Guidance on treatment for rare blood clots and low platelets related to COVID-19 vaccine

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Last Friday, the Centers for Disease Control and Prevention (CDC) and the U.S. Food & Drug Administration (FDA) lifted the pause in administration of the Johnson & Johnson (Janssen) COVID-19 vaccine in the U.S. The temporary pause was due to reports of a serious

condition called cerebral venous sinus thrombosis (CVST), which refers to blood clots in the brain's veins—not in the arteries, as is the case for most strokes—in combination with thrombocytopenia (low blood platelet count). CVST and thrombocytopenia together is called thrombosis-thrombocytopenia syndrome (TTS). When TTS is linked to receiving a COVID-19 vaccine, it is called vaccine-induced immune thrombotic thrombocytopenia (VITT). CVST has also been associated with cases of TTS in adults who received the AstraZeneca COVID-19 vaccine available in Europe, according to the European Medicines Agency, the agency responsible for the scientific evaluation, supervision and safety of medicines in the European Union.

The American Heart Association/American Stroke Association Stroke Council Leadership convened quickly to provide important guidance about CVST, TTS and VITT—the signs and symptoms and the best treatment options. The special report, "Diagnosis and Management of Cerebral Venous Sinus Thrombosis with Vaccine-Induced Thrombotic Thrombocytopenia," published today in *Stroke*, a journal of the American Stroke Association, a division of the American Heart Association.

"COVID-19 infection is a significant risk factor for CVST. A preliminary analysis of U.S. data during the COVID-19 pandemic, available online, preprint on April 15, 2021, found that the risk of CVST due to infection with COVID-19 is 8-10 times higher than the risk of CVST after receiving a COVID-19 vaccine," said Karen L. Furie, M.D., M.P.H., lead author of the special report, chair of the department of neurology at The Warren Alpert Medical School of Brown University, and chief of neurology at Rhode Island Hospital, The Miriam Hospital and Bradley Hospital in Providence, Rhode Island. "The public can be reassured by the CDC's and FDA's investigation and these statistics—the likelihood of developing CVST after a COVID-19 vaccine is extremely low. We urge all adults to receive any of the approved COVID-19

vaccines."

The analysis included data from 59 health care organizations, totaling 81 million patients, more than 98% of whom were in the U.S. Among the nearly 514,000 patients in the database who were diagnosed with COVID-19 infection from January 20, 2020 through March 25, 2021, 20 patients were diagnosed with CVST. This data was compared to the incidence of CVST in adults who received either the Pfizer or Moderna COVID-19 vaccine before March 25, 2021, excluding those who had previously been diagnosed with COVID-19. No cases of thrombocytopenia (low platelets) were diagnosed among almost 490,000 vaccinated adults.

"CVST blood clots are very rare adverse events. We recommend immediate screening of all patients who arrive in the ER with a suspected clot—did they receive a COVID-19 vaccine during the recent weeks prior to this event?" said Furie. "Patients who present with the symptoms of CVST or blood clots and who recently received the COVID-19 vaccine should be treated using non-heparin anticoagulants. No heparin products in any dose should be given for suspected CVST, TTS or VITT. With the right treatment, most patients can have a full recovery after CVST, TTS or VITT."

CVST is an extremely rare but serious type of stroke caused by a blood clot in a part of the brain known as the venous sinus, involving veins that carry blood away from the brain. CVST clot symptoms are very similar to several other neurological conditions, and the symptoms can include severe headache; blurry vision; fainting or loss of consciousness; weakness; sensory changes; confusion or trouble speaking; seizures; abdominal pain; leg pain; difficulty breathing or shortness of breath. CVST occurs in the veins of the brain; blood clots may also occur in other blood vessels, like those in the legs, lungs or abdomen. Among the cases reported in the U.S., the most common symptoms were severe

headaches; vomiting; back pain; fatigue; weakness or the inability to move one side of the body (hemiparesis); inability to speak or understand speech (aphasia); loss of consciousness; and abdominal pain.

If associated with the COVID-19 vaccine, cases of TTS/VITT occurred several days up to 2-1/2 weeks after being vaccinated with the Johnson & Johnson (Janssen) COVID-19 vaccine in the U.S., or up to 3-1/2 weeks after receiving the AstraZeneca COVID-19 vaccine in Europe.

The CDC and FDA's report on April 23, 2021, confirms the agencies investigated 15 reported cases of TTS in the U.S., in women ages 18-59 years, from the nearly 7 million adults who received the Johnson & Johnson COVID-19 vaccine before the temporary pause on April 13, 2021. The European Medicines Agency's investigation, reported on April 7, 2021, lists 62 cases of CVST, among adults ages 22-60 years, mostly women, from the more than 25 million people who received the AstraZeneca COVID-19 vaccine throughout the European Union .

The special report from the Stroke Council leaders details treatment for suspected CVST, TTS or VITT:

- All patients with suspected CVST due to a COVID-19 vaccine should be treated with non-heparin anticoagulants such as argatroban, bivalirudin, danaparoid, fondaparinux or a direct oral anti-coagulant (DOAC). **No heparin products in any dose should be given.**
- Magnetic Resonance Imaging with a venogram (MRI/MRV) or computed tomography with venogram (CT/CTV) is recommended to accurately detect and diagnose CVST.
- Blood tests should include a CBC (Complete Blood Count) plus:
- platelet count—to determine the number of platelets per liter of blood;
- a peripheral smear—examination under a microscope to count

the number of various types of blood cells and if they appear normal;

- a prothrombin time—to measure how long it takes the blood to clot;
- a partial thromboplastin time—a measurement of how long it takes the blood to clot, specifically measuring for these clotting factors: factor VIII, factor IX, factor 1V and factor XII;
- a fibrinogen test—to measure for the presence of fibrin, a protein found in the blood that indicates that blood clotting has been activated;
- a D-dimer test—to measure for the presence of D-dimer, a small protein that's made when blood clots are dissolving in the body; and
- a PF4 antibody ELISA test—to test for PF4 antibodies, which the body sometimes creates in the blood to fight against the anticoagulant heparin.
- Anticoagulation treatment doses may need to be tailored if platelet counts are extremely low (