New COVID vaccine recommendations for immunocompromised patients

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Featured topic and speakers

In today’s COVID-19 Update, a discussion with Sandra Fryhofer, MD, AMA’s liaison to Advisory Committee on Immunization Practices (ACIP) and a member of ACIP’s COVID-19 vaccine workgroup, discusses what physicians need to know about the recent FDA authorization for a third COVID-19 vaccine dose for immunocompromised patients.

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Speaker

- Sandra Fryhofer, MD, chair-elect, AMA Board of Trustees; AMA’s liaison to the Advisory Committee on Immunization Practices

Transcript

Unger: Hello, this is the American Medical Association’s COVID-19 Update. Today we’re discussing the latest news from ACIP, the Advisory Committee on Immunization Practices on vaccine boosters and who needs additional doses.

I'm joined today by Dr. Sandra Fryhofer, AMA's liaison to the ACIP and a member of ACIP’s COVID-19 vaccine workgroup. Dr. Fryhofer is also chair-elect of the AMA Board of Trustees. I'm Todd Unger, AMA's chief experience officer in Chicago.

Dr. Fryhofer, welcome back. The last time we talked, we spoke about boosters, so it was about the
end of July. What's happened since then?

**Dr. Fryhofer:** Well, on August 12 near the stroke of midnight, FDA made the announcement we've all been hoping for. FDA authorized an additional COVID vaccine dose for certain immunocompromised people. ACIP met the following day and also gave this extra dose a thumbs up. This extra dose gives these vaccinated but still vulnerable patients a greater chance of making enough antibodies to protect them from COVID.

But even with this third dose, protection's not guaranteed. Immunocompromised patients still need to follow prevention measures, wear a mask, practice social distancing and avoid crowds and poorly ventilated indoor spaces. Of course, all close contacts should be fully vaccinated.

**Unger:** That's an interesting point and not one that I'd read in the coverage of this, so very important addition. I'd like to know why the change? Are there different kinds of statistics and research that we're learning about and what kind of trends are we seeing?

**Dr. Fryhofer:** Well, new COVID cases and hospitalizations are on the rise. Since July, there's been a 700% increase in the seven-day average for COVID cases. We're also seeing more COVID related deaths. Delta continues to dominate and now makes up more than 90% of new COVID cases. Delta's a super spreader, it's super transmissible, it's super contagious. It's twice as contagious as previous variants, it's the most contagious variant we've seen yet. There's emerging evidence Delta causes more severe illness than previous strains.

The greatest risk of transmission is still among unvaccinated people but fully vaccinated people with Delta breakthrough infections can also spread virus to others. However, fully vaccinated people with Delta seem to be infectious for a shorter period of time than unvaccinated persons. Delta's also the reason masks are mostly back on for everyone. CDC says both unvaccinated and fully vaccinated people need to wear a mask in public indoor settings and areas of substantial or high transmission, which now is just about everywhere.

**Unger:** Well, on the topic of boosters, what age group does this apply to? Does the vaccine that someone initially received play a role in which booster they would get?

**Dr. Fryhofer:** Well, technically this is not a booster, it's an additional dose and the type of vaccine you initially received matters. For immunocompromised persons, ACIP recommends an additional dose of either Pfizer for those 12 and older or Moderna for those 18 and older following a primary mRNA vaccine series. Give the additional dose at least one month after the primary series and try to give the same type of additional dose as the original series if you can.

The recommendation only applies to those who got Pfizer or Moderna. It does not apply to those who received a single dose of Janssen's viral vector vaccine. There's not enough data there. An additional dose of Janssen’s viral vector vaccine is not one of the options. The effectiveness of two doses of
Janssen's vaccine is being studied, so more to come on that.

**Unger:** So, what do immunocompromised patients have to do to get the additional dose? Do they need to go to their doctor and get a note or some kind of documentation about their condition from a health care professional?

**Dr. Fryhofer:** It's the honor system, no prescriptions needed. A doctor's note is not required, patients just have to say that they're immunocompromised. CDC has posted detailed guidance on specifics of who qualifies as immunocompromised on the CDC website and at the ACIP meeting, the list of immunocompromised patients in this recommendation include active or recent treatment for solid tumor and hematologic malignancies, patients who've received organ or stem cell transplants, those with moderate to severe primary immunodeficiency or advanced or untreated HIV infection. Those with chronic medical conditions, such as asplenia and chronic renal disease were mentioned at the ACIP meeting but they're not on the CDC website. This omission may just be an oversight.

