PERSPECTIVE

A New Health Emergency: Monkeypox Outbreak

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Monkeypox, caused by a double-stranded DNA Orthopox virus has recently increased in non-endemic countries outside of Africa. At the time of this writing, 80,850 cases have been reported globally and 29,248 cases in the USA.[1] Endemic countries have also experienced a recent increase in monkeypox cases. In 2003, during an outbreak of monkeypox in Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 47 cases happened due to contact with prairie dogs. Before 2022, community transmission of monkeypox did not happen outside of Africa, as most cases occurred in the Democratic Republic of the Congo. In addition to the geographic difference between the current and previous monkeypox outbreaks, there are also significant demographic differences. Most recent outbreaks in West and Central Africa have affected individuals of all ages, while early outbreaks mainly affected children. According to the currently available data, 99% of U.S. monkeypox cases occurred in men.[2] The current outbreak of monkeypox is predominantly affecting gay, bisexual men, and other men who have sex with men (GBMSM).[2]

Monkeypox is a zoonotic infection. Interestingly, rodents are the most important animal reservoir despite the disease name.[3] Direct contact with the blood, body fluids, or mucosal lesions of animals can transmit this disease. The intimate skin-to-skin or skin-to-mouth contact with an infected patient's lesions, and respiratory droplets through kissing or coughing, can cause human-to-human transmission of this disease. In addition, contact objects used by an infected person like clothing, bedding, or sex toys can spread monkeypox.[4,6] It can remain stable on surfaces like linen in cool, dark environments. Monkeypox has been detected in anorectal swabs from asymptomatic MSM.[5,6] However, the importance of asymptomatic or subclinical infections in spreading the virus in the current outbreak is not known yet.

The rash is the most reported sign and symptom of monkeypox, which was most frequently reported on the genitals (46%).[2] In addition, rectal symptoms include rectal pain, and purulent or bloody stools have been frequently reported.[5] Prodromal symptoms (fever, chills, headache, arthralgia) can be present before or after the onset of the rash or not present at all. The CDC states that lesions are usually well-circumscribed, deep-seated, and often umbilicated.[7] The lesions evaluate through four stages – macular, papular, vesicular, and pustular before scabbing over and desquamation. Lesions are infectious until full healing of the rash with the formation of a fresh layer of skin.[7] Patients need counseling and space to isolate themselves until all symptoms have resolved. Clinicians should test patients with a rash suspicious of monkeypox, regardless of whether the rash is preceded by the prodrome or disseminated.[2] Lymphadenopathy is a key feature of monkeypox and a key distinguishing clinical feature from smallpox. Inguinal lymphadenopathy has been particularly prominent during this current outbreak.[7] Ocular

monkeypox can potentially cause blepharitis, conjunctivitis, keratitis, and loss of vision.

Per the Sept. 9 MMWR report of approximately 2,000 individuals with monkeypox in the US, 38% had HIV infection. Monkeypox co-infections with gonorrhea, syphilis, herpes, and chlamydia are frequently being seen. Individuals with poorly controlled HIV are at high risk for severe manifestations of monkeypox. It is crucial to encourage diagnostic tests for monkeypox, HIV, and other sexually transmitted infections (STIs) in every sexually active person if monkeypox is suspected.

Monkeypox typically takes between 3 to 17 days to manifest after exposure.[7] The illness typically lasts for 2-4 weeks, per CDC. The illness severity can depend on the initial health of the patient and the route of exposure.[7] Treatment is mostly supportive, focusing on the management of symptoms and prevention or treatment of complications. Potential serious complications include secondary bacterial infections, pneumonitis, and encephalitis. As of November 25, the CDC has reported 14 deaths in the U.S.[1]

Orthopox PCR from the skin lesions, or throat swabs in close contacts without lesions, are performed to diagnose monkeypox. Any lab that performs tests for monkeypox should report all results (positive, negative, equivocal) unless otherwise recommended by the applicable health department. Positive test results must be reported within 24 hours of testing to the appropriate state, tribal, local, or territorial (STLT) health departments.[8]

Antiviral tecovirimat (TPOXX), which has been approved by the Food and Drug Administration (FDA) to treat smallpox, is currently used to treat patients with severe monkeypox disease or who are at high risk of severe diseases like immunocompromised patients. It is worth remembering that TPOXX should not be prescribed to patients with milder monkeypox symptoms according to current guidelines. Clinicians should counsel patients to take fatty meals with oral tecovirimat to ensure adequate gastrointestinal absorption to maximize serum drug levels. Inadequate serum levels of oral tecovirimat can promote resistance. Patients who experience persistent or newly emergent monkeypox lesions after 14 days of tecovirimat treatment should undergo lesion swab specimens for tecovirimat resistance and plasma pharmacokinetic testing.[9] These two tests will help to determine if any cases of confirmed resistance are associated with drug levels below target concentrations. Of note, the pharmacokinetic test is done by a designated lab, not at the CDC.[9] Severe immunocompromised patients may need a longer course of tecovirimat than its standard 14-day course until their immune system can effectively clear monkeypox.[9]

Unvaccinated people had 14 times the risk of monkeypox compared to people who were vaccinated per CDC.[10] Two types of vaccines, JYNNEOS & ACAM2000, are now available for prevention and post-exposure prophylaxis. Past data from Africa suggests that these vaccines are at least 85% effective to prevent monkeypox.[10] There are no data on the clinical efficacy of these vaccines in the current outbreak.[11] It is critical to remember that vaccination within 4 days following exposure can prevent the onset of the disease. The CDC advises that if the vaccine is given within 4 to 14 days after the exposure, vaccination may reduce the severity of the disease but not prevent the disease onset. JYNNEOS, the Modified Vaccinia Ankara (MVA), is approved for the prevention of smallpox and monkeypox.[11,12] JYNNEOS vaccine is given as a series of two doses administered 28 days apart. It is expected to achieve peak immunity 14 days after the 2nd dose of the JYNNEOS vaccine. In contrast, the ACAM2000, a replicating vaccine, is licensed as a single dose, and peak immunity is expected to be reached 4 weeks after that one dose administration.[10] ACAM20000 is contraindicated in immunocompromised patients. Under the FDA-issued Emergency Use Authorization (EAU), the JYNNEOS vaccine has now been given 0.1 ml intradermally to patients 18 years or older in context 0.5 ml subcutaneously.[11] In

2015, an NIH-funded clinical study of the MVA vaccine evaluated a two-dose series and a lower dose (one-fifth) given intradermally compared to the subcutaneous route. This study demonstrated that a lower dose of the intradermal JYNNEOS vaccine had similar immune responses to subcutaneous administration.[12] The dose-sparing strategy will allow using one-fifth of what's traditionally given to have more doses out of the existing supply, which is expected to increase the vaccine dose availability up to fivefold compared to the usual subcutaneous route.

Endemic countries of monkeypox are still facing a lack of support from the international community to tackle outbreaks. Many of these affected countries have limited access to testing and vaccination. A remarkable difference exists between endemic and non-endemic countries regarding the political, scientific, and financial commitments to the monkeypox outbreak. Global health investment must focus on equitable distribution to prevent future outbreaks. Gay, bisexuals, and men who have sex with men (GBMSM) should be prioritized for testing, treatment, and prevention to ensure health equity. The California Department of Public Health announced it would avoid calling this virus monkeypox, instead referring to it as "MPOX" or "MPX" to make this less stigmatizing and discriminatory. Fact-based awareness to avoid stigma around our LGBTQ+ community is pivotal to optimizing appropriate patient care and prevention. We need health education to avoid behaviors that increase the risk of this new public health emergency.

Notes

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