Update on the Monkeypox Outbreak

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Multimedia

The current monkeypox outbreak was declared a Public Health Emergency of International Concern (PHEIC) by the World Health Organization (WHO) director-general on July 23, 2022. As of August 9, 2022, nearly 32,000 confirmed cases of monkeypox had been reported across 82 nonendemic countries.1 Given the rapid pace with which cases are being diagnosed, a coordinated international response is essential.2

The first US case of monkeypox was reported on May 7, 2022, and as of August 9, 2022, nearly 9,500 confirmed cases have been reported. On August 4, 2022, the Biden administration declared monkeypox a public health emergency, giving federal agencies the ability to quickly direct funds toward vaccines, therapeutics, and other immediate needs.

How Is Monkeypox Spread?

Monkeypox is transmitted primarily through direct skin-to-skin contact with infectious lesions. In the current outbreak, most cases have occurred among men who acquired the infection through sexual or intimate contact with other men. Contact with materials used by a person with monkeypox including clothing, bedding, or sex toys may lead to transmission.3

Monkeypox can be transmitted during sexual activity, but it is not considered to be a sexually transmitted infection because the virus can be acquired without having sex. In addition, even though the monkeypox virus has been detected in semen, it remains unclear if monkeypox can be transmitted through semen, vaginal secretions, urine, or feces.4 Transmission may occur across the placenta to the fetus in pregnant people. It is unknown if the virus can be transmitted by individuals without skin lesions or how often the virus is spread through respiratory secretions. The virus is not spread by casual contact.

Clinical Characteristics

As of July 25, 2022, the US Centers for Disease Control and Prevention (CDC) reported that 99.1% of US cases are among individuals assigned male sex at birth, with a median age of 35 years (range 18-76 years).5 Most of the cases have occurred among men who have sex with men but at least 13 cases have been reported among persons assigned female sex at birth, including one pregnant individual, and at least 2 children have become infected.6

The mean incubation period from time of exposure to first symptom onset has been estimated at 7.6 days (95% CI, 6.2-9.7),5 with 95% of individuals developing symptoms within 17.1 days. The initial symptoms are those of a flu-like illness with fever, malaise, headache, and fatigue often accompanied by lymphadenopathy. Shortly after the prodrome, a rash appears with lesions starting as macules that progress to papules, vesicles, and then pustules before scabbing.

In the current outbreak, common symptoms also include anorectal pain, proctitis with bleeding, and penile edema with balanitis and phimosis. Sore throat, odynophagia, epiglottitis, and tonsillitis are also reported.

The largest series published to date included 528 patients across 16 countries; 98% of the cases were among men who identified as gay or bisexual and 41% were living with HIV. The most common locations of lesions were the anogenital area (73%); trunk, arms, or legs (55%); face (25%); and palms and soles (10%). Most persons had fewer than 10 lesions and almost 10% presented with a single genital lesion.6

For most individuals, monkeypox is not life-threatening but it is disruptive and painful and could generate social stigma. Known complications of monkeypox may include pneumonia, encephalitis, and eye infections, which occur mostly in children younger than 8 years and individuals who are immunocompromised or pregnant. Hospitalization is uncommon and the major reason for admission has been pain control, typically from anorectal or oral pain. People with monkeypox should remain in isolation for the duration of illness, which typically lasts 2 to 4 weeks. Mortality is rare, but so far at least 4 people in nonendemic countries have died.7

Testing for Monkeypox

Any unusual skin lesion, particularly in the anogenital area, should be investigated. The rash may be limited to a few lesions or only a single lesion. The CDC’s nonvariola orthopoxvirus polymerase chain reaction test (cleared by the US Food and Drug Administration [FDA]) can detect monkeypox and is the test currently being performed. With testing expanded to 5 commercial laboratories, access to testing has increased; however, results are still taking 2 to 3 days in many places. There are no data supporting the use of other sample types such as blood, saliva, or genital secretions for testing.

Treatment

For most patients, the management is symptomatic, including treatment of pain. Monkeypox is a member of the Orthopoxvirus genus in the family Poxviridae, another member of that genus is the variola virus, which causes smallpox. As a result, while there are no antivirals currently approved for monkeypox, tecovirimat, an antiviral drug approved for the treatment of smallpox based on animal data, has been made available to treat monkeypox via an expanded access Investigational New Drug (IND) protocol. Tecovirimat is available as an oral capsule and as an injectable for intravenous administration.

