Sandra Fryhofer, MD, discusses new J&J vaccine recommendations

Watch the AMA’s daily COVID-19 update, with insights from AMA leaders and experts about the pandemic.

Featured topic and speakers

In today’s COVID-19 Update, Sandra Fryhofer, MD, AMA’s liaison to the Advisory Committee on Immunization Practices (ACIP) and chair-elect of the AMA Board of Trustees, provides updates about vaccine recommendations based on an increased, but still rare, risk of thrombosis with thrombocytopenia with the Johnson & Johnson vaccine. Also, covering the latest on Omicron and vaccine effectiveness, a vaccine safety update for children aged 5-11 and the status of a COVID vaccine for toddlers.

Learn more at the AMA COVID-19 resource center.

Speakers

- Sandra Fryhofer, MD, physician, AMA trustee and AMA liaison to CDC’s Advisory Committee on Immunization Practices

Transcript

Unger: Hello, this is the American Medical Association’s COVID-19 update video and podcast. Today, we have a special update coming out of the recent ACIP meeting, that’s CDC’s advisory committee on immunization practices, including updated COVID vaccine recommendations, a vaccine safety update for kids five to 11, and what we know about Omicron. I’m joined today by Dr. Sandra Fryhofer, AMA’s liaison to ACIP, and a member of the ACIP’s COVID-19 vaccine work group. 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, ACIP had an emergency meeting on December 16. Can you tell us what was decided and why the hurry?

**Dr. Fryhofer:** Well, new data raises more safety concerns for Janssen’s viral vector vaccine and risk of TTS, thrombosis with thrombocytopenia syndrome, a rare but deadly condition. The bottom line, mRNA COVID vaccines, the ones by Pfizer and Moderna, are now preferred over Janssen's viral vector vaccine.

ACIP reviewed new safety data and made this preferential recommendation. It was endorsed by the CDC director just hours later and is now official CDC policy. A similar preference for mRNA vaccines is already in place in Canada. CDC’s preference for mRNA vaccines applies to all authorized age groups, and for both females and for males. FDA also expanded its TTS warning language to include both males and females across a wider age range. The highest reporting rate is for females age 30 to 49, about one case per 100,000 doses administered. The warning also points out that 15% of TTS cases have been fatal.

**Unger:** Well, let’s dig into that just a little bit. How was the TTS warning identified and when was it first recognized?

**Dr. Fryhofer:** Well, the first warning was back in April 2021. A safety signal from VAERS, which is CDC’s vaccine adverse event reporting system, revealed a curious and concerning combination. Six females, age 18 to 48, with a rare type of blood clot, cerebral venous sinus thrombocytosis, aka CVST. In combination with thrombocytopenia, really low platelet counts. One of these patients had died. All six patients had received Janssen's single dose viral vector COVID vaccine within the previous two weeks.

Back then, the supply of mRNA vaccine was limited. ACIP continue to recommend Janssen vaccine for those 18 and older, under an amended FDA EUA, emergency use authorization, with a warning about TTS. Women under 50 needed to be made aware of this risk and know that TTS had not been seen with any mRNA vaccines.

Also, in July 2021, another concern about Janssen, a safety signal for GBS, Guillain-Barré syndrome, was linked to Janssen vaccine, the risk being highest for males aged 50 to 64 within 42 days after Janssen vaccination.

**Unger:** So there was, then, updated evidence that was reviewed. What did it show about TTS risk with a Janssen vaccine?

**Dr. Fryhofer:** The December 2021 update amplifies Janssen's TTS risk. The case reporting rate is higher than previously presented. Initially the concern was mainly for young women, those under 50. We now know case reporting rates for men 40 to 49 and women 50 to 64, are similar to the risk for
women aged 18 to 29, about four to five TTS cases per million Janssen doses administered. So there’ve been more TTS cases.

The increased risk also applies to males, and the risk also applies to a wider age range. This reveal demonstrates honesty and transparency in vaccine safety surveillance, and should inspire and instill more confidence in the vaccine surveillance process.

**Unger:** When we think back to a year ago or so, vaccine supply played a big role in decisions. How did it apply then, versus where we are right now?

