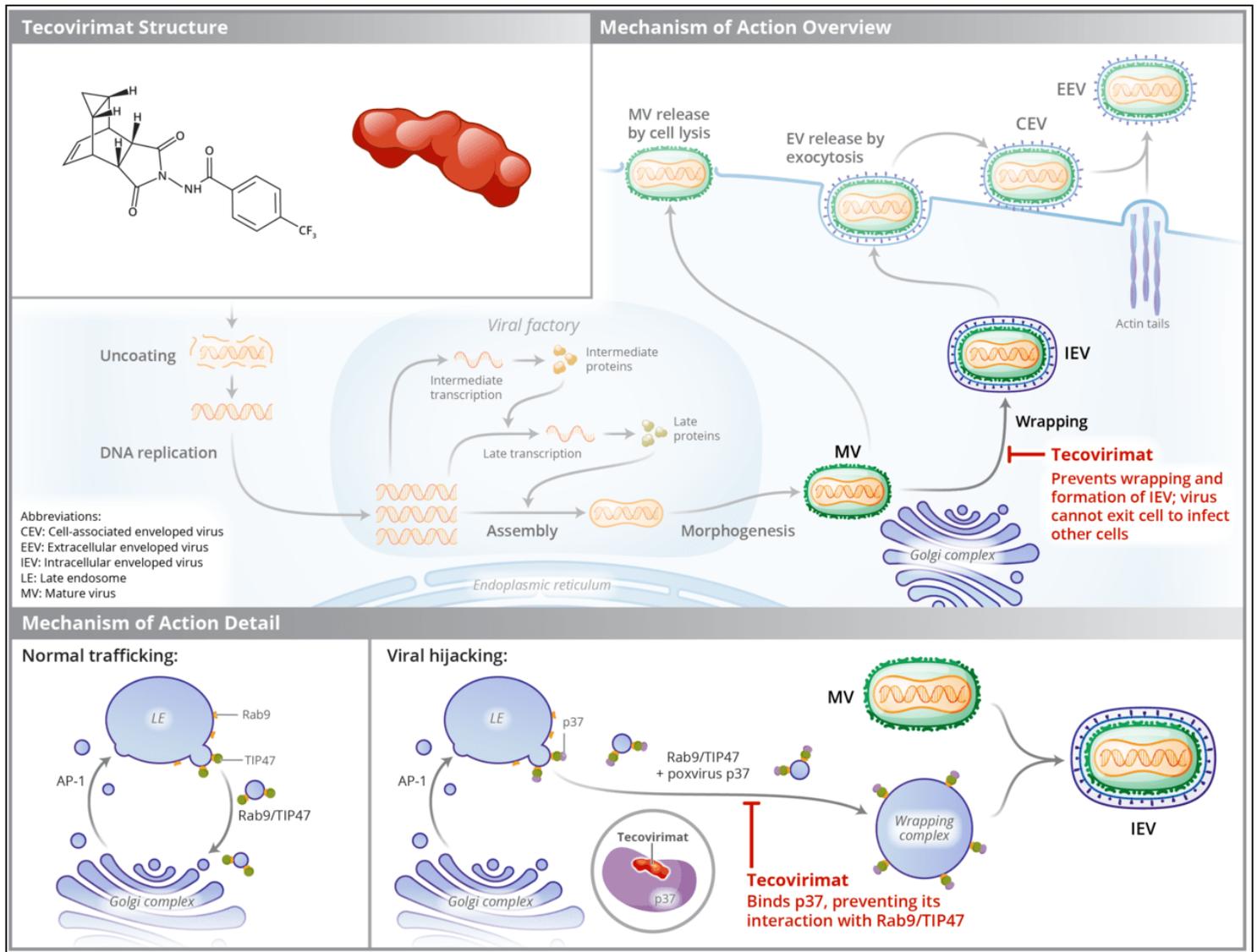


Figure 8 Brincidofovir Mechanism of Action Against Monkeypox Virus

Illustration: Cognition Studio, Inc., David H. Spach, MD, and Raaka G. Kumbhakar, MD