In addition, those on active treatment with high-dose corticosteroids, that means about 20 milligrams per day or higher, or other immunosuppressive treatments including alkylating agents, antimetabolites, tumor necrosis factor inhibitors and other biologic agents that are immunosuppressive should also receive an additional vaccine dose. Vaccine doses should be given at least two weeks prior to the initiation of immunosuppressive therapies.

Now, CDC does acknowledge that the patient's clinical team is best able to assess the degree of altered immunity and the optimal timing of vaccination for those on immunosuppressive therapies.

**Unger:** Should the physicians be checking antibody levels before vaccination in immunocompromised patients?

**Dr. Fryhofer:** That's a question I get asked all the time, CDC says no. I specifically asked CDC and FDA representatives about this again. Right now, there's no established correlator protection. FDA has not authorized any test for checking post vaccination response. So for immunocompromised patients, just get the additional mRNA vaccine dose, you don't need to check for antibodies. Antibody testing post vaccination is not recommended. None of the current FDA authorized serological tests are cleared for this purpose.

**Unger:** Well, earlier in the segment you talked about the difference between an additional dose and a booster. How are they different or are they the same in general?

**Dr. Fryhofer:** Well, they're sort of the same, but not really, and here's why. Immunocompromised patients can't build enough protective immunity with the routine primary series. Their initial immune response is insufficient. That's why immunocompromised patients need an additional dose to augment their primary vaccine series and increase their immune response.
On the other hand, the term “booster” infers the immune response to the primary vaccine series is sufficient. A booster is then given when protection begins to wane over time. The need for COVID vaccine boosters for everyone is still under study but no boosters quite yet. Right now we’re talking about additional doses for immunocompromised patients because they don’t respond sufficiently to a two-dose mRNA vaccine regimen. For immunocompromised patients, this is an additional vaccine dose, it’s not a booster.

**Unger:** So, will you just take us a little bit through the thought process of how ACIP came to this conclusion and the science behind it?

**Dr. Fryhofer:** Sure. Remember that immunocompromised persons were not included in the phase three trials, so these studies are happening in real time. We now know that COVID vaccines don’t work as well in immunocompromised patients. Vaccine effectiveness ranges from 59% to 71% in immunocompromised patients, as compared to 90% to 94% effectiveness in patients who are not immunocompromised.

Immunocompromised patients are more likely to have breakthrough infections. Studies show 40% to 44% of hospitalized breakthrough cases are immunocompromised people. They’re more likely to transmit COVID to people they live with, as well as other household contacts. Immunocompromised patients are also more susceptible to infection with COVID variants, they’re also more likely to stay sick with COVID longer. We know that prolonged infections gives the virus more time to evolve and mutate and transform into new variants.

There’s new observational data that additional COVID vaccine dose enhances antibody response in immunocompromised patients. It increases protection, it also seems to be well-tolerated. Those pesky side effects we expect after COVID vaccination, fatigue, muscle aches, fever, chills and a sore arm still apply. However, the reactogenic side effects of the additional dose are about the same as for prior doses. A number of other countries, France, United Kingdom, Israel and now Germany are either already giving additional doses to immunocompromised patients or plan to give them in the near future.

**Unger:** So supply was a huge issue, obviously for a good period of time. A question in the minds, I think, of people would be is there enough vaccine to do this or will our supply hold up?

**Dr. Fryhofer:** Fortunately, we have enough vaccine. At least 2.7% of all U.S. adults are immunocompromised and that’s about seven million people. The U.S. government has purchased 600 million mRNA vaccine doses. Vaccine’s available at no cost to us and it’s already been paid for with our U.S. tax dollars. And so far as of August 10, 2021, we’ve already administered more than 350 million vaccine doses.

Pfizer and Moderna were authorized in mid-December. About 90 million people have received two
Pfizer mRNA doses. About 64 million people have received two Moderna mRNA doses. Janssen single dose vaccine was authorized at the end of February. Janssen's also run into some production issue problems, so not as many doses have been available as initially expected and only about 14 million people have received it so far.

We are so fortunate here in the U.S. to even be discussing additional doses. So many people around the world have not received even a first COVID vaccine dose and what happens in the rest of the world does affect us. The next variant is only a plane ride away. We need to get everyone in the world vaccinated. An additional vaccine dose for immunocompromised patients is not a booster, it's part of an augmented primary series because the regular primary series was not protected for these patients.

