



A conference that is for us and by us

Pandemic Response Team: Lessons from Mpox

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Disclosures

- This contents and views of this presentation are of the speaker and do not necessarily represent the US Centers for Disease Control, Department of Health and Human Services or any other federal agency

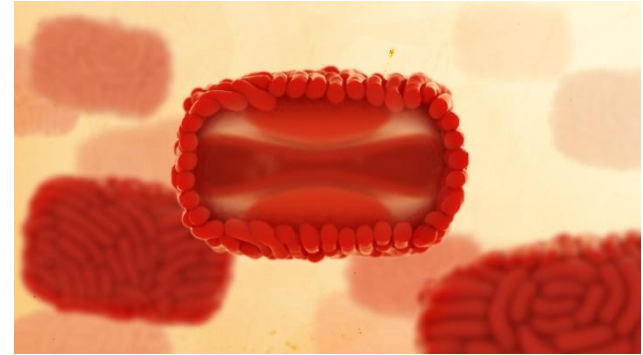
Objectives

- Describe the epidemiology and pathophysiology of mpox
- Discuss the CDC's pandemic response team structure and activities
- Summarize the available medical countermeasures for orthopoxviruses

Background

Monkeypox virus

- Genus: *Orthopoxvirus*
- Family: *Poxviridae*
- Discovered in 1958 after two pox-like disease outbreaks in research monkey colonies
- Specific animal reservoir unknown, but likely small African mammals
- On November 28, 2022, WHO implemented the preferred term “mpox”



Other notable *Orthopoxviridae*

- *Variola virus* (smallpox agent)
- *Vaccinia virus* (used in the smallpox vaccine)
- *Cowpox virus*

Historical Clinical Manifestations (1/2)

- Incubation period: 3–17 days¹
 - Illness duration: 2–4 weeks²
 - Development of initial symptoms marks beginning of prodromal period
 - Fever
 - Malaise
 - Headache
 - Weakness
 - Lymphadenopathy: generalized or localized to several areas (e.g., neck and armpit)
1. <https://www.cdc.gov/poxvirus/monkeypox/symptoms/index.html>
 2. <https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html>

Historical Clinical Manifestations (2/2)

- Rash appears shortly *after* prodrome
 - Lesions develop anywhere on the body but most commonly on the face and extremities, including palms and soles
 - Clusters of lesions in one area begin simultaneously and evolve together

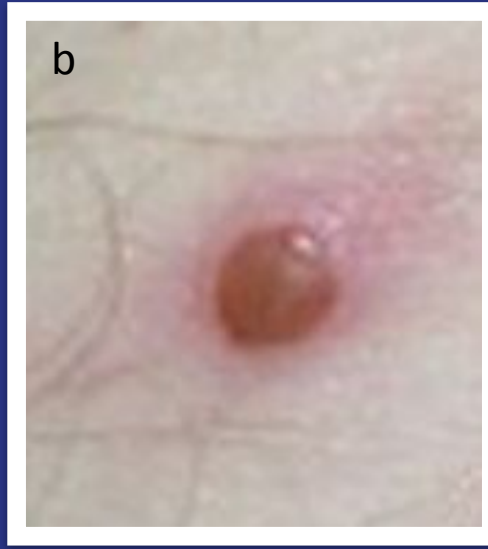
— Lesion evolution



- Lesions are
 - Well circumscribed, deep seated, and often umbilicated
 - Often painful, then become pruritic during the healing phase

Classic Rash Presentation

Mpox lesions are typically **firm** because they arise from deep in the epidermis



Lesions seen in the 2003 U.S. mpox outbreak

Lesions seen in endemic countries

Mpox Complications

- Severe lesions
 - Mucosal lesions may appear as painful ulcers and result in
 - Inability/difficulty to eat, urinate, or defecate due to pain and/or development of strictures
 - Myonecrosis and/or secondary infection if ulcers penetrate deep tissue
 - Skin lesions may
 - Become confluent or necrotic
 - Require specialized wound care/transfer to burn unit
- Other complications
 - Neurologic, myopericarditis, obstructions, sepsis/hemorrhagic disease

