The Johnson & Johnson vaccine and blood clots: What you need to know

April 23 2021, by Kathy Katella

Infectious diseases expert Jaimie Meyer, MD, MS, says she has gotten questions from people about taking “pre-emptive” aspirin if they have received the Johnson & Johnson vaccine to prevent the blood clots. “That is not recommended unless they are supposed to be taking aspirin for other conditions,” she says. Credit: Anthony DeCarlo

In the minds of many, the halt of the Johnson & Johnson vaccine in April delivered doubt just as the mass COVID-19 vaccinations were making progress. There are three vaccines authorized for use in the United States, but Johnson & Johnson's was a particularly important one, partly because its one-shot dose made it seem as though we might achieve herd immunity faster. Then, the government recommended pausing the company's vaccine after six women who received it developed rare blood clots—and one woman died.

But six cases is a small number, considering that over 6.8 million Johnson & Johnson shots had been administered as of April 12.

Focusing on the word "pause" is key to understanding what's happening, because scientists need time to understand the risks and what they do or do not mean to people who get this shot. "Putting a pause on a new vaccine or medication is not unusual. Even after it has completed its clinical trials, a vaccine still must be monitored in the real world," says Yale Medicine infectious diseases specialist Jaimie Meyer, MD, MS. "If there are serious adverse events, we need to stop, take a deep breath, collect and analyze the data—and really try to understand why this is happening. Then, we can decide whether we should proceed."

Transparency is also important, Dr. Meyer adds. "People should know that there are these events that have been observed—even if they are very rare events—so they can make informed choices," she says.

We will know more about what those choices will be once the Centers for Disease Control and Prevention (CDC) advisory committee concludes its investigation into the clots out of "an abundance of caution." They could decide to lift the halt or choose another strategy, such as releasing it with new recommendations on who should and who should not get the vaccine. It's a challenge, since at this point, there is not enough evidence yet to say whether the vaccine caused or is related to

the blood clots.

What we know so far

Pausing the Johnson & Johnson vaccine was a response to six cases of a rare type of blood clot developing in people who'd had the shot. The cases were reported in late March and early April to the Vaccine Adverse Events Reporting System (VAERS), a national early reporting warning system to detect safety problems with U.S.-licensed vaccines. All six people were women aged 18–48 years who experienced onset of symptoms between 6–13 (a median of nine) days. One woman died. There were also reports of blood clots in a seventh woman (after the pause was announced) and earlier in a man during clinical trials for the vaccine.

What's troubling about the reported clots

A blood clot is what it sounds like—a gel-like clump of blood. Small blood clots form whenever you cut or scrape your skin to plug up the injured area and stop the bleeding. But they are dangerous when they form within a blood vessel, where they can cause thrombosis (meaning they block blood flow), a condition that kills up to 100,000 people a year in the United States. "Those clots typically occur in people who are bedridden or hospitalized, or have other medical issues related to inflammation or infection or cancer," says Yale Medicine hematologist Robert Bona, MD. They are also more likely to occur in women who are pregnant or on oral contraceptives, or in people who have hereditary disorders that predispose them to blood clotting.

The type of blood clot developed by seven of the eight Johnson & Johnson vaccine recipients was a particularly rare and dangerous blood clot in the brain, known as cerebral venous sinus thrombosis (CVST)

because it appears in the brain's venous sinuses. Yale doctors diagnose only about a couple of patients a year with CVST—its usual causes include dehydration, inherited disorders, and infections or obstructions in the brain, Dr. Bona says.

But another concern is that these same vaccine recipients also developed thrombocytopenia, a condition characterized by abnormally low platelet levels in their blood. This is unusual in someone with a major blood clot because platelets are colorless blood cells that have the function of helping blood clot.

"The mechanism of the action of these clots has been quite unusual and, frankly, that has surprised me," says Dr. Bona. "There are definitely a lot of questions."

We saw this before—with the AstraZeneca vaccine

A small number of serious blood clots also were reported in people who received the AstraZeneca vaccine, which is not authorized for use in the United States. In March, countries in Europe and elsewhere put a pause on that vaccine after a handful of people—mostly women younger than 60—also developed CVST and low platelet counts. The European Medicines Agency (EMA) investigated the situation and concluded that these complications should be listed as very rare side effects of the AstraZeneca vaccine, and said the benefits still outweighed the risks. But several countries now are administering that vaccine only to older people.

Both the AstraZeneca and Johnson & Johnson vaccines, as well as the Sputnik V vaccine in Russia (also not approved for use in the U.S.) are carrier—or vector—vaccines, which instruct human cells to make the SARS CoV-2 spike protein. For this vaccine technology, scientists engineer a harmless inactivated common adenovirus (which can cause

colds and other illnesses when it is active) into a sort of Trojan Horse that carries genetic code to a vaccine recipient's cells. The code then instructs the cells to produce a spike protein that trains the body's immune system, which then creates antibodies and memory cells to protect against an actual SARS-CoV-2 infection.

