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When the COVID-19 Delta variant became the dominant strain of SARS-CoV-2 in the United States, it was found that people's immunity against infection started to wane months after they finished the two-dose series of the Pfizer-BioNTech COVID-19 vaccine.

This led to the emergency use authorization (EUA) of Pfizer COVID-19 vaccine booster shots from the Food and Drug Administration (FDA) and recommendation from the Centers for Disease Control and Prevention (CDC). Now, with all three COVID-19 vaccines—Pfizer, Moderna and Johnson & Johnson—having received EUA for booster shots and the Omicron variant taking Delta’s spot as the dominant strain of SARS-CoV-2 in the country, many are left with more questions than answers. One physician expert aims to clear the air about COVID-19 vaccine boosters.

The AMA’s What Doctors Wish Patients Knew™ series provides physicians with a platform to share what they want patients to understand about today’s health care headlines, especially throughout the COVID-19 pandemic.

For this installment, AMA member Rambod A. Rouhbakhsh, MD, took time to discuss what patients need to know about COVID-19 vaccine boosters. Dr. Rouhbakhsh is a faculty physician and program director at the Forrest General Hospital Family Medicine Residency Program and the principal investigator for Hattiesburg Clinic MediSync Clinical Research. He is also one of the leading physicians over the Moderna COVID-19 vaccine trial at Hattiesburg Clinic—a member of the AMA Health System Program.

All adults should get a booster

“Originally, the CDC said all people should get a booster if they are 50 and older,” Dr. Rouhbakhsh explained. “Additionally, the CDC said people 18 and older should get a booster if they have specific risk factors like a high-risk living environment or workplace.
“Otherwise, it advised that anyone 18 and older ‘may’ get a booster,” he added, noting that “now the word ‘should’ applies to everyone 12 and older” who is at least five months past their second shot of an mRNA vaccine.

For adults who got the Johnson & Johnson vaccine at least two months ago, they too should get a booster dose. The CDC, though, recommends individuals get an mRNA COVID-19 vaccine over Johnson & Johnson’s COVID-19 vaccine. This came after the FDA revised the fact sheets for J&J COVID-19 vaccine providers and recipients, which now include a contraindication for people with a history of thrombosis with thrombocytopenia (TTS) following the J&J vaccine. Women 30–49 years old are at highest risk, with one in 100,000 developing TTS after J&J vaccination.

“The FDA determined the benefits of the booster—especially as more infectious variants arise—outweigh any potential risks like myocarditis, in this age group,” Dr. Rouhbakhsh explained.

**Older adults may get a second booster**

As the highly transmissible SARS-CoV-2 BA.2 Omicron subvariant now accounts for more than half of COVID-19 cases in the United States, the FDA has authorized a second booster dose of either the Pfizer-BioNTech or Moderna COVID-19 mRNA vaccines for people over 50 and for certain people with compromised immune systems, which may be administered four months after receiving an initial booster dose. The CDC followed suit with a recommendation that these people may receive a second booster dose.

Additionally, the CDC is recommending that adults who got the J&J vaccine for their primary series and booster dose at least four months ago may now receive a second booster dose of an mRNA COVID-19 vaccine.

**Booster offers added protection**

“What we have seen is that the efficacy of the vaccine diminishes over time, which is to be expected—all vaccines do to some degree,” said Dr. Rouhbakhsh, noting “it takes some time for us to figure out how many doses and at what intervals we need.
“Think about childhood vaccines. We’re supposed to get five TdaP—tetanus, diphtheria and acellular pertussis—and those have differing intervals,” he added. “It takes time to establish an optimal interval.”

For COVID-19 vaccines, “we’re figuring this out as we go along. Fortunately, we have ongoing clinical trials,” said Dr. Rouhbakhsh. “I’m a part of the Moderna clinical trial, where the participants in our trial are actively re-evaluated to assess their [antibody] titers post-vaccination. Then we follow them to see how many wind up getting sick to determine if there is a correlation between antibody levels and likelihood for illness.”

“As we noticed—especially with the Delta variant—the infection numbers going up, we’re starting to speculate that maybe it's time for a booster,” he explained. “A small group of people in the Pfizer, Moderna and Johnson & Johnson trials have started getting boosters and we’re seeing how well it works out for them.”

In the face of the Omicron variant, the CDC found that, compared with people who are fully vaccinated with booster doses, unvaccinated adults 50–64 years old were 45 times more likely to be hospitalized from COVID-19. Unvaccinated seniors were 51 times likelier to land in the hospital.

Research published in *Morbidity and Mortality Weekly Report* also shows that during both Delta- and Omicron-predominant periods, receipt of a third vaccine dose was highly effective at preventing COVID-19-associated emergency department and urgent care encounters as well as preventing hospitalization.