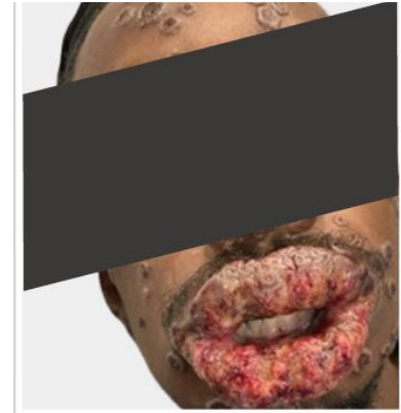


Photo credits: CDC

Emergence of the 2022 Multinational Mpox Outbreak



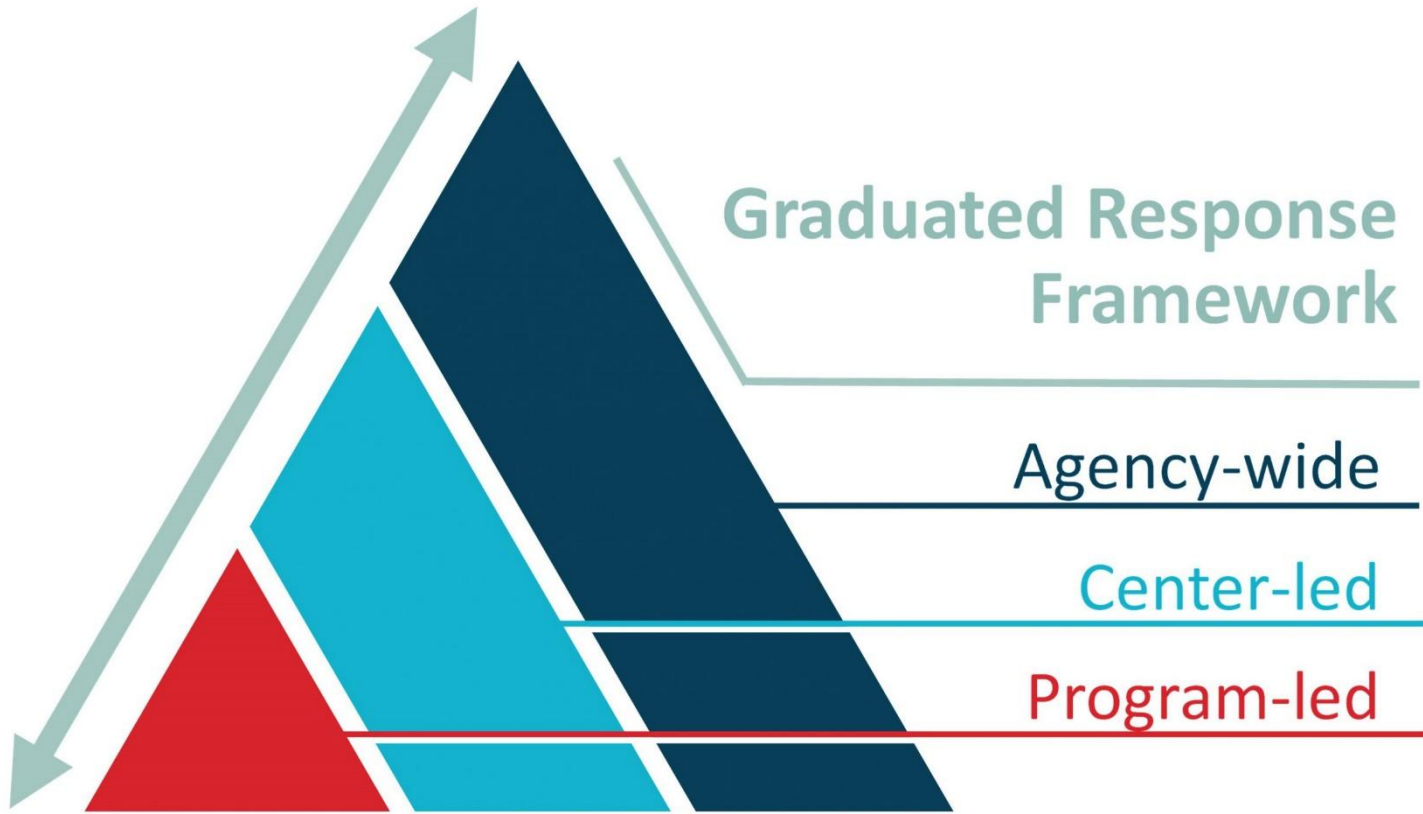
UK Cluster



US Case



**Increasing
Cases**

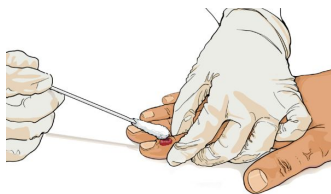


Main Priorities



Enhance
surveillance

Expand
lab testing



Use MCM for
PEP and
treatment

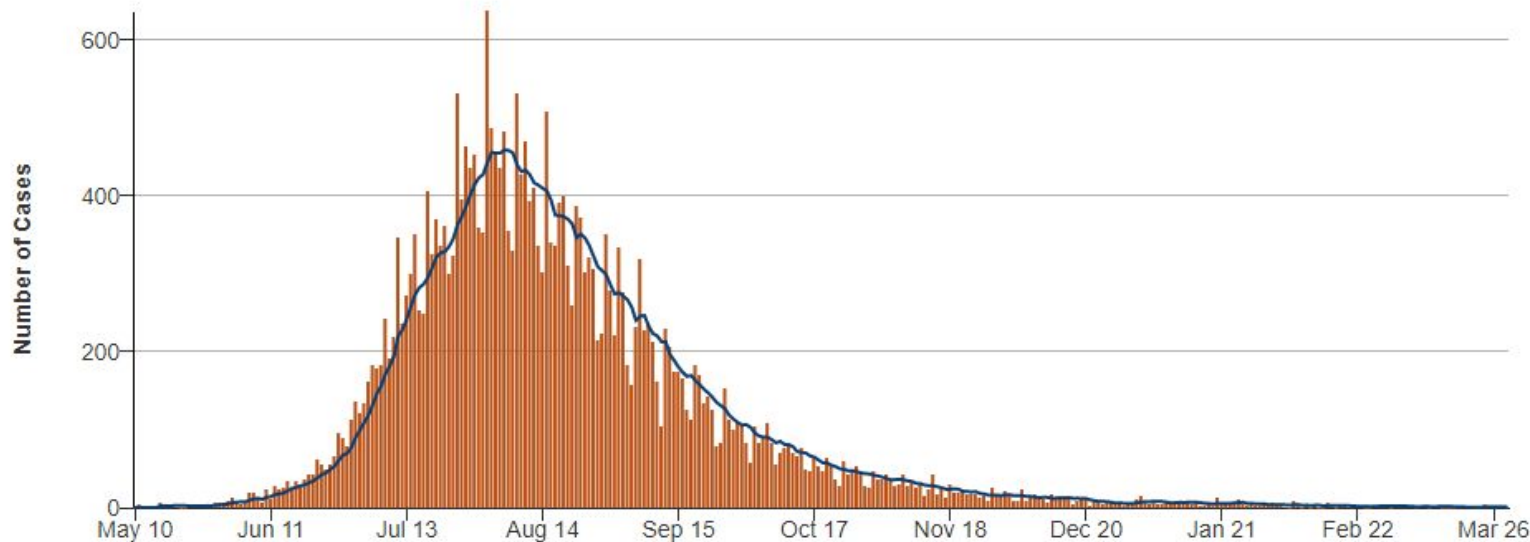
Disseminate
information





Enhance Surveillance

Daily Mpox Cases and 7 Day Daily Average

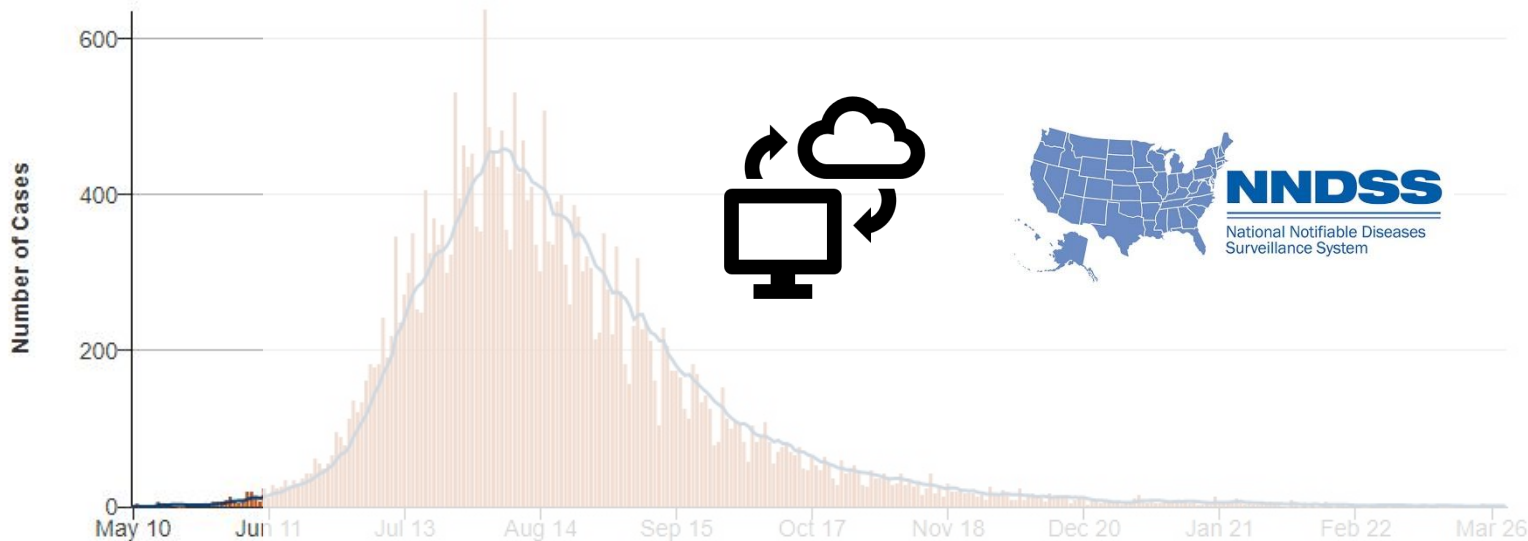


1. <https://www.cdc.gov/poxvirus/monkeypox/response/2022/us-map.html>



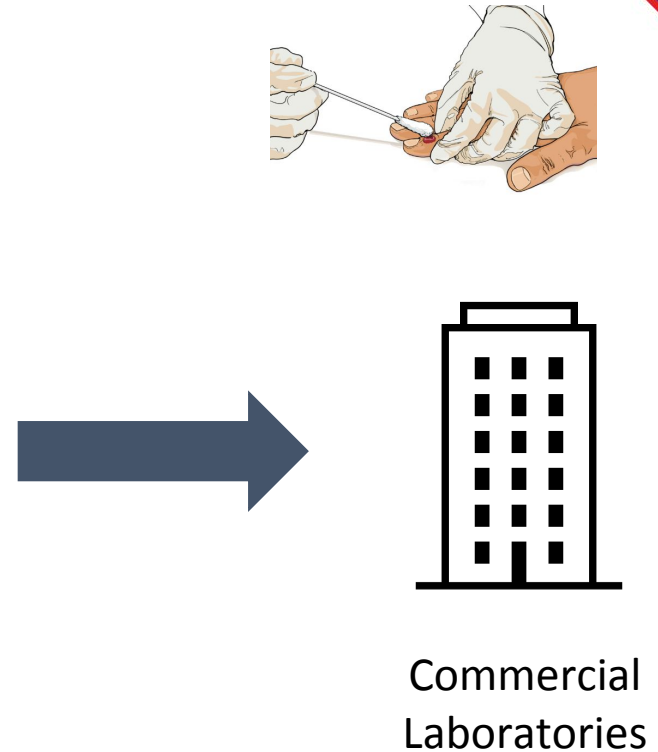
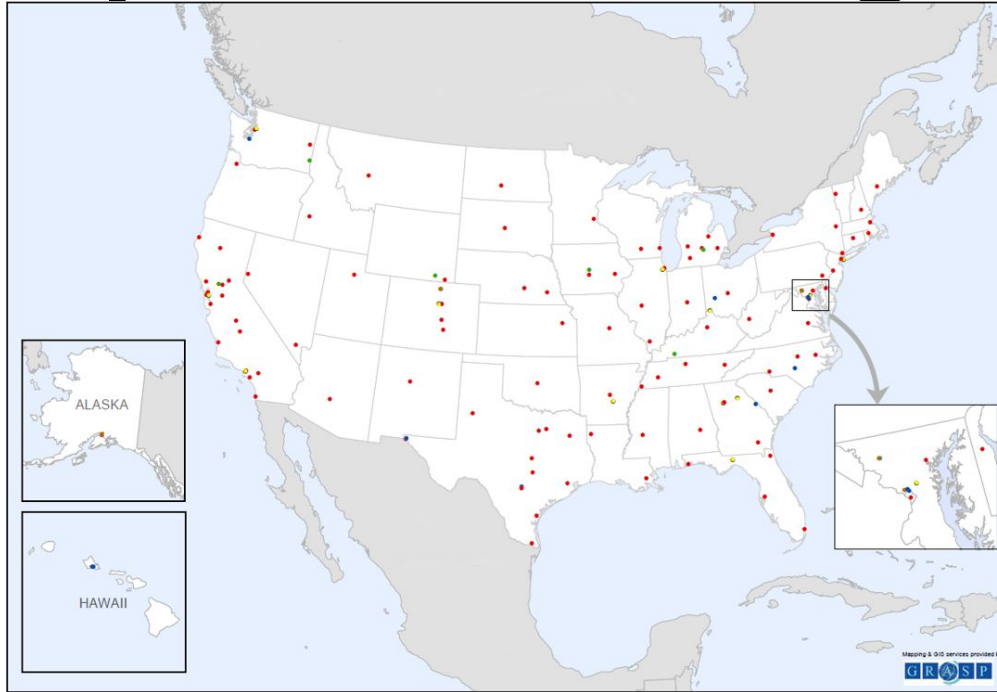
Enhance Surveillance

Daily Mpox Cases and 7 Day Daily Average



1. <https://www.cdc.gov/poxvirus/monkeypox/response/2022/us-map.html>