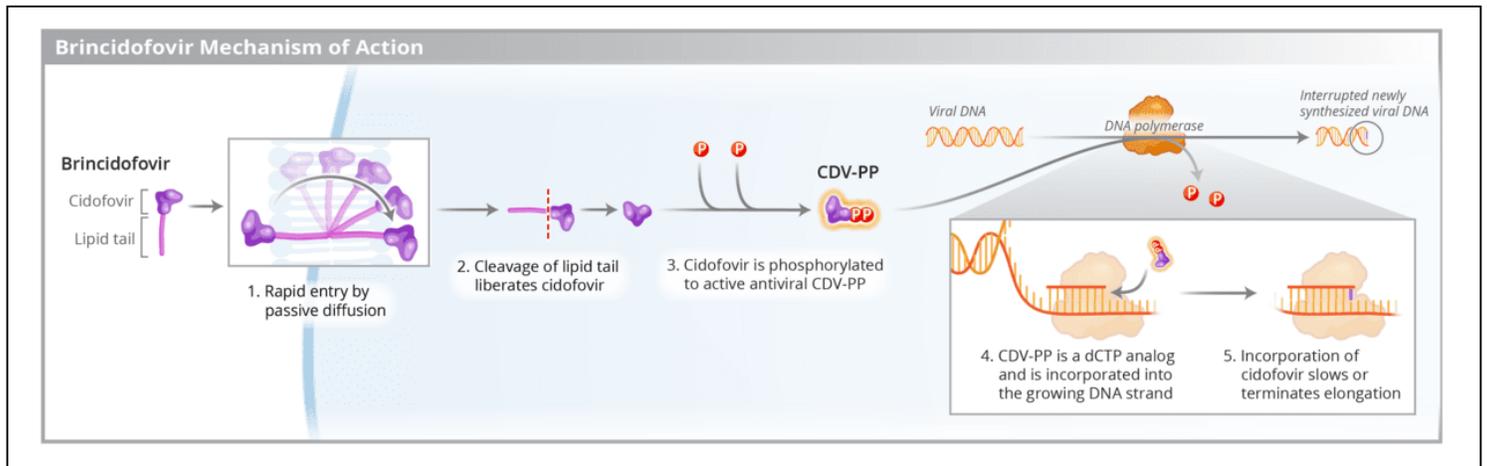


Figure 9 Recommended Personal Protective Equipment (PPE) When Encountering a Patient with Confirmed or Suspected Mpox

Illustration: Cognition Studio, Inc., Raaka G. Kumbhakar, MD, and David H. Spach, MD



Figure 10 Mpox Vaccine

This vaccine can be administered as either a 0.5 mL/dose subcutaneous injection or a 0.1 mL/dose intradermal injection. The intradermal dosing is an option only for persons 18 years of age and older.

