Most People With HIV Respond Well to COVID Vaccines

COVID-19 vaccines are highly effective, but people with a low CD4 count or detectable viral load are at risk for poor response.

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People living with HIV generally respond well to COVID-19 vaccines, according to recent studies. But some HIV-positive people may have weaker responses, including those who are not on antiretroviral treatment and those who have a detectable viral load or a low CD4 T-cell count. Experts stress that people with HIV should get vaccinated as soon as possible.

“Vaccines remain the most important intervention for preventing morbidity and mortality from COVID-19, including among people living with HIV,” Matthew Spinelli, MD, of the University of California at San Francisco, told POZ. “I would encourage people living with HIV to pursue vaccination and, if available, seek a booster.”

Studies of COVID-19 outcomes among people living with HIV have yielded conflicting results, but some show that HIV-positive people—many of whom are older and have other chronic health conditions—are at greater risk for severe illness and death. Immunocompromised people are at greater risk for COVID-19 complications, and they can have slower and weaker immune responses after infection or vaccination. Studies have shown, for example, that organ transplant recipients and cancer patients treated with immunosuppressive medications may not be fully protected.

Research has shown that a majority of people with HIV produce an adequate immune response against SARS-CoV-2, the coronavirus that causes COVID-19. In a small study presented at this summer’s International AIDS Society Conference on HIV Science, Juan Tiraboschi, PhD, of Bellvitge University Hospital in Spain, and colleagues assessed immune responses in 11 people on antiretroviral therapy who had recovered from COVID-19. Three months after SARS-CoV-2 infection, 73% had detectable antibodies, compared with 94% of HIV-negative people.

But antibody levels don’t tell the whole story. Antibody levels normally decline after infection or vaccination, but memory B cells are left behind to produce more antibodies if the virus is encountered again. T cells also play a role. In this study, all HIV-positive people had memory B cells, and both groups had similar levels of virus-fighting T cells.

On the other hand, there have been reports of people with advanced HIV who had prolonged

SARS-CoV-2 infection. In one case, a South African woman had persistent infection for more than six months and cleared the coronavirus only after she switched to more effective antiretroviral therapy.

Vaccine Response in People With HIV

The ability to mount a natural immune response against SARS-CoV-2 bodes well for a good vaccine response, and this is indeed what studies have generally shown.

Advocates fought to get people with HIV included in clinical trials of the vaccines, but the numbers were small and limited to those with good immune function. The pivotal trials of the Pfizer-BioNTech (BNT162b2, or Comirnaty) and Moderna (mRNA-1273, or Spikevax) vaccines included 196 and 179 HIV-positive people, respectively, among their tens of thousands of participants. No safety concerns were reported for people with HIV, but there were too few of them to draw conclusions about effectiveness.

More recent studies looking specifically at people living with HIV shed more light on vaccine safety and efficacy in this population.

First, as seen in the clinical trials, subsequent studies have shown that COVID-19 vaccines are safe for people with HIV. Side effects are similar to those of HIV-negative people, mostly temporary soreness at the injection site and mild to moderate symptoms, such as headache and fatigue.

The Pfizer-BioNTech, Moderna and Johnson & Johnson vaccines do not contain live virus—only genetic instructions for making the SARS-CoV-2 spike protein—so they do not pose a risk for immunocompromised people. These vaccines also do not use an adenovirus type 5 vector, which was linked to an increased likelihood of HIV acquisition in a trial of an HIV vaccine that used similar technology.

Turning to vaccine effectiveness, John Mellors, MD, of the University of Pittsburgh School of Medicine, and colleagues analyzed vaccine response in 107 healthy health care workers and 489 immunocompromised individuals, all fully vaccinated with one of the three authorized vaccines. While only 37% of organ transplant recipients and 55% of blood cancer patients produced antibodies against the coronavirus, 95% of people with well-controlled HIV did so—similar to the 98% response rate for healthy participants.

Two research groups at Johns Hopkins University School of Medicine looked at responses in HIV-positive and HIV-negative people who received the Pfizer-BioNTech or Moderna messenger RNA (mRNA) vaccines.

As described in the journal AIDS, William Werbel, MD, and colleagues evaluated immune response in 14 people with HIV. The median age was 62, all had been on antiretroviral therapy for at least six months, all but one had an undetectable viral load and all but two had a CD4 count above 200. After the second dose, all had high SARS-CoV-2 antibody levels, similar to those seen in HIV-negative people and much higher than those of severely immunocompromised people. The strength and breadth of T-cell responses were also similar.