Expand Lab Testing

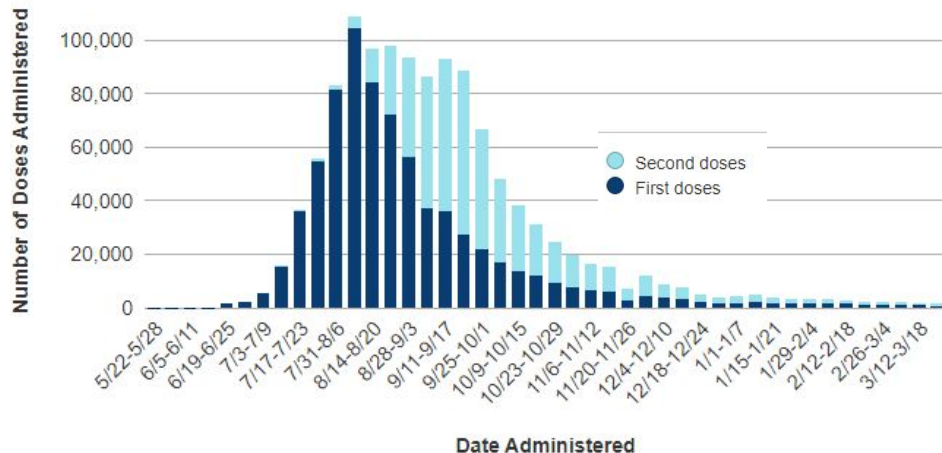


6. <https://www.cdc.gov/poxvirus/monkeypox/cases-data/lab-testing.html>

Use MCM for PEP and Treatment



Total JYNNEOS Vaccine Second Doses and First Doses Reported to CDC



Tecovirimat



Brincidofovir
Cidofovir



Vaccinia Immune
Globulin Intravenous

4. <https://www.cdc.gov/poxvirus/monkeypox/response/2022/vaccine-admin.html>

Disseminate Information



2022 Mpox Outbreak Signs and Symptoms

- During this outbreak, mpox may present atypically
 - Characteristic rash present but often starts in mucosal areas
 - Genital
 - Perianal
 - Oral
 - Skin lesions are scattered or localized to a specific body site but not disseminated



<https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html>

Rash Presentations (1/2)