Illustration: Cognition Studio, Inc. and David H. Spach, MD

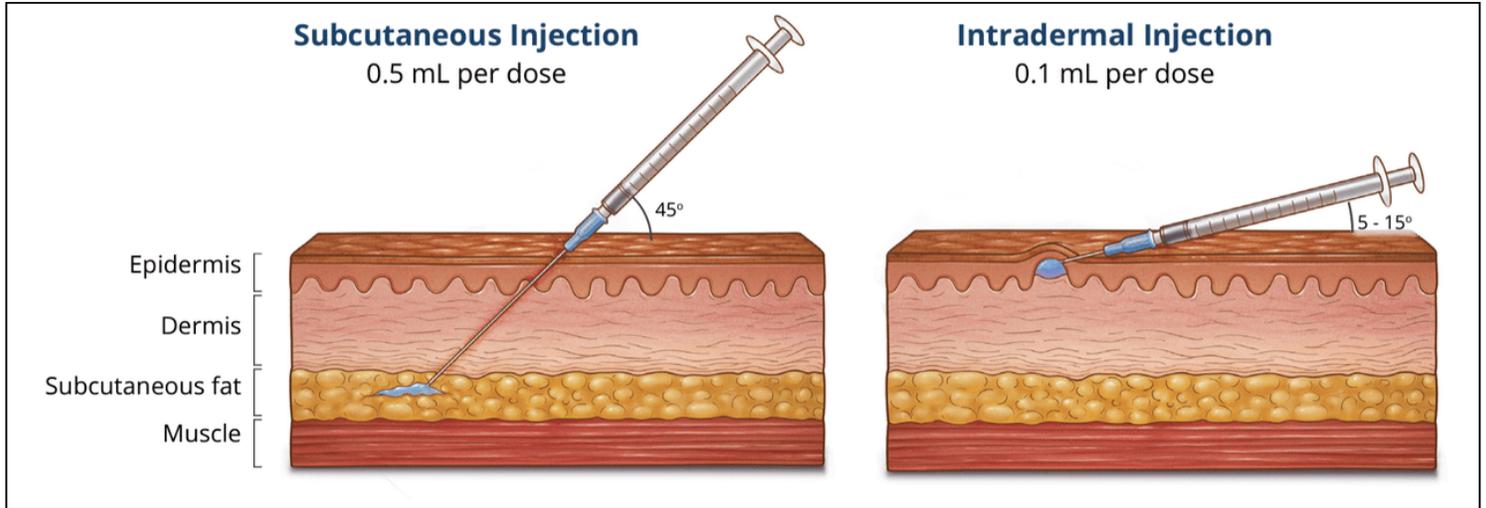


Figure 11 Recommended Mpox Vaccine Schedule

Illustration: Peter Harrison, MPH and David H. Spach, MD

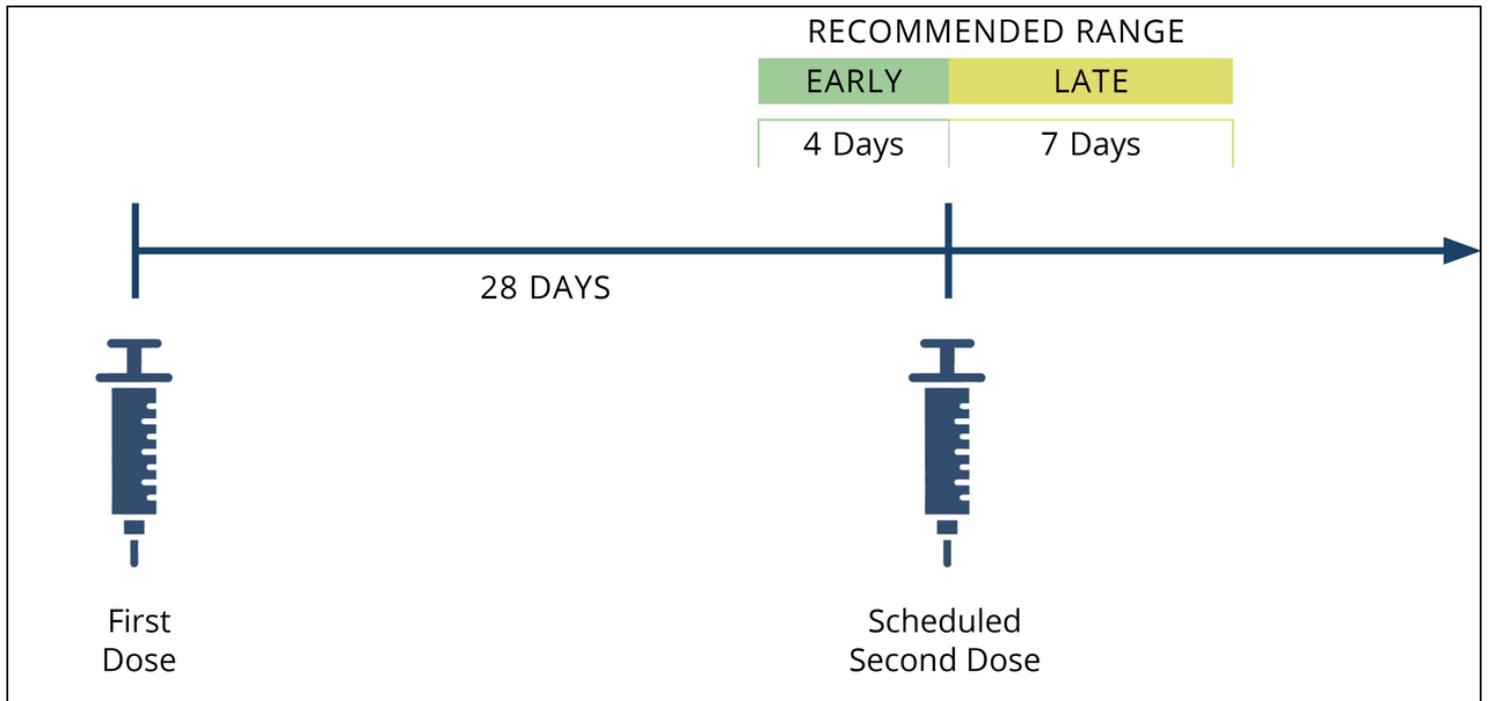


Table 1. Tecovirimat Oral Dosing for the Treatment of Mpox in Adults

Table 1.		
Tecovirimat Recommended Oral Dosing for the Treatment of Mpox in Adults*		
Weight (kg)	Weight (lbs)	Oral Dosing (Capsules) ^{^+}
*Recommendations listed in this table are based on Expanded Access IND Protocol: Use of Tecovirimat (TPOXX®) for Treatment of Human Non-Variola Orthopoxvirus Infections in Adults and Children. IND No. 116,039 CDC IRB No. 6402 Version 6.3 Updated on January 31, 2025		
25 kg to <40 kg	55 lbs to <88 lbs	400 mg every 12 hours
40 kg to <120 kg	88 lbs to <264 lbs	600 mg every 12 hours
≥120 kg	≥264 lbs	600 mg every 8 hours
[^] Each tecovirimat capsule = 200 mg ⁺ Tecovirimat capsules should be taken within 30 minutes after a full meal containing moderate or high fat. Carefully open the required number of capsules and mix contents of capsule(s) with 30 mL of liquid (e.g., milk, chocolate milk, water) or soft food (e.g., apple sauce, yogurt). Administer the entire mixture within 30 minutes of preparation.		

Source:

- Centers for Disease Control and Prevention (CDC). Mpox. Tecovirimat (TPOXX) for Treatment of Mpox. Updated February 6, 2025 [[CDC](#)]

Table 2. Tecovirimat Intravenous Dosing for the Treatment of Mpox in Adults

Table 2.					
Tecovirimat Recommended Intravenous Dosing for the Treatment of Mpox in Adults*					