In the second study, published in Clinical Infectious Diseases, Joel Blankson, MD, PhD, and colleagues looked at antibody and cellular responses in 12 HIV-positive and 17 HIV-negative people who received two doses of the Pfizer-BioNTech vaccine. All the people with HIV were taking antiretrovirals, had an undetectable or very low viral load and had a CD4 count above 600. People with and without HIV had similar binding and neutralizing antibody levels and comparable T-cell responses.

In an larger study, Galia Rahav, MD, of Sheba Medical Center in Tel Aviv, and colleagues compared vaccine response in 143 HIV-positive people on antiretroviral treatment and 400 HIV-negative health care staff. Most had an undetectable viral load, and the average CD4 count was around 700. Here, 98% of people with HIV (including the small number with a CD4 count below 350) produced antibodies after two doses of the Pfizer-BioNTech vaccine, and antibody levels were similar in HIV-positive and HIV-negative people. The four people with HIV who did not respond were older and had other underlying health conditions.

There has been less research on the Johnson & Johnson vaccine, which uses an adenovirus type 26 vector. The pivotal clinical trials in the United States, South Africa and Latin America included more than 1,200 people with HIV (2.8% of the study population). Among them, there were five cases of COVID-19 in the vaccine group and five in the placebo group, but these numbers were too small to draw conclusions about effectiveness.

Two studies evaluated the AstraZeneca-Oxford COVID-19 vaccine (not authorized in the United States), which uses a chimpanzee adenovirus vector, in people with HIV. The first study, which included 54 men in London who were on antiretroviral treatment with an undetectable viral load and a high CD4 count, showed that HIV-positive people had antibody and T-cell responses similar to those of HIV-negative people. The second study, which included 104 people with well-controlled HIV in South Africa, found that participants who previously had COVID-19 showed stronger antibody responses after the first vaccine dose than those without COVID-19 did after two doses. The researchers cautioned, however, that they could not assume responses would be equally good in people with a low CD4 count.

In contrast, a South African study of the Novavax vaccine (also not yet authorized in the United States) found that its effectiveness rose from 49% to 60% when the more than 200 participants with medically stable HIV (6% of the study population) were excluded from the analysis, suggesting that this group had a substantially lower response rate.

Risk Factors for Poor Response

Experience with vaccines for other diseases shows that some people with HIV, including older people and those with low CD4 counts, do not have as strong or as durable a response as HIV-negative people, and this is the case for COVID-19 vaccines as well.

Spinelli and colleagues analyzed stored samples from 100 HIV-positive adults at the Ward 86 HIV clinic at Zuckerberg San Francisco General Hospital and 100 HIV-negative patients receiving care

for other chronic conditions who received two doses of the Pfizer-BioNTech or Moderna vaccine. In the HIV-positive group, the median age was 59, the CD4 count was 511 and five people had a detectable viral load.

As reported at IDWeek 2021, people with HIV were more than twice as likely to have a poor vaccine response: 12% did not produce SARS-CoV-2 antibodies, compared with 5% of HIV-negative people. A SARS-CoV-2 neutralization test showed nonresponse rates of 24% versus 12%, respectively. What's more, antibody levels were 43% lower in the HIV-positive group.

Looking at factors associated with poor response, people with detectable HIV had an 86% lower antibody level, and each 100-cell increase in CD4 count was associated with a 28% rise in antibody levels. All seven people with a CD4 count below 200 were nonresponders. People who received the Moderna vaccine had stronger responses than those who got the Pfizer-BioNTech vaccine; in fact, no Moderna recipients were nonresponders.

This study did not measure T-cell responses and did not look at clinical outcomes, such as how many people developed symptomatic COVID-19 or required hospitalization. Patients at the HIV clinic are now receiving third doses, and Spinelli's team will evaluate responses after the additional shot.

Another study, presented at the 2021 European AIDS Conference, likewise showed that people with a low CD4 count were less likely to respond to the mRNA vaccines. Andrea Antinori, MD, of the National Institute for Infectious Diseases in Rome, and colleagues compared antibody and cellular immune responses in 32 HIV-positive people with severe immune deficiency (CD4 count below 200), 56 with moderate immune deficiency (CD4 count between 200 and 500) and 78 with a normal CD4 count (above 500). The median age was approximately 55. All were on antiretroviral therapy, but people with a low CD4 count were more likely to have a detectable viral load.

