A GUIDE FOR FRONT-LINE CLINICIANS

INTRODUCTION

Human mpox (monkeypox) is an infection characterized by rash and fever. Mpox has historically been reported in Central and Western Africa, and in early 2022, additional cases were identified in Europe and North America. By late November 2022, more than 80,000 cases had been identified in 110 countries, most of which had never previously reported the infection [1].

This document provides an overview of terminology, epidemiology and transmission, clinical manifestations, diagnosis, treatment and prevention of mpox for this most recent outbreak.

A NOTE ON TERMINOLOGY

The illness known as "monkeypox" was named decades ago when the infection was identified in a colony of laboratory monkeys [2]. However, the name is considered inaccurate because the virus' animal reservoir is likely rodents, not monkeys. In addition, the name "monkeypox" has been experienced as stigmatizing and racist [2]. On November 28, 2022, the World Health Organization announced that it was phasing out the name "monkeypox" and replacing it with "mpox" over the course of one year [3]. This document will use the term "mpox".

EPIDEMIOLOGY & TRANSMISSION

The global outbreak of mpox that began in 2022 has predominantly affected cisgender men who have sex with men (MSM), although people of any sexual orientation or gender identity can and have been affected. In early reports on the outbreak, cisgender MSM represented more than 90% of those affected by the virus [4]. Mpox has also been prevalent among those already diagnosed with HIV, with 57% of affected individuals in the United States having HIV [5].

Mpox can be spread in a number of ways. The most common mode of transmission in the recent outbreak is close, skin-to-skin contact, such as during sex. The virus can also be spread through contact with fomites, such as blankets or clothing, used by a person with mpox. People with mpox are considered capable of spreading the infection to others until all skin lesions have healed. However, presymptomatic transmission has also been shown to occur. Asymptomatic transmission – in other words, transmission from people who never develop symptoms – has not been documented [6].

Weekly case counts of mpox peaked in early August, 2022 and have declined since [7]. The decrease in cases likely stems from three factors: natural immunity among those who have had the infection, vaccine-induced immunity, and behavior changes, including reduction in the number of sexual partners and one-time sexual partnerships among gay, bisexual, and other MSM [8].

CLINICAL MANIFESTATIONS

Classically, mpox began with a viral prodrome consisting of fever, malaise, and lymphadenopathy followed by development of a rash. However, in the current outbreak, the prodrome may not occur, or fever and other systemic symptoms may begin after the development of the rash [9].

Ultimately, nearly all affected people develop a rash. The skin lesions of mpox begin as macules and then progress to become papules, vesicles, and deep-seated pustules, often with central umbilication, before eventually scabbing and healing [10].

To see examples of skin lesions due to mpox, view https://www. cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html from the Centers for Disease Control and Prevention.

Scarring may occur. The rash may take two weeks or more to evolve and heal. More than 70% of people in the recent outbreak have anogenital mpox lesions [4]. Significant rectal pain and proctitis, which may interfere with bowel movements, may also occur.

While most people with mpox have a self-resolving infection and do not require hospitalization, severe illness can occur and is more common in those with untreated HIV and low CD4 T cell counts [11]. Severe manifestations of mpox include: confluent, necrotic skin lesions; urinary retention; secondary bacterial infections; ocular infections; encephalitis; and rarely death [11].

Concurrent sexually transmitted infections (STIs) such as gonorrhea, chlamydia, and or syphilis are common among people with mpox, occurring in approximately one-third of people at the time of mpox diagnosis [4].

DIAGNOSIS

Clinicians can test for mpox by swabbing crusts and/or fluid from an open lesion or dryswabbing intact vesicles or pustules. Unroofing of vesicles or pustules is not necessary and is not recommended, because it may be a source of mpox transmission to health care workers. Because people with suspected mpox may have more than one skin process simultaneously, it is recommended to obtain multiple samples from different-appearing lesions, if possible [12]. There is no clinically available way to test for mpox prior to the development of a visible skin or mucosal lesions.