Weight (kg)	Weight (lbs)	Recommended Dose	Volume of IV Tecovirimat	Volume of Diluent	Total Volume for Infusion
*Recommendations listed in this table are based on Expanded Access IND Protocol: Use of Tecovirimat (TPOXX®) for Treatment of Human Non-Variola Orthopoxvirus Infections in Adults and Children. IND No. 116,039 CDC IRB No. 6402 Version 6.3 Updated on January 31, 2025					
<35 kg	<77 lbs	6 mg/kg every 12 hours by IV infusion over 6 hours	0.6 mg mL/kg	1.2 mL/kg	Varies by weight
35 kg to <120 kg	77 lbs to <264 lbs	200 mg every 12 hours by IV infusion over 6 hours	20 mL	40 mL	60 mL
≥120 kg	≥264 lbs	300 mg every 12 hours by IV infusion over 6 hours	30 mL	60 mL	90 mL
When clinical improvement has occurred, patients should be switched to tecovirimat oral capsules to complete the standard 14-day treatment course as soon as oral therapy can be tolerated.					

Source:

- Centers for Disease Control and Prevention (CDC). Mpox. Tecovirimat (TPOXX) for Treatment of Mpox. Updated February 6, 2025 [[CDC](#)]

Table 3. Brincidofovir Oral Dosing

Table 3.

Brincidofovir Recommended Oral Dosing for the Treatment of Mpox*

Weight (kg)	Weight (lbs)	Oral Tablet [^] Dosing
*Recommendations listed in this table are based on Brincidofovir (<i>Tembexa</i>) Prescribing Information		
<10 kg	<22 lbs	NA
10 kg to <48 kg	22 lbs to 106 lbs	NA
≥48 kg	≥106 lbs	200 mg once weekly for 2 doses
*Doses of brincidofovir are given on days 1 and 8		
[^] Each tablet of brincidofovir = 100 mg		

Source:

- Centers for Disease Control and Prevention (CDC). Mpox. Clinical Treatment of Mpox. Updated January 30, 2025 [[CDC](#)]