**Dr. Fryhofer:** When the first alert occurred, vaccine supply was limited. Also, Janssen single shot dosing was an attractive option for people who might have trouble getting a second vaccine dose. Now, a second dose of any COVID vaccine is recommended two months later for everyone who received a Janssen single dose. So the one dose convenience no longer applies.

Vaccine supply is no longer an issue. There's plenty of mRNA COVID vaccine that does not pose this risk, and which also has greater vaccine efficacy. ACIP looked at the risk-benefit balance and voted to preferentially recommend mRNA vaccines over Janssen's viral vector vaccine, for both their primary series and for boosters.

**Unger:** In terms of that comparison, how does Janssen’s TTS risk compare to the risk of myocarditis after mRNA vaccines?

**Dr. Fryhofer:** Well, there is a risk of myocarditis after mRNA COVID vaccines but by three months, 90% of patients are fully recovered and there have been no confirmed deaths. Risk for Janssen vaccine are much more serious. TTS after Janssen vaccine has a 15% mortality rate. Of those who lived, 17% require discharge to a post-acute care facility or a rehab facility.

The Janssen vaccine has also been linked to GBS, which has a 1% mortality, 10% of those patients require mechanical ventilation. So if you look at and compare the severity of vaccine-associated events, there are more severe health impacts from TTS and GPS after Janssen vaccine, as compared to the impact of myocarditis after mRNA vaccine.

Also, compared to mRNA vaccines, Janssen vaccine prevents fewer COVID hospitalizations, ICU admissions and deaths. The benefit-risk balance for mRNA vaccines is more favorable across all age and sex groups.

**Unger:** Based on that data, I'm curious about the breakdown of the ACIP committee votes. Did some members no longer want to recommend the Janssen vaccine at all after reviewing this data?
Dr. Fryhofer: Well, the ACIP vote count was unanimous in favor of a preferential recommendation for mRNA vaccines over Janssen’s viral vector vaccine. In the discussion, at least one committee member did say that they tell their patients not to get the Janssen vaccine.

But Todd, we’re in a pandemic. People are dying from COVID. We want everyone to get vaccinated. Some people may have an allergic reaction or an allergy or a contraindication to mRNA vaccines. Janssen’s viral vector vaccine may provide a way to get those patients protected.

ACIP was clear, mRNA vaccines are preferred, but Janssen vaccine still needs to be available. In some cases, Janssen COVID vaccine is the only vaccine available for some harder to reach populations. This however could result in an equitable distribution of the risk for TTS and GBS.

I have to say, I agree with the ACIP vote. I do think this vaccine needs to be available for ease of storage and transportation. We also need to have a variety of vaccine platforms. We don't know what variant is next, or what twist and turns the COVID pandemic will take. At the same time, we need to make sure that patients are aware of this rare but deadly risk, and that the risk is not just limited to young women.

Also, Janssen is not just a one dose and you’re done vaccine. If you get one dose, you still need another. The need for a second vaccine dose was emphasized by several ACIP members.

Unger: Well, speaking of variants, we've got a new layer of pandemic with Omicron, in terms of that variant. Do you have any updates coming out of the ACIP meeting regarding Omicron?

Dr. Fryhofer: Well, that was on our agenda. Omicron is here and the case count is growing but, for now, Delta is still dominant in the United States, but that could change. Omicron seems to be spreading like wildfire. Omicron is the B.1.1.529 variant. It was first detected in Botswana in South Africa in mid-November, and is now a variant of concern. The first U.S. case was identified on December 1. As of December 8, 22 states had identified at least one Omicron case. As of December 18, a CDC graphic shows detection in at least 45 states.

There's a lot we don't know about Omicron, but here's what we do know. Omicron has 30 mutations in the spike protein. And this is where many of our vaccines, our antibodies, and many treatments are directed. It also has 15 mutations in the receptor binding domain, which could trigger increased transmissibility. And it does seem more transmissible than the original strain for sure.

We know Delta is a super spreader. There’s concern that transmission from Omicron could be turbocharged. We still need more data on its clinical severity and how severity is affected by preexisting immunity by vaccination and by previous infection. We also need more data about how well monoclonal antibody treatments work against Omicron.
There's a suggestion from data in South Africa that Omicron leads to milder infections, but even if cases are milder, the sheer numbers of cases could potentially overwhelm health care systems. Now, this is all coming around the holidays when health care personnel really need a little time off to be with their families.