Treatment is currently recommended for people infected with monkeypox with severe disease or who are at high risk for severe disease (individuals who are immunocompromised, pregnant or lactating, or have atopic
dermatitis; children <8 years) and those with 1 or more complications. The CDC and FDA recently simplified the protocol by streamlining the postadministration monitoring and data requirements. In addition, several clinical trials (PALM-007, PLATINUM, WHO/ARNS, and ACTG5418) are underway or planned to provide necessary data on the safety and efficacy of tecovirimat for monkeypox. Optimal drug absorption of the oral formulation requires concurrent intake of a high-fat meal (ideally about 600 calories and 25 g of fat).

Vaccines
Currently, 2 vaccines can be used to prevent monkeypox: the Bavarian Nordic JYNNEOS vaccine, which is FDA approved for smallpox and monkeypox, and ACAM2000, approved only for smallpox but granted an expanded-access IND protocol allowing use against monkeypox. The JYNNEOS vaccine uses a live, attenuated vaccinia virus that is incapable of replicating, and it is administered as a 2-dose series. Peak antibody response occurs 2 weeks after receipt of the 2-dose JYNNEOS vaccine. The ACAM2000 vaccine uses a live vaccinia virus capable of replicating and is administered as a single dose but requires multiple skin punctures. Both vaccines are thought to be at least 85% effective at preventing monkeypox. The ACAM2000 vaccine has comparable immunogenicity to that of the Dryvax vaccine (the previously licensed smallpox vaccine) and, like Dryvax, it has been associated with an unexpectedly high rate of myocarditis and pericarditis. A helpful feature of both vaccines is that they can be administered as postexposure prophylaxis. When administered up to 4 days after exposure, vaccination can prevent disease onset altogether, but even receipt of vaccination up to 2 weeks following exposure can reduce symptom severity.

The Biden administration is working to increase availability of the JYNNEOS vaccine, but vaccine supply is still severely limited with around 1 million doses available in the US. In contrast, more than 100 million doses of ACAM2000 are available in the Strategic National Stockpile. Given the urgency of the situation, some have advocated for use of the ACAM2000 but the high risk of adverse events, risk if administered to people who are immunocompromised or with certain skin conditions like eczema, and operational issues (administration requires a bifurcated needle) make JYNNEOS a better choice. Given limited supplies, most health departments are currently only administering a single dose of JYNNEOS vaccine. On August 9, 2022, the FDA issued an Emergency Use Authorization (EUA) for the JYNNEOS vaccine to allow clinicians to use the vaccine by intradermal injection for individuals aged 18 years or older who are determined to be at high risk for monkeypox infection. This is expected to increase the total number of doses available for use by up to 5-fold. The lower dose is immunologically noninferior to the standard dose, but it is more reactogenic.

Preventing Spread of Infection
With appropriate use of personal protective equipment, the risk of transmission of monkeypox in the health care setting is low. Health care workers should wear a gown, gloves, eye protection, and a N95-approved particulate respirator equipped with N95 filters or higher. A patient with suspected or confirmed monkeypox infection should be masked immediately, have lesions covered with a gown or sheet, and be placed in isolation in a single-person room. A person with monkeypox infection should avoid close contact with others until the skin lesions are completely healed, which can take several weeks. It is unknown whether recovery from monkeypox protects against subsequent infection but given the limited supply of vaccine, individuals already infected should not be prioritized for vaccination.

Public Health Lessons
The current monkeypox outbreak illustrates why global health cannot be ignored. Despite monkeypox being endemic in Africa for decades, clinical trials on treatments and vaccines were not done. Now more than 3 months into the global monkeypox outbreak, there is much to learn. While test capacity has been increased, more is needed. Contact tracing is not happening, and data systems are not informing the response in rapid fashion. Many individuals at risk for monkeypox may not be engaged with the health care system, making diagnosis, containment, and prevention challenging. The demand for vaccines far exceeds availability. Although the supply of tecovirimat has increased, this drug must still be used under an IND protocol, which limits access. In addition, a decentralized and wholly underresourced public health infrastructure is even more strained as officials must now respond to both COVID-19 and monkeypox.

REFERENCES