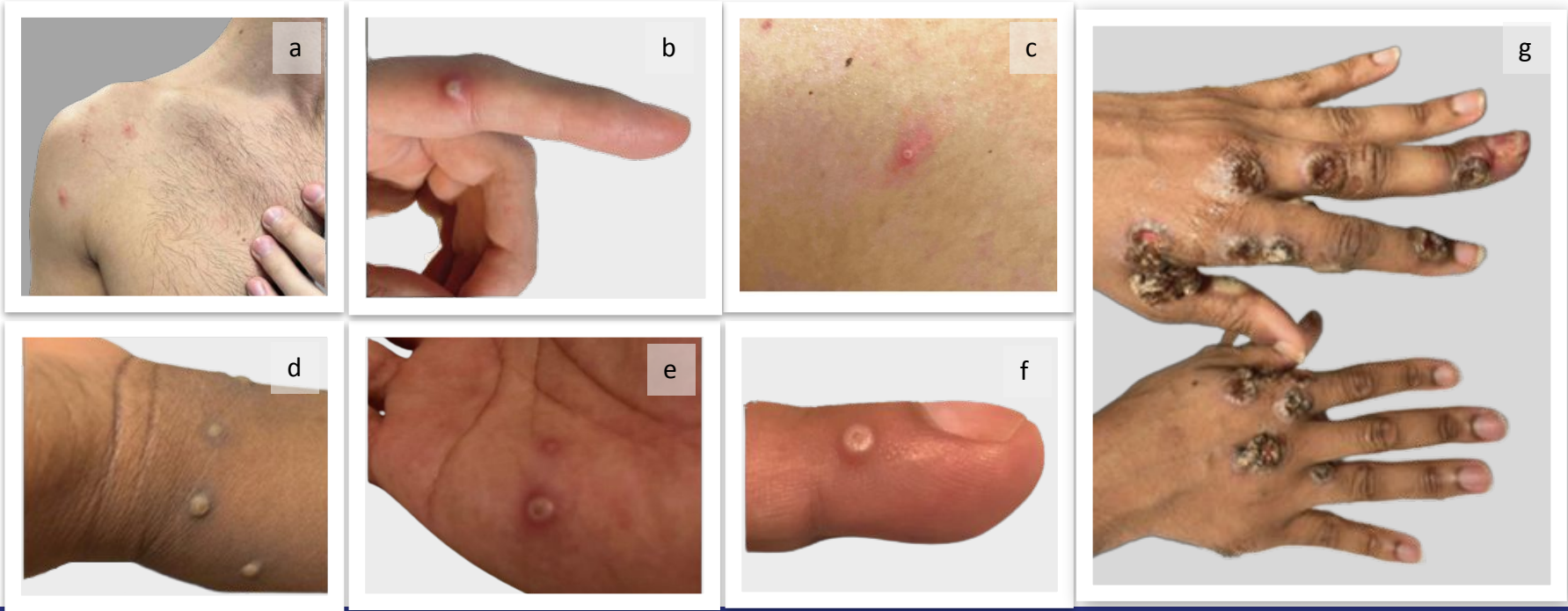


Photo Credits: a-c) Photos appear in Basgoz et al.¹; d-f) CDC; g) Photo appears in Miller MJ et al.²

Rash Presentations (2/2)



Photo Credits: a-f) UK Health Security Agency, g) CDC

Genital Lesions (1/2)

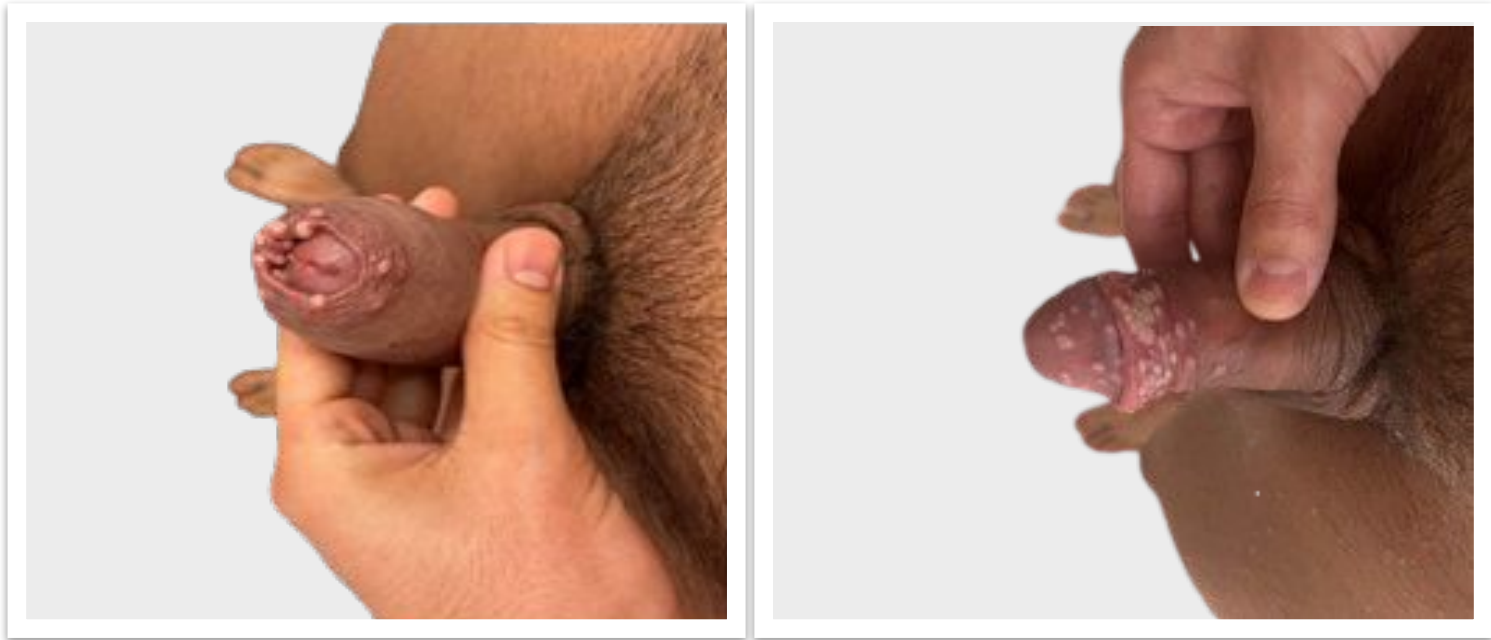


Photo Credits: DC Health and Wellness Center

Genital Lesions (2/2)



Photo Credits: a) Photo appears in Basgoz et al., b) DC Health and Wellness Center

Perianal Lesions



Photo Credit: DC Health and Wellness Center

Treatment and Interim Clinical Considerations

Mpox Prognostic Indicators

- Mpox prognosis depends on multiple factors such as
 - Previous mpox vaccination
 - Immune status (e.g., CD4+ count/viral load)
 - Concurrent illnesses and comorbidities
- Mpox infection is often mild and self-limiting without specific antiviral therapy¹
- Pain management,² skin care,³ and wound care are often vital components of mpox treatment plans