**Unger:** Absolutely. You can't help but read every day a question about whether Omicron is affected by the vaccine. Is there any additional news about vaccine effectiveness and the Omicron variant?

**Dr. Fryhofer:** At the ACIP meeting, there was a discussion about Pfizer vaccine effectiveness. At about six months post-vaccination, VE, which is vaccine effectiveness, is about 35% for Omicron as compared to 64% for Delta. VE two weeks after a third dose Pfizer booster is 93% against Delta but only 76% against Omicron.

Preliminary data from South Africa for Pfizer vaccine during the Omicron wave show 70% protection against hospitalization, but only 33% protection against infection. Vaccine manufacturers are looking at boosters, Moderna's testing a higher booster dose of 100 micrograms of its existing vaccine against Omicron. Both Pfizer and Moderna are working on Omicron specific vaccines. And just this morning, there was some breaking news about Moderna.

The company reports Moderna boosters significantly increased antibodies that could help fight Omicron. A 50 microgram dose boosted antibodies roughly 37 fold. A 100 microgram booster dose increased antibodies levels 83 fold but had more side effects. Again, this is just from press releases. Moderna does say it's in the process of putting a manuscript together to post online. So stay tuned, and I look forward to reading that manuscript.

**Unger:** Anything else on the horizon in terms of new treatments, new vaccines?

**Dr. Fryhofer:** Well, two new oral medications are being reviewed by FDA. Merck's Molnupiravir, four pills twice a day for five days started within five days after first symptoms, decreased the risk of hospitalization from COVID by 30%. A press release about Pfizer's Paxlovid claims an 89% reduction in hospitalization and death if started within three days of symptoms.

Now, both of these medications are under reviewed by FDA. There's some new vaccines in the pipeline. Sanofi, GSK's recombinant COVID vaccine, which is a new vaccine platform, reports positive preliminary results as a COVID vaccine booster. A 9 to 43 fold increase in antibody titers was seen, no matter which primary vaccine was received, so more to come about that.

And finally, there's disappointing news about Pfizer's COVID vaccine for toddlers. A three microgram two dose series didn't work. They're now testing the addition of a third dose booster in the two- to four-year-old trial and the trial for those six months to two years old. This delay means we won't have a vaccine for these little ones as soon as we had hoped.
Now remember that children age five to 11 are given a lower kiddie dose version of 10 micrograms, which is one third of the dose given to adults. The 10 microgram kiddie dose series works well in 5- to 11-year-olds.

**Unger:** Has there been any safety update regarding kids in that 5- to 11-year-old group?

**Dr. Fryhofer:** We did hear a safety updated at the ACIP meeting, and fortunately, there were no surprises. The most common adverse effects were the kinds of symptoms and the kinds of side effects that had been observed in the preauthorization clinical trials. In VAERS, there were only 14 reports of myocarditis in more than 7 million doses administered. In VSD, which is CDC’s vaccine safety data link, there were no reports of myocarditis. So, very reassuring data.

**Unger:** Any final thoughts as we head into the holidays this week?

**Dr. Fryhofer:** The COVID pandemic could get worse, and it could become a twindemic of Delta variant and the flu. The emergence of Omicron poses a triple threat.

Symptoms of COVID and flu are similar. Masking, vaccination and testing are so important. Once you've had a primary COVID vaccine series, please get boosted. Get your flu vaccination. You can get both COVID and flu shots at the same time if you need to.

So far, COVID vaccines are remarkably effective against severe disease, hospitalization and death. But understand, you can still get COVID even if you've been fully vaccinated and even if you've been previously infected, so that’s why wearing mask is important for prevention, especially with the Omicron variant on the rise.

If you have symptoms, get tested. PCR is the gold standard, but especially over the holidays, try to have some of those home tests available. Happy holidays, stay safe, get vaccinated and get boosted.

**Unger:** Dr. Fryhofer, thank you so much for the special update coming out of ACIP's meeting. On behalf of everyone here at the AMA, we'd like to wish you safe and healthy holiday. Please take care, please get boosted and see your doctor if anything happens. Thanks so much for watching. For resources on COVID-19, you can always go to ama-asn.org/COVID-19. Take care.

**Disclaimer:** The viewpoints expressed in this video are those of the participants and/or do not necessarily reflect the views and policies of the AMA.