A Large Proportion of Men with Monkeypox Are Living With HIV

People with well-controlled HIV do not appear to have more severe illness, but HIV-positive people might not respond as well to monkeypox vaccines.

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Around 40% of people with monkeypox are living with HIV, but the proportion can be substantially higher in some areas, according to recent reports on the ongoing global outbreak. The Centers for Disease Control and Prevention (CDC) and the British HIV Association (BHIVA) recently issued new guidance for the prevention and treatment of monkeypox in people with HIV.

The good news is that people with well-controlled HIV and a high CD4 count do not appear to have more severe monkeypox illness. But HIV-positive people, especially those with a lower CD4 count, may not respond as well to monkeypox vaccines, suggesting they should receive the most effective regimen available.

As of August 22, the CDC has identified 15,433 monkeypox cases in the United States. Worldwide, there are now nearly 43,000 cases, mostly outside of countries in Central and West Africa where the virus was reported before the current outbreak.

While anyone can get monkeypox through close physical contact, cases remain overwhelmingly concentrated among gay, bisexual and other men who have sex with men. A new report from the CDC shows that 99% of cases with available data have been among men, more than 90% of whom reported sex or close intimate contact with other men. The epidemiological picture is similar in other countries outside of Africa.

The proportion of people with monkeypox who are living with HIV is high and remarkably consistent in several large case series.

According to the World Health Organization, 41% of people with monkeypox whose status is known are HIV positive. The CDC report also shows that 41% of those with a known status in the U.S. have HIV. A recent analysis of more than 500 cases in multiple countries, published in The New England Journal of Medicine (NEJM), also put the proportion at 41%. A recent report in The Lancet, looking at nearly 200 cases in Barcelona and Madrid, found that 40% were HIV positive, and the European Centre for Disease Prevention and Control reports that 38% of people with monkeypox across Europe are living with HIV.

There is some regional variation, however. An analysis from the U.K. Health Security Agency (UKHSA) found that 26% of monkeypox cases in the United Kingdom with a known status are HIV positive.

Georgia, which was among the first U.S. states to report HIV status, found that 67% of people with monkeypox are living with HIV; 85% had viral suppression (less than 200 copies), and 92% had a CD4 count above 200. Like other southern states, Georgia has a high HIV rate, especially among African Americans. The state recently reported that 71% of people with monkeypox are Black, a group that is also heavily overrepresented among HIV cases, at 73%.

Among HIV-negative men with monkeypox, a majority were on pre-exposure prophylaxis (PrEP). In the NEJM case series, the proportion was 57%. The UKHSA analysis found that 79% of HIV-negative men with monkeypox had ever taken PrEP.

The proportion of HIV-positive people in these reports is substantially higher than the HIV rate among men who have sex with men overall, which is estimated to be around 15% in the United States. The reasons for the heavy overrepresentation of men living with HIV among monkeypox cases are not fully understood.

HIV-positive people are more likely to be engaged with health care, and the HIV and sexual health clinics where they receive care are clued in about monkeypox. This may also explain the high rate of viral suppression. It is not clear how many HIV-positive people who are not in care have monkeypox. Because people with an undetectable viral load don't transmit HIV, HIV-positive people—as well as HIV-negative people on PrEP—may be more likely to forgo using condoms, which may provide some protection against sexual transmission of monkeypox (though this, too, remains unclear).

Finally, while people with well-controlled HIV and a high CD4 count generally are not considered immunocompromised, they may have more subtle immune impairment or persistent inflammation that might increase their susceptibility to monkeypox.

The good news is that HIV-positive people in these case series did not have worse monkeypox outcomes. "Whilst people with HIV account for more than 40% of cases so far, it is reassuring that HIV status was not linked with monkeypox severity," says BHIVA chair Laura Waters, MD.

The NEJM report, by Chloe Orkin, MD, of Queen Mary University of London, and colleagues, gave more detail about people with HIV and monkeypox. Almost all (96%) were on antiretroviral treatment, with a majority taking integrase inhibitors. Most had well-controlled HIV; 95% had an undetectable viral load (less than 50 copies), and the median CD4 count was high, at 680.

"The clinical presentation was similar among persons with HIV infection and those without HIV infection," the study authors wrote. HIV-positive people were not more likely to be admitted to a hospital, however two of the more serious complications occurred in people living with HIV. One man with a CD4 count below 200 developed epiglottitis, or inflammation of the flap of tissue at the

back of the throat. There were two cases of myocarditis (heart muscle inflammation), one in an HIV-positive person with a high CD4 count and one in an HIV-negative person.

In the Spanish case series, by Oriol Mitjà, MD, of University Hospital Germans Trias i Pujol near Barcelona, and colleagues, 99% of HIV-positive people with monkeypox were on antiretroviral therapy, and 89% had a CD4 count of 500 or higher. “We did not notice any difference in clinical features, including the number of lesions or incubation period between patients who reported being HIV-positive and those who did not,” the researchers wrote.