Unger: I think that's a really important way of talking about it and it makes it very, very simple to understand in that context of that question. Do you find … is there kind of a general sense among immunocompromised patients that this is a very, very positive element and that they're in favor of it?

Dr. Fryhofer: Well, overall the initial intent to vaccinate is high among immunocompromised populations, they seem very supportive of getting an additional vaccine dose. As of August 8, Black adults had the largest difference in the percentage of fully vaccinated persons compared with the percentage in the overall U.S. population.

Concerns about safety and possible side effects are the most commonly stated reasons for vaccine hesitancy in this subpopulation. Vaccine hesitancy in immunocompromised populations is associated with younger age, female gender within racial and ethnic minorities and among those with less formal education.

Unger: Looking at the Federation House of Medicine, is there a broad scale viewpoint that people are supportive of augmenting this primary vaccine series?

Dr. Fryhofer: Yes, the Infectious Disease Society of America, the American Society of Transplantation, the American Society of Transplant Surgeons, the International Society for Heart and Lung Transplantation and the American College of Rheumatology all strongly support giving this additional dose. For kids, the Pediatric Infectious Disease Society and the Children's Oncology Group are also on board.

Unger: So, we talked about earlier about the rest of us. Do you expect boosters for the rest of us at some point in the future?

Dr. Fryhofer: Many kinds of booster studies are underway and we should expect to see some results any day now, certainly in the next month or so, so stay tuned. Decision points affecting when to boost were discussed at our August 13 ACIP meeting. They include risk of waning immunity, risk of COVID exposure, risk of COVID variant and risk of COVID complications. We also have to make sure booster doses are safe and immunogenic. Sometimes additional boosters can actually blunt immune
response but we have not seen evidence of that so far with mRNA vaccines, but this has been seen with other vaccines.

As for waning immunity with time, how does this vary by disease severity? We have the Delta variant today but what variant is on the menu for tomorrow? We also need to look at data on specific subpopulations, particularly health care personnel. Health care personnel were vaccinated in early stages of vaccine rollout and we continue to be exposed to COVID. We don't want to be passing COVID to our patients, so we may need earlier boosters to keep our patients safe. We don't want to be transferring COVID to vulnerable patients, so there are lots of questions and CDC is studying all of this in real time.

Unger: Well, speaking of unvaccinated populations, one of the big obstacles to that was the full FDA approval of the Pfizer and Moderna vaccines. We know a lot of organizations are kind of waiting on this approval to implement vaccine mandates. Do you have any news on when we can expect full approval?

Dr. Fryhofer: Well, news reports say FDA may release its decision on full licensing for Pfizer’s vaccine before Labor Day and FDA approval for Moderna vaccine should soon follow. News reports also say Pfizer plans to submit EUA for 5- to 11-year-olds by the end of September and for children under five, shortly thereafter.

There are also more vaccines in the pipeline. For example, Novavax is using recombinant nanoparticle vaccine technology, along with the proprietary adjuvant Matrix-M to boost immune response. Novavax will likely apply for FDA authorization at the end of the year.

Delta has really fed the pandemic fire. Momentum for vaccine mandates has been building and many companies and federal agencies are now requiring COVID vaccination. AMA joined forces with more than 50 other major medical organizations, including the American College of Physicians, the American Academy of Pediatrics, the American Academy of Family Physicians, the American Public Health Association and many sub-specialty societies calling for mandatory COVID vaccination for all health care workers. More and more companies may make vaccination mandatory once the vaccines are fully licensed by FDA. That could happen any day now. The sooner, the better.

Unger: Dr. Fryhofer, thank you so much for this incredible update. Do you have any final thoughts before we close?

Dr. Fryhofer: Well, I am relieved our immunocompromised patients can now be offered an additional COVID vaccine dose. The need for a booster for everyone is still under study. We may all need a booster eventually, but one thing is for sure, we all need to be fully vaccinated now.

As of August 11, only 58.9% of those 12 and older have been vaccinated. Those of us who can, need to be vaccinated to protect the young for whom vaccine is not yet available and to protect the
vaccinated but still vulnerable. So, please get vaccinated. Encourage your family, your patients, your friends to get fully vaccinated. That's the only way we can end this pandemic and get life back to normal.

**Unger:** Absolutely. Dr. Fryhofer, thanks again for being here and providing us with all of this, the update and the data. That wraps up our COVID-19 Update for today, we'll be back with another segment soon. In the meantime, for resources on COVID-19, visit ama-assn.org/COVID-19. Thanks for joining us and please take care.

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