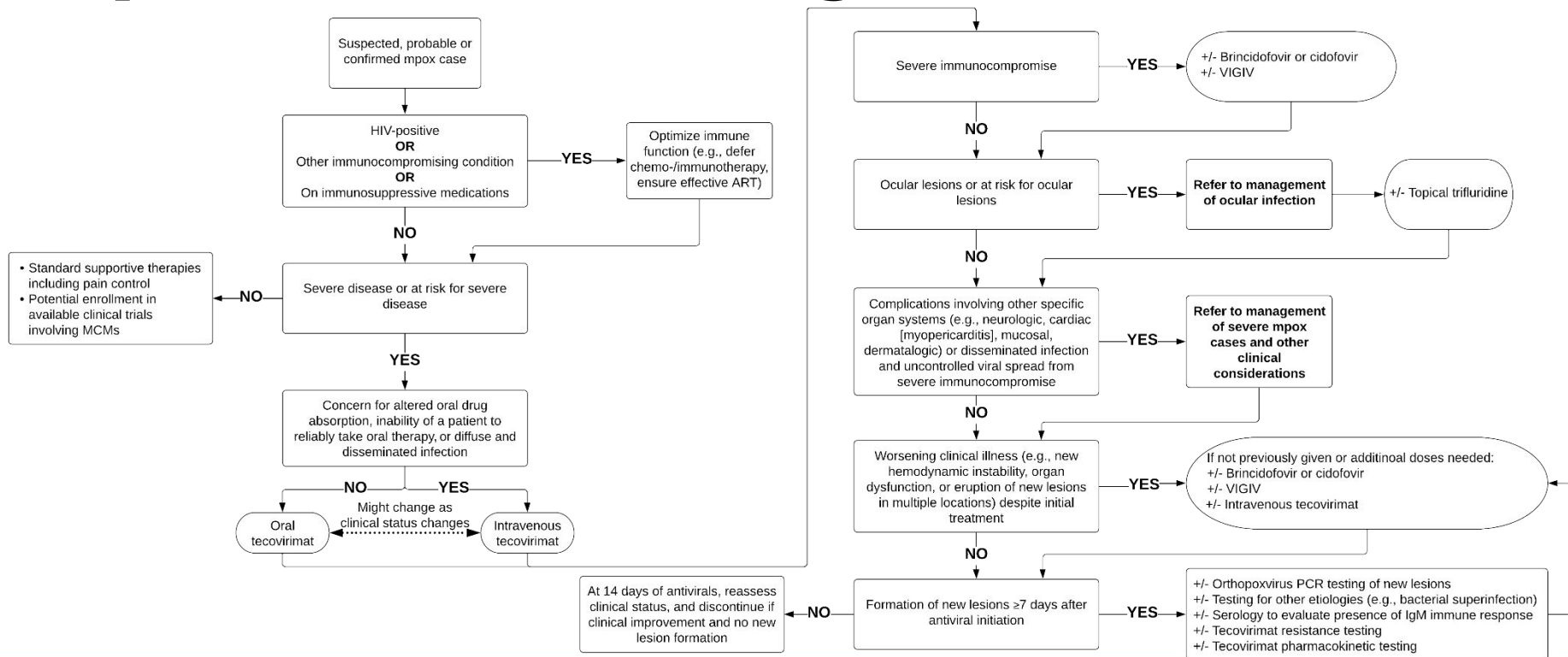


Photo Credits: Photo appears in Miller MJ et al.

Patients at Risk for Severe Mpox

- People with underlying medical conditions (e.g., severe or moderate immunocompromise) are at risk for severe, systemic, protracted illness and death and likely need combination therapy
 - Inadequately treated HIV (CD4+ counts < 350 cells/mm³)
 - Moderate or severe primary immunodeficiency
 - Immunosuppression (e.g., organ transplant, therapy for autoimmune disorder, chemotherapy)
- Prompt consultation with CDC is advised (CDC Emergency Operations Center Phone: 770-488-7100; Email: poxvirus@cdc.gov)

Mpox Treatment Algorithm

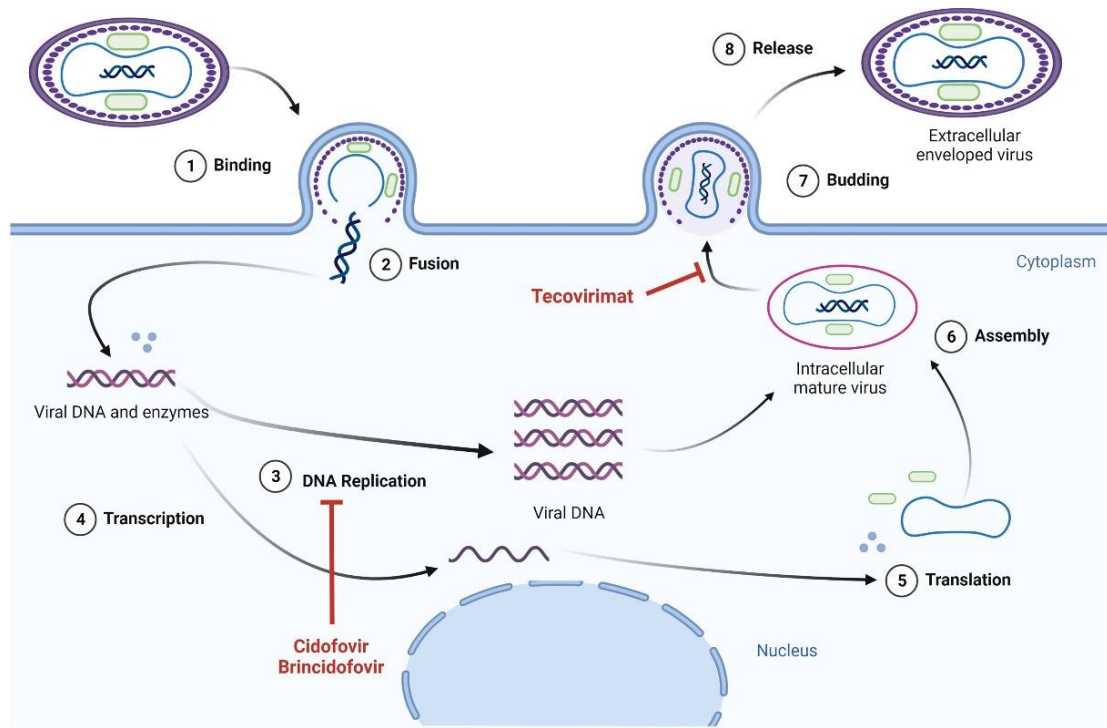


Optimize Immune Function

- For immunocompromised patients
 - Facilitate competent native immunity (e.g., ensure persons with HIV are receiving effective antiretroviral therapy)
 - Limit the use of immunocompromising therapies (e.g., chemotherapy, corticosteroids)
- Doing this may
 - Decrease duration of mpox therapies
 - Minimize morbidity and mortality

<https://www.cdc.gov/mmwr/volumes/72/wr/mm7209a4.htm>

Mpox Antiviral Mechanisms



Siegrist EA, Sassine J. Antivirals With Activity Against Mpox: A Clinically Oriented Review. Clin Infect Dis. 2023 Jan 6;76(1):155-164.

