Sandra Fryhofer, MD, on the J&J Janssen COVID-19 vaccine pause

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In today’s COVID-19 Update, Sandra Fryhofer, MD—the AMA liaison to the CDC’s Advisory Committee on Immunization Practices (ACIP) and the AMA’s representative on the COVID-19 vaccine work group—provides a quick and comprehensive look at the emerging details regarding the Johnson & Johnson/Janssen COVID-19 vaccine, and what physicians need to know about the vaccine pause.

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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. Today, we're discussing the decision to pause distribution of the Johnson & Johnson COVID-19 vaccine. I'm joined today by Dr. Sandra Fryhofer, an internal medicine physician, adjunct associate professor of medicine at Emory University School of Medicine and an AMA trustee from Atlanta.
Dr. Fryhofer is the AMA liaison to the CDC's Advisory Committee on Immunization Practices, or ACIP, and serves as the AMA's representative on the COVID-19 Vaccine Work Group. I'm Todd Unger, AMA's chief experience officer in Chicago. Dr. Fryhofer, when we last spoke about the J&J singledose vaccine, it was good news, but just two days ago, we learned that distribution has been paused. Can you start by explaining specifically what prompted that decision?

Dr. Fryhofer: Well, a lot has happened since we last talked. On February 27, 2021, FDA authorized an emergency use of Janssen's viral vector COVID vaccine for those age 18 and older. Now Janssen is the pharmaceutical arm of Johnson & Johnson. This "one dose and you're done" option has been very popular. More than 6.8 million doses of the Janssen vaccine have already been administered in the U.S. But now, just six and a half weeks after its authorization, FDA and CDC called for a pause in Janssen vaccine administration. A safety cynical signal in VAERS, which is CDC's Vaccine Adverse Event Reporting System, revealed a cluster of six patients with a rare type of blood clot, cerebral venous sinus thrombosis, aka CVST, in combination with thrombocytopenia, really low platelet counts.

Unger: So let's talk about the facts around the individuals who have had these adverse reactions.

Dr. Fryhofer: Well, all six cases were women age 18 to 48. One of them died. All six patients had received Janssen's COVID vaccine within the previous two weeks. Now, these findings are very similar to recent European reports of unexpected blood clots in patients within weeks of receiving AstraZeneca's viral vector vaccine. AstraZeneca's vaccine has not yet been authorized for use in the United States. CDC and FDA acted quickly and issued a joint statement recommending the pause. CDC released additional information through HAN, it's Health Alert Network. Now, these actions will likely lead to more cases being reported as a result of increased awareness.

Unger: So you talk about the term pause, how long should we expect to wait for more information? Can you give us some flavor of what pause means in this case?

Dr. Fryhofer: Well, the pause means, hold off on administering this vaccine for now. It's a recommendation. It's not a mandate, but it's being made out of an abundance of caution. ACIP, the Advisory Committee on Immunization Practices convened an emergency meeting on April 14 to review these safety concerns. And after presentations from Janssen Pharmaceuticals and the CDC, many ACIP committee members said they were not yet ready to vote on next steps. They needed more information in order to make an evidence-based decision. So no action vote was taken.
This means the status quo, the pause, is still on for now. But this will give CDC more time for risk refinement, to identify specific risk factors like age, gender, as well as the effect of other factors, including use of estrogen-containing products like birth control pills and hormone replacement therapy. The pause is not indefinite. The plan is for ACIP to reconvene after additional risk refinement is completed, hopefully in about 7 to 10 days.

**Unger:** Okay. So, according to the announcement by the CDC and the FDA, the adverse effects that you've talked about are extremely rare. Can you give some more background on that?

**Dr. Fryhofer:** Well, some might say this pause is an overreaction. Six people afflicted out of more than 6.8 million doses administered. So about one in a million. However, cerebral venous sinus thrombosis is a very rare, but very serious clotting disorder. CDC says the background rate of CVST is somewhere between two and 15 per million, but that includes all CVST cases. CVST is not usually associated with low platelet counts. So the combination of the two conditions, both blood clots and low platelets is the red flag. And as FDA's Dr. Peter Marks explained, it's not just the cerebral venous sinus thrombosis, it's not just the thrombocytopenia. It's the combination of them occurring together that makes a pattern. And this pattern looks very similar to what's recently been seen in Europe. The proposed syndrome seen in Europe after the AstraZeneca vaccine has been given the acronym VITT. V-I-T-T, Vaccine-Induced Thrombotic Thrombocytopenia. And recent reports in the New England Journal of Medicine suggest it's similar to auto-immune heparin-induced thrombocytopenia, aka HIT.