There have been no reports of blood clots from recipients of the Pfizer-BioNTech or Moderna vaccines, both of which are mRNA vaccines and use a different method to protect against the virus.

Blood clots are also a complication of COVID-19

Researchers have also seen a strong association between blood clots and COVID-19 infection itself, says Hyung Chun, MD, a Yale Medicine cardiologist. "Unfortunately, in those who are sick enough with COVID-19 to be in the intensive care unit [ICU], blood clots have been a major factor in their illness," Dr. Chun says. Close to 20% of COVID-19 patients in the ICU develop blood clots, he says. "That's far higher than what you'd expect for patients who are in the ICU for different conditions. Estimates I've seen are in the 3 to 10% range for patients admitted for other reasons," adds Dr. Chun.

COVID-19 infection seems to cause the blood vessels and the blood itself to behave in a way that promotes formation of blood clots, which is likely a key driver for poor outcomes, sometimes damaging vital organs and even leading to death, Dr. Chun says.

Dr. Chun and colleagues published a study in The Lancet Haematology after identifying a leading mechanism behind blood clots in COVID-19 patients. Yale Medicine hematologist Alfred Lee, MD, Ph.D., and George Goshua, MD, a hematology-oncology fellow, were also authors of the study. They found that endothelial cells (cells that line the blood vessels) play a surprising role in the formation of blood clots, especially

as a COVID-19 patient becomes critically ill. They hope the finding will eventually contribute to determining treatment for the blood clots. So far, "there is not a clear-cut answer," Dr. Chun says.

CVST must be treated differently

One unique aspect of CVST, as it has developed in these individuals, is its similarity to the way some patients react to heparin, an anticoagulant (or blood thinner medication) commonly used to treat clots—and one that is not being recommended for vaccine-related CVST.

Studies suggest that clots linked to the AstraZeneca vaccine resemble a similar condition that has been seen in some patients after treatment with heparin. "The pathophysiology of the blood clots appears to mirror that of the unusual clotting with heparin," says Dr. Bona. He explains that a small number of patients treated with heparin develop an antibody to a protein called platelet factor 4. Heparin binds to platelet factor 4, and that binding creates a new spot on the platelet factor 4 that is immunogenic, he says. "For a variety of reasons, the antibodies cause the platelet count to go down and cause blood clotting."

But the AstraZeneca vaccine recipients developed antibodies to platelet factor 4 in the absence of heparin. "So, heparin is the wrong anticoagulant to use," Dr. Bona says. "Luckily, we have other anticoagulants that will likely work well in this situation."

Should you get the Johnson & Johnson vaccine if it becomes available to you?

It's important to remember that for the vast majority of people, the benefits of the Johnson & Johnson vaccine outweigh the harms, Dr. Meyer says. The blood clots have been very rare and unusual. The fact

that the vaccine requires only one shot is an important benefit for many people. "There are other advantages of the Johnson & Johnson vaccine as well. It has less refrigeration requirements than the Moderna or Pfizer vaccines, so it's amenable to pop-up facilities—and in Connecticut there have been a lot of mobile health deliveries that carried Johnson & Johnson prior to the pause," Dr. Meyer says. "This could be quite disabling to those programs, which are so important because they are trying to reach the people and places most severely impacted by COVID-19."

Dr. Bona agrees. "I don't mean to minimize the effect of the clots on the people who get them, because obviously for those people it's a devastating consequence," he says. "But this is going to be infrequent, while the clotting rate is going to be much higher among those who have a COVID-19 infection." Dr. Chun adds that people are more likely to develop a serious blood clot if they are infected with COVID-19 than they are from a vaccine to prevent the disease.

CVST symptoms to look for

If the pause is lifted on the Johnson & Johnson vaccine, everyone needs to be aware of early symptoms of the rare blood clots. The CDC recommends seeking immediate medical care if you develop any of the following symptoms:

- Severe headache
- Backache
- New neurologic symptoms
- Severe abdominal pain
- Shortness of breath
- Leg swelling
- Tiny red spots on the skin (petechiae)
- New or easy bruising

Dr. Meyer says she has gotten questions from people about taking "pre-emptive" aspirin if they have received the Johnson & Johnson vaccine to prevent the blood clots. "That is not recommended unless they are supposed to be taking aspirin for other conditions," she says.

Meanwhile, researchers are working on learning more about the blood clots. Dr. Bona, for one, is eager for answers, since he has patients calling his office who are wondering if they should get the vaccine at all. "If the FDA releases the Johnson & Johnson vaccine, after they have reviewed the data, then I certainly would agree with their advice," he says.

Anyone who experiences signs of a blood clot or any adverse reaction to a vaccine should contact VAERS.

More information: Anyone who experiences signs of a blood clot or any adverse reaction to a vaccine should contact VAERS . vaers.hhs.gov/reportevent.html

Provided by Yale University