Tecovirimat

- Antiviral approved by the FDA for treatment of human smallpox
 - Also known as TPOXX or ST-246
 - Approved for adults and children weighing at least 3 kg
 - May be used for non-variola orthopoxvirus infections (e.g., mpox) under a CDC-held Expanded Access Investigational New Drug Protocol ([EA-IND](#))
- Mpox treatment efficacy
 - Animal studies suggest mortality benefit
 - Human case reports suggest reduced illness duration and viral shedding
- Mpox postexposure prophylaxis (PEP) efficacy is unstudied

<https://www.cdc.gov/poxvirus/monkeypox/clinicians/Tecovirimat.html>

Tecovirimat is Indicated for Patients With

Severe Disease

- Hemorrhagic disease
- Encephalitis
- Confluent lesions
- Other conditions requiring hospitalization
- Sepsis

Involvement of anatomic areas which might result in serious sequelae

- Eyes*
- Genitals
- Anus

High Risk for Severe Disease

- Severely immunocompromised
- Pediatric
- Pregnant
- Has a condition affecting skin integrity
- Breastfeeding

One or more complications

- Secondary bacterial skin infection
- Broncho-pneumonia;
- Gastroenteritis with severe nausea/ vomiting, diarrhea, or dehydration
- Concurrent disease or other comorbidities

Tecovirimat: Availability

- Oral capsules
 - Must be taken with a full, fatty meal for adequate absorption¹
 - May be opened and mixed with soft food for pediatric patients <13kg
 - Available through
 - Study of Tecovirimat for Human Mpox Virus ( **STOMP**)²
 - Some health departments (limited supplies)
- Oral and intravenous (IV) formulations available through the Strategic National Stockpile (SNS) via consultation/email with CDC



Tecovirimat: Safety and Side Effects

- IV formulation contraindicated for creatinine clearance <30 mL/min
- Minor side effects in healthy subjects
 - Headache
 - Nausea
 - Abdominal pain
- Not studied in pregnant, breastfeeding, or pediatric patients



Cidofovir and Brincidofovir

Cidofovir

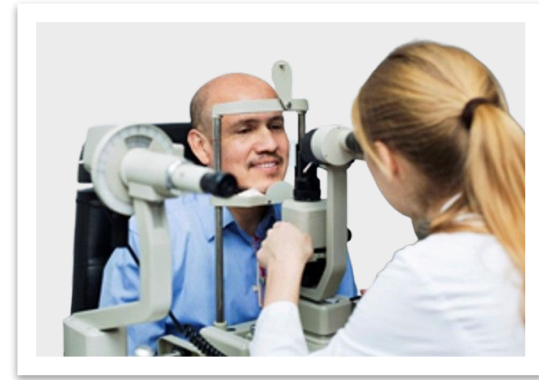
- FDA approved for cytomegalovirus retinitis
- Demonstrated in vivo efficacy against orthopoxviruses
- Commercially available
- Limitations
 - Unknown efficacy
 - Renal toxicity

Brincidofovir

- FDA approved for treatment of smallpox in children of all ages and adults
- In vitro data suggests efficacy against orthopoxviruses
- Available through SNS following FDA authorization for single patient use
- Limitations
 - Unknown efficacy
 - Hepatotoxicity

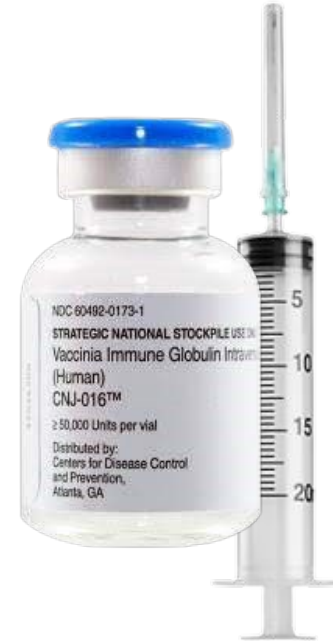
Ocular Mpox Treatment

- Ophthalmology referral strongly encouraged
- Tecovirimat dose needed to achieve therapeutic ocular concentration is unknown
- Avoid topical steroids to prevent viral persistence and corneal damage
- Trifluridine
 - FDA-approved nucleoside analogue for treatment of epithelial keratitis caused by herpes simplex virus
 - Preferred treatment for ocular orthopoxvirus infection (e.g., keratitis and conjunctivitis)
 - Use beyond recommended duration may cause corneal toxicity



Vaccinia Immune Globulin Intravenous (VIGIV)

- FDA-approved for the treatment of vaccinia vaccination (e.g., ACAM2000) complications such as
 - Eczema vaccinatum
 - Progressive vaccinia
 - Severe generalized vaccinia
- **May be used for prevention and treatment of orthopoxvirus infection complications** under a CDC-held Expanded Access Investigational New Drug Protocol
- Efficacy as pre-exposure prophylaxis (PrEP), PEP, or mpox treatment is unknown