Testing is available at both public health and commercial laboratories; the instructions for specimen collection, packaging, and shipment may vary among laboratories, so clinicians should check the instructions for their particular laboratory prior to using the test.

TREATMENT

Most people with mpox will recover on their own, with supportive care only. It is crucial for clinicians to assist with pain management in those affected by mpox. Pain management strategies depend upon the location of mpox lesions and may include topical therapies, such as sitz baths for those with proctitis, or systemic analgesics, up to and including opioid medications should other analgesics provide insufficient relief [13].

Clinicians should test for STIs such as HIV, gonorrhea, chlamydia, and syphilis in people with mpox. HIV pre-exposure prophylaxis (PrEP) should be considered for those without HIV, and those with HIV who are not yet taking antiretroviral therapy should be engaged in care.

The primary medication used for treatment of mpox has been tecovirimat. Tecovirimat is an antiviral drug approved for treatment of smallpox in children and adults. It is not approved for the treatment of mpox, but it is anticipated to have activity against mpox based on its mechanism of action. Currently, tecovirimat is available through an expanded access-investigational new drug (IND) application process for those with severe manifestations of mpox, those who are at risk for severe manifestations of mpox (e.g., people with untreated HIV, pregnant people), and those whose mpox lesions pose a risk for serious sequelae or scarring (e.g., anal lesions precluding normal bowel movements, pharyngeal lesions precluding eating) [14]. Because the clinical efficacy of tecovirimat in mpox is unknown, a clinical trial is also underway to assess the drug's impact. Agents such as brincidofovir or vaccinia immune globulin can be administered in special circumstances, for people with or at risk for severe manifestations of mpox.

VACCINATION

Mpox vaccination is currently recommended for those who have had a confirmed or presumed exposure to mpox within the past 14 days, and those who are at risk for mpox going forward. Eligible individuals include MSM, transgender, and nonbinary people who, in the past 6 months, have had 1) an STI and/or more than one sex partner; 2) sex at a commercial sex venue or large public event; or 3) sex partners with any of the aforementioned behaviors. In addition, people who anticipate any risks for mpox going forward are eligible. To mitigate the impacts of stigma, people should be able to self-attest to meeting criteria for vaccination without having to stipulate the nature of their risks [15].

The vaccine used in response to the global mpox outbreak is the modified vaccinia Ankara-Bavarian Nordic (MVA-BN) vaccine, also known as JYNNEOS. It is a live, non-replicating viral vaccine. The vaccine is generally well-tolerated; the only known contraindication is severe allergy to a vaccine component, which includes ciprofloxacin, gentamicin, or egg. Primary vaccination with MVA-BN consists of two doses given four weeks apart [16].

The preferred route of administration is intradermal, because this requires a smaller dose of vaccine and thus stretches the vaccine supply; intradermal administration was shown to produce similar immune responses to subcutaneous administration [17], which is the standard route. Intradermal administration can cause local inflammatory reactions. People with a history of keloid scars and those younger than 18 years are not candidates for intradermal vaccination; they should receive the vaccine subcutaneously.

MVA-BN appears to be effective at reducing the risk of mpox, with one analysis showing that mpox incidence is 14 times lower in people who had received at least one dose of MVA-BN compared to unvaccinated people [18]. Remote smallpox vaccination may not protect against mpox in the current outbreak, so people with childhood smallpox vaccinations should still receive MVA-BN if they are eligible for mpox vaccination.

SUMMARY

- Mpox is a viral infection which caused a global outbreak beginning in 2022, predominantly affecting cisgender MSM.
- Nearly all people affected by mpox will develop a rash as part of the illness, and in a majority of cases, involvement of the anogenital area occurs.
- Most people with mpox will recover with supportive care only, but people with HIV or other immunocompromising conditions can develop severe disease.
- Vaccination with MVA-BN (JYNNEOS) is recommended for people with exposure to mpox or who are at risk for mpox.

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