Meanwhile, a *JAMA* study shows that receipt of three doses of a mRNA COVID-19 vaccine—compared with being unvaccinated or having received two doses—was associated with protection against both the Omicron and Delta variants.

### Expect the same side effects

For those who are eligible for a COVID-19 vaccine booster, the side effects will be similar to their initial full series.

Some of those side effects include “injection-site pain and swelling, fatigue, headache, possibly some muscle aches, or what we’d call myalgias or joint aches, and arthralgias,” said Dr. Rouhbakhsh. “The myocarditis cases have been very rare, mostly seen in young males.”

With myocarditis, it “would be more shortness of breath-type symptoms and sometimes chest pain,” he said. “Fortunately, the cases of myocarditis have been mild, and people have gotten better on their own.”
Adolescents are now eligible

While it may seem like teenagers and younger children are being left out, they are not. That’s because “those trials started after the adult trials, so they’re going to lag behind in terms of the data acquired,” Dr. Rouhbakhsh explained. “What you’re likely going to see is the same kind of pattern as the initial EUA of the COVID-19 vaccines.”

That means “Pfizer adults, then Moderna adults, then Johnson & Johnson adults, and then subsequent to that will be Pfizer 12–16 year-olds and so forth,” he said. “So that’s likely the pattern in which it’s going to go, because they likely have continued on that same pace and are in that order in terms of starting and finishing their trials.”

With that, children 12–17 years old who completed the primary series of the Pfizer mRNA COVID-19 vaccine are now eligible for a booster dose five months after their second shot. Data examined by the FDA and CDC found no new safety concerns following a Pfizer mRNA vaccine booster in this group. There were also no new cases of myocarditis or pericarditis in these individuals.

Mixing and matching is OK for boosters

Through the FDA’s authorization and the CDC’s recommendation, heterologous boosting—aka “mixing and matching”—is allowed with a single dose of any of the authorized COVID-19 vaccine boosters. For example, those who got Johnson & Johnson’s one-dose series can receive a booster shot from Moderna or Pfizer.

Physicians will look at the clinical considerations, including rare adverse events, and perform an individual benefit-risk assessment to inform patients about which booster vaccine to use. Mixing and matching may only be considered for the booster dose.

Third doses are for immunocompromised

For patients with compromised immune systems, rather than a booster, they are receiving a third dose of a COVID-19 vaccine. This can be either Pfizer or Moderna mRNA COVID-19 vaccines.

“A third dose is not the same as a booster dose,” explained Dr. Rouhbakhsh. “There had been a group of individuals who had already been recommended to get a third dose. And it’s those people with immunocompromised states or those less likely to mount an adequate immune response.”
“We know the older you are, the less robust your immune response is, and you have to have more of the vaccine,” he said. “This is what we do with the flu shot, where people above the age of 65 get four times the potency that people under the age of 65 get.”

“A third dose is recommended four weeks after your last dose,” said Dr. Rouhbakhsh.

Additionally, the CDC recommends that children 5–11 years old with moderately or severely compromised immune systems get an additional primary dose of vaccine 28 days after their second shot. The Pfizer-BioNTech COVID-19 vaccine is the only one authorized and recommended for 5–11-year-olds. This is consistent with the CDC’s previous recommendation for adults who have compromised immune systems.

**Bring your vaccine card**

There are extra spaces on the COVID-19 vaccine cards for a reason. Those who are eligible for a COVID-19 vaccine booster are being “asked to bring their cards and provide the reasons why they need a COVID-19 vaccine booster,” said Dr. Rouhbakhsh.

“It’s pretty much going on an attestation. In other words, an honor system—you must attest that you need the booster dose,” he added. That means “you’re one of the people who fits these categories and you’ve had the second dose six months prior” for Moderna and Pfizer. For Johnson & Johnson, it is two months after their initial shot in the one-dose series.

**More people must get their first shots**

Part of the reason why we're talking about boosters right now is because of the rise of the Delta and Omicron variants, Dr. Rouhbakhsh said, noting that it increased the frequency of breakthrough COVID-19 infections.

It’s imperative that as many people get vaccinated as possible to avoid a SARS-CoV-2 variant “that could outwit our vaccines,” he said.

The next variant could be “even more deadly than what we've seen,” said Dr. Rouhbakhsh. “So, if you are eligible or you are a high-risk person, you should consider yourself lucky to be in a place that has rapid access to vaccines—whether it’s at your doctor’s office or your local pharmacy. Unfortunately, that's not the case in other areas of the world.”


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“Sometimes, we don't value that which comes easily. And the fact that we have this brand-new technology that was rapidly acquired and available virtually on every corner pharmacy in the entire country is a remarkable feat that we may be taking for granted,” he added. “Please don't. It is a luxury that we have as Americans, and I would recommend everyone take advantage of it if they can.”

Visit the AMA COVID-19 resource center for clinical information, guides and resources, and updates on advocacy and medical ethics.