Mpox Vaccination

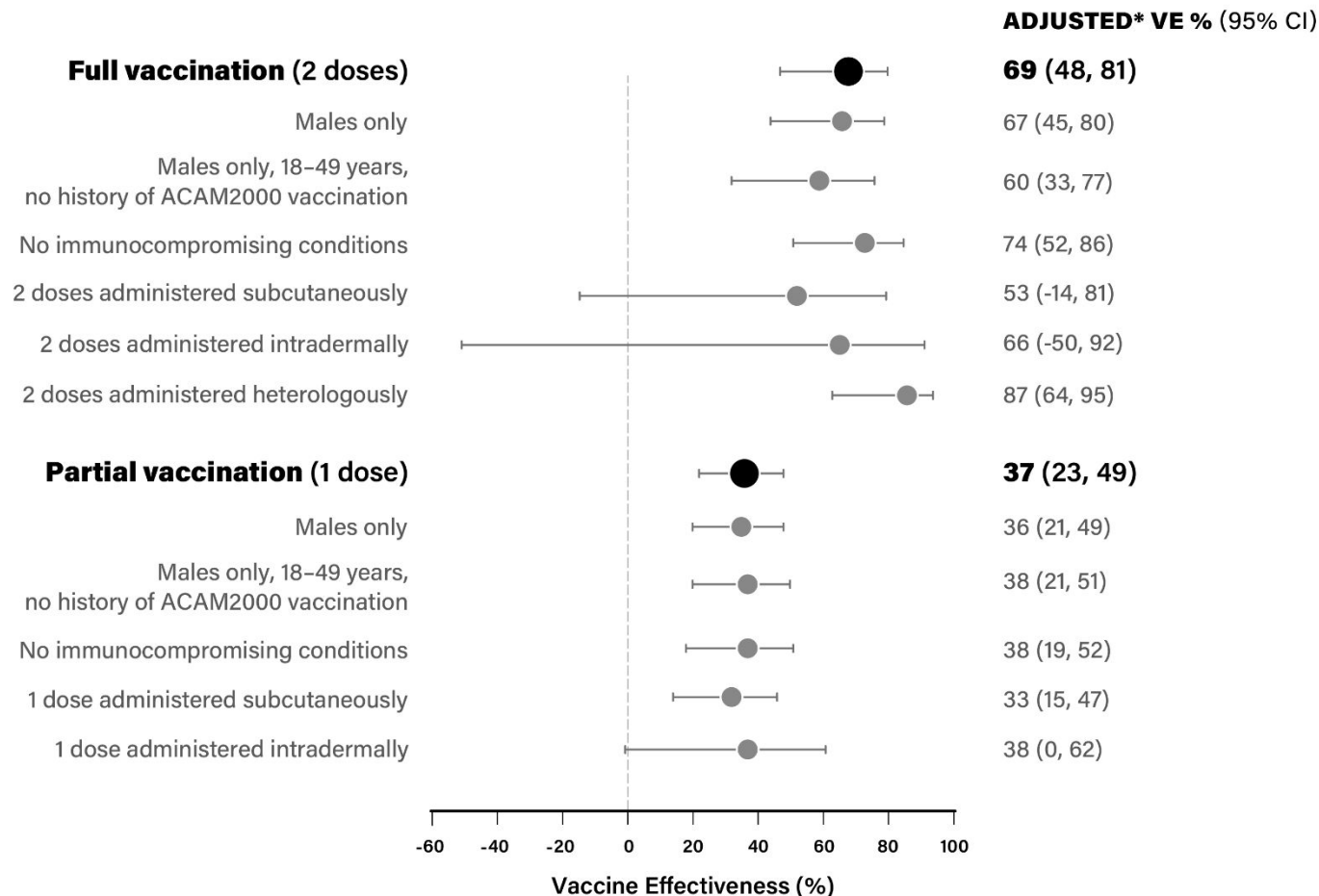
Summary: ACAM2000* and JYNNEOS Vaccines

	ACAM2000	JYNNEOS
Vaccine virus	Replication-competent vaccinia virus	Replication-deficient modified vaccinia Ankara
“Take”	“Take” occurs	No “take” after vaccination
Inadvertent inoculation and autoinoculation	Risk exists	No risk
Serious adverse event	Risk exists	Fewer expected
Cardiac adverse events	Myo/pericarditis in 5.7 per 1,000 primary vaccinees	Risk believed to be lower than that for ACAM2000
Effectiveness	FDA assessed by comparing immunologic response and “take” rates to Dryvax*	FDA assessed by comparing immunologic response to ACAM2000 & animal studies
Administration	Percutaneously by multiple puncture technique in single dose	Subcutaneously or intradermally in 2 doses, 28 days apart

JYNNEOS Vaccine

- Live virus vaccine
- Produced from the *replication-deficient* vaccinia virus strain Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN; also known as IMVAMUNE, IMVANEX, MVA)
- FDA licensed in 2019 to prevent smallpox and mpox in adults ≥ 18 years old¹
- May be intradermally for persons ≥ 18 and subcutaneously for persons < 18 under Emergency Use Authorization
- Administration in 2 doses at least 4 weeks apart
 - Standard regimen: subcutaneous² injections
 - Use only subcutaneous route for people with keloid history
 - **Preferred alternate** regimen: intradermal³ injections
- Can be used for both vaccination prior to exposure and postexposure prophylaxis (PEP)

Preliminary vaccine effectiveness (VE) estimates against medically attended mpox disease



*Vaccine effectiveness estimates were adjusted for age, race/ethnicity, social vulnerability index, and immunocompromising conditions. Cases and controls were matched on week of index event, HHS region, and gender identity.

Summary

- Mpox is generally a self-limiting illness, and cases have declined since their peak last summer
- Interim clinical considerations for treatment of mpox are available for severe cases
- Public health responses to emerging outbreaks are complex, involving significant resources and coordination

For clinical consultation, please contact

CDC Emergency Operations Center Phone: (770) 488-7100
Email: poxvirus@cdc.gov



The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Assessment Question

What is true about mpox?

- A. There is a prolonged viremia which can cause blood to be infectious until it is cleared
- B. The mpox rash is typically superficial, and resolves within 1 week
- C. Mpox is rarely fatal, but severe outcomes can occur in immunocompromised persons
- D. Monkeypox virus often infects only the skin without systemic symptoms

Assessment Question

What is true about mpox?

- A. There is a prolonged viremia which can cause blood to be infectious until it is cleared
- B. The mpox rash is typically superficial, and resolves within 1 week
- C. Mpox is rarely fatal, but severe outcomes can occur in immunocompromised persons**
- D. Monkeypox virus often infects only the skin without systemic symptoms

Explanation:

C. Monkeypox is rarely fatal, but severe outcomes can occur in immunocompromised persons.

Monkeypox is a rare viral disease that typically presents with mild-to-moderate symptoms but can cause more severe outcomes in immunocompromised individuals. The other options are incorrect because: (A) viremia duration varies and is often short, and replication competence in blood is lower than other sample types; (B) the monkeypox rash is deep-seated and generally lasts longer than a week; and (D) monkeypox can cause systemic symptoms (e.g., fever, lymphadenopathy) in addition to skin manifestations.

Assessment Question

Which of the following is not part of the CDC Response Priorities?

- A. Research on the available therapeutics
- B. Enhance surveillance
- C. Disseminate information
- D. Expand laboratory testing

Assessment Question

Which of the following is not part of the CDC Response Priorities?

A. Research on the available therapeutics

B. Enhance surveillance

C. Disseminate information

D. Expand laboratory testing

Explanation: The CDC's main focus is on public health surveillance, laboratory testing, and information dissemination. While research on therapeutics is important, it is not one of the CDC's primary responsibilities. The other options are incorrect because they are part of the CDC's core response priorities: (1) enhancing surveillance to monitor disease trends and detect outbreaks, (2) disseminating information to educate the public and healthcare providers, and (3) expanding laboratory testing to improve diagnostic capabilities and support public health decision-making.

Assessment Question

Which of the following is first line for treatment of mpox?

- A. Brincidofovir
- B. Cidofovir
- C. Tecovirimat
- D. VIGIV

Assessment Question

Which of the following is first line for treatment of mpox?

- A. Brincidofovir
- B. Cidofovir
- C. Tecovirimat**
- D. VIGIV

Explanation: Tecovirimat is an antiviral medication that has been specifically developed for the treatment of smallpox and related orthopoxvirus infections, including mpox. It has been shown to be safe and is currently the preferred treatment option.

The other options, Brincidofovir, Cidofovir, and VIGIV (Vaccinia Immune Globulin Intravenous), are not considered first-line treatments for mpox. Brincidofovir and Cidofovir are broad-spectrum antiviral agents that have shown activity against orthopoxviruses, but due to adverse effects and limited efficacy data are not first line. VIGIV is best used for patients with a compromised immune system who fail to respond to initial treatment.



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References

Background

Slide 6: Historical Clinical Manifestations (1/2)

1. CDC [2022]. Signs and Symptoms
<https://www.cdc.gov/poxvirus/monkeypox/symptoms/index.html>
2. CDC [2022]. Clinical Recognition
<https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html>

Slide 7: Historical Clinical Manifestations (2/2)

- CDC [2022]. Clinical Recognition
<https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html>

Slide 10: Mpox Complications: Other

- Rao AK, Schrodtt CA, Minhaj FS, et al. Interim Clinical Treatment Considerations for Severe Manifestations of Mpox — United States, January 2023. MMWR Morb Mortal Wkly Rep. forthcoming 2023.