However, this may not be the case for people with poorly controlled HIV. Prior reports from Nigeria, where fewer people are on optimal treatment, showed that people with HIV had more severe and prolonged illness and higher mortality. One recent report from the current outbreak describes a 40-year-old man in Germany with untreated HIV (CD4 count 127) and syphilis who developed severe monkeypox, including necrosis of the nose. He was treated with the antiviral medication TPOXX (tecovirimat) and is recovering.

Monkeypox among people with unsuppressed HIV and greater immune impairment is likely to become a growing concern as the outbreak increasingly moves into lower-income communities with more Black and Latino people, groups that have higher HIV rates but are less likely to be in care and on effective antiretroviral therapy.

HIV and Monkeypox Guidance

The CDC released its Interim Guidance for Prevention and Treatment of Monkeypox in Persons with HIV Infection, which includes information about vaccination and treatment, in the August 12 edition of Morbidity and Mortality Weekly Report.

“Persons with and without HIV infection should follow the same guidance to protect themselves from monkeypox,” the guidance states. Some people have been concurrently diagnosed with monkeypox, HIV and other sexually transmitted infections, “highlighting the importance of testing for these infections when monkeypox is suspected or diagnosed.”

The British HIV Association also recently issued rapid guidance on monkeypox. While HIV-positive people overall do not appear to be at greater risk for worse outcomes, the guidance advises specialist care for those with a CD4 count under 200, a persistent detectable viral load or recent HIV-related illnesses or other conditions or treatments that may cause immune suppression.

Monkeypox is related to smallpox, and smallpox vaccines can prevent monkeypox too.Because the monkeypox virus has a long incubation period, vaccines may be used either as post-exposure prophylaxis within four days after exposure (although it may reduce symptoms if taken within two weeks) or as pre-exposure prophylaxis for those at risk.

Jynneos, a new vaccine that uses a nonreplicating virus, is safe and well tolerated for people living with HIV. ACAM2000, an older live-virus vaccine, should not be used by people with a weakened immune system, including people with HIV.

The original Jynneos indication calls for two doses administered as subcutaneous injections four weeks apart. In an effort to stretch the limited vaccine supply, some jurisdictions have resorted to a one-dose strategy to give twice as many people partial protection as soon as possible, rather than holding second doses in reserve. In addition, the Food and Drug Administration this month issued an emergency use authorization that allows Jynneos to be administered by intradermal injection, splitting a single vial into five doses. Limited research shows that subcutaneous and intradermal administration lead to similar antibody responses, but the intradermal method requires training on how to administer the shot at an angle under the upper layer of skin.

Some experts caution that the one-dose strategy and intradermal administration may not be appropriate for people living with HIV, who may have weaker immune responses even if they're on effective antiretroviral treatment. Small studies indicate that Jynneos provides protection for HIV-positive people with an adequate CD4 count, but they may have lower antibody levels and may not respond as well after the first dose. Little is known about responses in people with a CD4 count under 100. This suggests that people with HIV—especially those with a lower CD4 count— should be prioritized to receive the optimal number of doses using the most effective administration method. Maximum protection occurs two weeks after the second dose.

Monica Gandhi, MD, MPH, medical director of the Ward 86 HIV clinic at Zuckerberg San Francisco General Hospital, says the intradermal injection technique should not be used for people with a low CD4 count, suggesting a cut-off of 350. The intradermal method also should not be used for people with keloids, an overgrowth of scar tissue that is more common among Black people.

TPOXX, which is FDA-approved for smallpox, is being used under an expanded access protocol to treat monkeypox. Data about its effectiveness comes from animal studies, though early reports from this outbreak suggest it may improve symptoms. Small studies in humans showed that TPOXX is safe and well tolerated with only minor side effects. Other treatments that can be considered for severe monkeypox cases include cidofovir, brincidofovir and vaccinia immune globulin, but again data are limited. According to the CDC, monkeypox treatment should be considered for HIV-positive people based on their disease severity and degree of immunosuppression.

People with HIV who contract monkeypox should continue their antiretroviral therapy. "Treatment interruption might lead to rebound HIV viremia that could complicate the management of monkeypox, including worsening illness severity," the guidance states. Those who are newly diagnosed with HIV and monkeypox at the same time should start antiretroviral treatment as soon as possible. People taking PrEP for HIV prevention should also continue.

The CDC guidance notes that no drug interactions have been identified that would preclude administration of TPOXX with antiretrovirals. Cidofovir, however, can cause kidney toxicity and should not be used with tenofovir disoproxil fumarate.

In summary, the guidance states, "Although data are limited for monkeypox in patients with HIV, prompt diagnosis, treatment and prevention might reduce the risk for adverse outcomes and limit

monkeypox spread.”

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