A month after the second vaccine dose, five people—four of whom had fewer than 250 CD4 cells—had no detectable SARS-CoV-2 antibodies. Antibody levels, neutralization responses and T-cell responses were substantially lower in people with a CD4 count below 200. Those in the middle range did not have significantly lower antibody responses than HIV-positive people with a normal CD4 count, but they did have weaker responses than HIV-negative health care workers.

Finally, Zabrina Brumme, PhD, of Simon Fraser University, and colleagues looked at vaccine response in 100 HIV-positive and 152 HIV-negative people in Vancouver. The HIV-positive participants were mostly white men without chronic health conditions; the median age was 54. All were on antiretroviral treatment with an undetectable viral load, the median current CD4 count was 710 and the median lowest-ever count was 280. Most received two Pfizer-BioNTech or Moderna shots, but some got the AstraZeneca-Oxford vaccine.

As reported in a preprint, people with HIV had somewhat lower antibody levels and neutralization responses than the HIV-negative group after the first dose, but they mostly caught up after the second shot. In fact, after controlling for other factors, HIV itself was not associated with weaker vaccine response, nor was current or lowest-ever CD4 count (though only two people had a

current count below 250). However, older people and those with more underlying chronic health conditions had less robust responses.

Vaccines and Boosters a High Priority

Experts now recommend that all adults and many children should be vaccinated against SARS-CoV-2, but this is even more important for people living with HIV. And it's essential to get both doses.

Studies showing poor vaccine response among people with a detectable viral load or a low CD4 count are a concern, given that around a third of people living with HIV in the United States are not in care, and about 40% have not achieved viral suppression.

For HIV-positive people who are not on treatment, starting antiretroviral therapy is a key step toward protection against COVID-19 and better overall health. Those who have a detectable viral load or a low CD4 count despite being on treatment should talk with their doctor about optimizing their regimen. For those who still don't have adequate CD4 recovery, COVID-19 pre-exposure prophylaxis using monoclonal antibodies—and potentially antiviral pills—could soon be an option.

"There are likely millions of immunocompromised people, including some with HIV, who cannot mount an immune response to the vaccines," Dorry Segev, MD, PhD, of Johns Hopkins University, told POZ. "Pre-exposure prophylaxis with monoclonal antibodies could be the miracle they have been waiting for."

COVID-19 vaccines are more effective at preventing severe illness and death than they are at preventing SARS-CoV-2 infection, and even people who respond well can still have breakthrough infections. While circulating antibodies respond to the virus immediately, these wane over time. B-cell and T-cell responses, which take days to kick in, may not prevent initial infection, but they can stop the virus from taking hold in the body. Nonetheless, some people with breakthrough infections develop serious illness or long COVID, though the risk is much lower compared with unvaccinated people.

Now that a majority of Americans have received their initial vaccines, attention has turned to boosters in an effort to reduce that risk even further as well as to curb transmission.

In August 2021, the Food and Drug Administration (FDA) authorized and the Centers for Disease Control and Prevention (CDC) recommended an additional Pfizer-BioNTech or Moderna vaccine dose for moderately to severely immunocompromised people, including those with advanced or untreated HIV. (For such individuals, the extra shot is considered part of the initial series needed to achieve full protection, not a booster.)

The FDA and CDC later went further, recommending boosters for all Pfizer-BioNTech and Moderna recipients six months after their last dose and for J&J recipients two months after their initial dose. Immunocompromised people who received an additional dose can also receive a booster six months later, for a total of four doses.

While this is good news for residents of the United States, people in many low- and middle-income countries still do not have access to first vaccines. For countries where vaccines are in short supply, medical experts and advocates urge that people living with HIV should be among those prioritized for vaccination.

“All of the authorized vaccines are safe and effective for people with HIV, and vaccination should be a very high priority,” Melanie Thompson, MD, of the AIDS Research Consortium of Atlanta, told POZ. “Advocates should be insisting on equitable and convenient access to vaccines for all HIV-positive people, and people with HIV should feel confident about rolling up their sleeves to get the jabs. We have two pandemics to fight now, but at least we have effective vaccines for one of them.”

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