Epidemiology

Slide 15: Enhanced Surveillance

1. CDC [2023]. 2022 U.S. Map & Case Count
<https://www.cdc.gov/poxvirus/monkeypox/response/2022/us-map.html>
2. CDC [2023]. U.S. Mpox Case Trends Reported to CDC
<https://www.cdc.gov/poxvirus/monkeypox/response/2022/mpx-trends.html>
3. CDC [2023]. Mpox Outbreak Global Map
<https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html>
4. CDC [2023]. Mpox Cases by Age and Gender, Race/Ethnicity, and Symptoms
<https://www.cdc.gov/poxvirus/monkeypox/response/2022/demographics.html>
5. CDC [2023]. Vaccination uptake by dose
<https://www.cdc.gov/poxvirus/monkeypox/response/2022/vaccine-admin.html>
6. CDC [2022]. Lab Testing Data <https://www.cdc.gov/poxvirus/monkeypox/cases-data/lab-testing.html>
7. CDC [2022]. Mpox Technical Reports
<https://www.cdc.gov/poxvirus/monkeypox/cases-data/technical-report.html>

2022 Mpox Outbreak

Slide 20: 2022 Mpox Outbreak Signs and Symptoms

- CDC [2022]. Clinical Recognition

<https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html>

Slide 21: Rash Presentations (1/2)

1. Basgoz N, Brown CM, Smole SC, Madoff LC, Biddinger PD, Baugh JJ, Shenoy ES [2022]. Case 24-2022: A 31-Year-Old Man with Perianal and Penile Ulcers, Rectal Pain, and Rash. N Engl J Med. 387(6):547-556. doi: <http://dx.doi.org/10.1056/NEJMcp2201244>
2. Miller MJ, Cash-Goldwasser S, Marx GE, et al. Severe Monkeypox in Hospitalized Patients — United States, August 10–October 10, 2022. MMWR Morb Mortal Wkly Rep 2022;71:1412–1417. doi: <http://dx.doi.org/10.15585/mmwr.mm7144e1>

Slide 24: Current U.S. Outbreak Response

1. CDC [2022]. Monitoring and Risk Assessment for Persons Exposed in the Community
<https://www.cdc.gov/poxvirus/monkeypox/clinicians/monitoring.html#exposure>

Treatment

Slide 28: Mpox Prognostic Indicators (1/2)

1. CDC [2022]. Treatment Information for Healthcare Professionals
<https://www.cdc.gov/poxvirus/monkeypox/clinicians/treatment.html>
2. CDC [2022]. Clinical Considerations for Pain Management of Mpox
<https://www.cdc.gov/poxvirus/monkeypox/clinicians/pain-management.html>
3. American Academy of Dermatology and the American Academy of Dermatology Associates [2022]. Monkeypox Caring for the Skin.
<https://assets.ctfassets.net/1ny4voiyrgia/205qKUkE21zKDDSL3KBDq/46124bcc4bf0c0fabbe7a84a490efe73/AAD-Monkeypox-Caring-for-Skin.pdf>
4. Miller MJ, Cash-Goldwasser S, Marx GE, et al. Severe Monkeypox in Hospitalized Patients — United States, August 10–October 10, 2022. MMWR Morb Mortal Wkly Rep 2022;71:1412–1417. DOI:
<http://dx.doi.org/10.15585/mmwr.mm7144e1>
5. Emily A Siegrist, Joseph Sassine, Antivirals With Activity Against Mpox: A Clinically Oriented Review, Clinical Infectious Diseases, Volume 76, Issue 1, 1 January 2023, Pages 155–164,
<https://doi.org/10.1093/cid/ciac622>

Treatment

Slide 29: Mpox Prognostic Indicators (2/2)

- CDC [2022]. Severe Monkeypox in Hospitalized Patients — United States, August 10–October 10, 2022
<https://www.cdc.gov/mmwr/volumes/71/wr/mm7144e1.htm#contribAff>

Treatment

Slide 30: Mpox Treatment Algorithm

- Rao AK, Schrodtt CA, Minhaj FS, et al. Interim Clinical Treatment Considerations for Severe Manifestations of Mpox — United States, January 2023. MMWR Morb Mortal Wkly Rep. forthcoming 2023. <https://www.cdc.gov/mmwr/volumes/72/wr/mm7209a4.htm>

Slide 31: Optimize Immune Function

- CDC [2022]. Update on Managing Monkeypox in Patients Receiving Therapeutics <https://emergency.cdc.gov/han/2022/han00481.asp>

Slide 33: Tecovirimat

- CDC [2022]. Guidance for Tecovirimat Use <https://www.cdc.gov/poxvirus/monkeypox/clinicians/Tecovirimat.html>

Slide 34: Tecovirimat is Indicated for Patients With

- CDC [2022]. Guidance for Tecovirimat Use <https://www.cdc.gov/poxvirus/monkeypox/clinicians/Tecovirimat.html>

Treatment

Slide 35: Tecovirimat: Availability

1. U.S. Department of Health and Human Services and National Institutes for Health [2022]. Study of Tecovirimat for Human Mpox Virus <https://www.stomptpoxx.org/main>
2. CDC [2022]. Guidance for Tecovirimat Use <https://www.cdc.gov/poxvirus/monkeypox/clinicians/Tecovirimat.html>

Slide 37: Cidofovir and Brincidofovir

- CDC [2022]. Treatment Information for Healthcare Professionals. <https://www.cdc.gov/poxvirus/monkeypox/clinicians/treatment.html>

Slide 38: Ocular Mpox Treatment

- CDC [2022]. Interim Clinical Considerations for Management of Ocular Mpox Virus Infection <https://www.cdc.gov/poxvirus/monkeypox/clinicians/ocular-infection.html>

Treatment

Slide 39: Vaccinia Immune Globulin Intravenous (VIGIV) Mpox Treatment

- U.S. Food and Drug Administration (FDA) [2018]. Vaccinia Immune Globulin Intravenous (Human) <https://www.fda.gov/vaccines-blood-biologics/approved-blood-products/vaccinia-immune-globulin-intravenous-human>
- CDC [2022q]. Treatment Information for Healthcare Professionals https://www.cdc.gov/poxvirus/monkeypox/clinicians/treatment.html#anchor_1655488353796

Mpox Vaccination

Slide 41: JYNNEOS Vaccine

1. U.S. Food and Drug Administration (FDA) [2022]. Jynneos
<https://www.fda.gov/vaccines-blood-biologics/jynneos>
2. CDC [2022]. JYNNEOS Smallpox and Monkeypox Vaccine: ALTERNATIVE REGIMEN Standing Orders for Administering Vaccine Intradermally
<https://www.cdc.gov/poxvirus/monkeypox/files/interim-considerations/monkeypox-jynneos-standing-orders-alt-dose.pdf>
3. CDC [2022]. JYNNEOS Smallpox and Monkeypox Vaccine: STANDARD REGIMEN Standing Orders for Administering Vaccine Subcutaneously
<https://www.cdc.gov/poxvirus/monkeypox/files/interim-considerations/monkeypox-jynneos-standing-orders-stand.pdf>