**Unger:** Well that is actually the most complete answer to the question that I've heard to date. And that is a lot of great information there about the background. I imagine that patients who have already received this vaccine are concerned. How are patients reacting to this news?

**Dr. Fryhofer:** Well, patients who were already signed up to get the Janssen's one dose vaccine, are likely disappointed. Their appointment's been canceled. They remain not protected because they have not yet been vaccinated. Patients who've already received the vaccine are concerned and I've already received several phone calls from patients. With this safety signal, those who received the Janssen vaccine and the last couple of weeks are still in the window of risk. After vaccination, patients should expect flu-like symptoms, mild to moderate headache, fatigue, fever, muscle aches. These symptoms are expected and usually resolve within one to two days. For patients who received Janssen vaccine within the past three weeks, here's what to look for. Severe headache, abdominal pain, leg pain or swelling, shortness of breath, and also tell patients to look for petechiae. Those little tiny red spots under the skin, other than just at the site where the vaccination was given.
Unger: All right. And that is an important thing, that differentiation you talked about in terms of expected symptoms after vaccination and the timeframe that you've outlined for those other symptoms. Well, for the physician, this obviously does change things in terms of what they do. What recommendations do you have for physicians out there?

Dr. Fryhofer: If a patient comes to your office or the emergency room with a very severe headache, or with blood clots and gives a history of recent COVID vaccination, be sure to think about this syndrome and evaluate and manage appropriately. Usually when we find blood clots, we use blood thinners like heparin, but for these types of blood clots, CDC has emphasized heparin could cause tremendous harm. Check a CBC, look for low platelets. Also, check for platelet activating antibodies by doing a platelet factor 4 antibody HIT test. The CDC says that the ELISA version of this test is the best. Do not, I repeat, do not treat with heparin unless HIT testing for heparin-induced thrombocytopenia is negative. If the HIT testing is positive, or if you can't run this test, use non-heparin anticoagulants and high dose IV immunoglobulin. These should be considered. And it's probably best to get a hematology consult.

Unger: Excellent advice. One of the concerns that you see out there is the impact that the pause is going to have on building patient trust in vaccines, how do you address that?

Dr. Fryhofer: This pause demonstrates honesty and transparency. It should inspire trust and confidence in the vaccine evaluation process. A safety signal concerned was identified. CDC and FDA acted quickly. The vaccine safety surveillance system is working. This pause gives ACIP, the Advisory Committee on Immunization Practices, time to fully review the situation and make recommendations.

Unger: That's so important. Have we seen this kind of problem with other COVID vaccines that are authorized in the United States?

Dr. Fryhofer: Well, the United States has authorized use of two other safe and highly effective COVID vaccines, which use a completely different platform. Pfizer and Moderna's mRNA vaccines are work completely differently and more than 180 million doses of mRNA COVID vaccines have been administered. There have been no reports of cerebral venous sinus thrombosis, combined with thrombocytopenia in patients who have received mRNA vaccines by Pfizer or Moderna. I repeat, this rare, but deadly combination of blood clots and low platelets has not been seen with Pfizer and Moderna mRNA COVID vaccines. And fortunately, based on current projections, the current supply of both of these mRNA vaccines is fairly high and looks stable, for at least the near future. So please, we need to encourage our patients to get vaccinated. This is the only way we can end this pandemic.

Unger: Well, Dr. Fryhofer, thank you so much for the very thoughtful and complete explanation about the situation that we're facing right now. And thank you for the work that you're doing and the rest of
the committee. That completes our COVID-19 Update for today. We'll be back with another segment shortly. In the meantime, for more resources on COVID-19, visit ama-assn.org/COVID-19. Thanks for joining us, please take care.

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