LOUISIANA DEPARTMENT OF HEALTH Public Health	**Health Alert Network Message 21-34: Recommendations for Clinicians & the Public Regarding the Johnson & Johnson COVID-19 Vaccine**
Origination Date: *April 15, 2021*	**Revision Dates (List All Revision Dates):**

Recommendations for Clinicians and the Public: Cerebral Venous Sinus Thrombosis with Thrombocytopenia after Receipt of the Johnson & Johnson (J&J) COVID-19 Vaccine

Recommendations For Clinicians

1. Pause the use of the J&J COVID-19 vaccine until further notice.
2. Maintain a high index of suspicion for symptoms that might represent serious thrombotic events or thrombocytopenia in patients who have recently received the J&J COVID-19 vaccine, including severe headache, backache, new neurologic symptoms, severe abdominal pain, shortness of breath, chest pain, leg swelling, petechiae (tiny red spots on the skin), or new or easy bruising. Obtain platelet counts and screen for evidence of immune thrombotic thrombocytopenia.
3. In patients with a thrombotic event or thrombocytopenia after the J&J COVID-19 vaccine, evaluate initially with a screening PF4 enzyme-linked immunosorbent (ELISA) assay as would be performed for autoimmune heparin-induced thrombocytopenia (HIT). Consultation with a hematologist is strongly recommended.
4. Do not treat patients with thrombotic events and thrombocytopenia following receipt of J&J COVID-19 vaccine with heparin, unless HIT testing is negative.
5. If HIT testing is positive or unable to be performed in patient with thrombotic events and thrombocytopenia following receipt of J&J COVID-19 vaccine, non-heparin anticoagulants and high-dose intravenous immune globulin should be strongly considered.
6. Report adverse events to the Vaccine Adverse Events Reporting System (VAERS), including serious and life-threatening adverse events and deaths in patients following receipt of COVID-19 vaccines as required under the Emergency Use Authorizations for COVID-19 vaccines.
7. **Please report any clinical significant thrombotic event or thrombocytopenia in an individual who received the J&J COVID-19 vaccine within the past 6 weeks to the Louisiana Department of Health, Infectious Disease Epidemiology Clinician Hotline: 800-256-2748.**
8. Serious and life-threatening adverse events and deaths in patients following receipt of COVID-19 vaccines should also be reported to the Louisiana Department of Health, Infectious Disease Epidemiology Clinician Hotline: 800-256-2748.

Recommendations For Clinicians to give to the Public

1. If you have received the J&J COVID-19 vaccine and develop severe headache, abdominal pain, leg pain, chest pain, or shortness of breath within six weeks after vaccination, contact your healthcare provider, or seek medical care.
2. Report adverse events, including severe headache, abdominal pain, leg pain, or shortness of breath within six weeks after vaccination, following receipt of any COVID-19 vaccine to your healthcare provider as well as to the CDC's V-Safe After Vaccination Health Checker app.
3. If you are scheduled to receive the J&J vaccine, please contact your healthcare provider, vaccination location, or clinic to learn about additional vaccine availability.

Summary

As of April 12, 2021, approximately 6.85 million doses of the Johnson & Johnson (J&J) COVID-19 vaccine (Janssen) have been administered in the United States. The Centers for Disease Control and Prevention (CDC) and the U.S. Food and Drug Administration (FDA) are reviewing data involving six U.S. cases of a rare type of blood clot in individuals after receiving the J&J COVID-19 vaccine that were reported to VAERS. In these cases, a type of blood clot called cerebral venous sinus thrombosis (CVST) was seen in combination with low levels of blood platelets (thrombocytopenia). All six cases occurred among women aged 18–48 years. The interval from vaccine receipt to symptom onset ranged from 6–13 days. One patient died. Providers should maintain a high index of suspicion for symptoms that might represent serious thrombotic events or thrombocytopenia in patients who have recently received the J&J COVID-19 vaccine. When these specific type of blood clots are observed following J&J COVID-19 vaccination, treatment is different from the treatment that might typically be administered for blood clots. Based on studies conducted among the patients diagnosed with immune thrombotic thrombocytopenia after the AstraZeneca COVID-19 vaccine in Europe, the pathogenesis of these rare and unusual adverse events after vaccination may be associated with platelet-activating antibodies against platelet factor-4 (PF4), a type of protein. Usually, the anticoagulant drug called heparin is used to treat blood clots. In this setting, the use of heparin may be harmful, and alternative treatments need to be given.

CDC will convene an emergency meeting of the Advisory Committee on Immunization Practices (ACIP) on Thursday April 22, 2021, to further review these cases and assess potential implications on vaccine policy. FDA will review that analysis as it also investigates these cases. Until that process is complete, CDC and FDA are recommending a pause in the use of the J&J COVID-19 vaccine out of an abundance of caution. The purpose of this Health Alert is, in part, to ensure that the healthcare provider community is aware of the potential for these adverse events and can provide proper management due to the unique treatment required with this type of blood clot.

Background

VAERS is a national passive surveillance system jointly managed by CDC and FDA that monitors adverse events after vaccinations. The six patients (after 6.85 million vaccine doses administered) described in these VAERS reports came to attention in the latter half of March and early April of 2021 and developed symptoms a median of 9 days (range = 6–13 days) after receiving the J&J COVID-19 vaccine. Initial presenting symptoms were notable for headache in five of six patients, and back pain in the sixth who subsequently developed a headache. One patient also had abdominal pain, nausea, and vomiting. Four developed focal neurological symptoms (focal weakness, aphasia, visual disturbance) prompting presentation for emergency care. The median days from vaccination to hospital admission was 15 days (range = 10–17 days). All were eventually diagnosed with CVST by intracranial imaging; two patients were also diagnosed with splanchnic* and portal vein thrombosis. Unusual for patients presenting with thrombotic events, all six patients showed evidence of thrombocytopenia (<150,000 platelets per microliter of blood), consistent with a condition known as thrombotic thrombocytopenia, with platelet nadir counts ranging from 10,000 to 127,000 during their hospitalizations. Four patients developed intraparenchymal brain hemorrhage and one subsequently died. All data presented in this HAN are preliminary and investigations of these VAERS reports are ongoing. The Clinical Immunization Safety Assessment (CISA) project which includes experts in infectious disease and hematology are also reviewing these cases. To date, VAERS has received no reports of CVST

with thrombocytopenia among persons who received either of the two mRNA-based COVID-19 vaccines (Pfizer or Moderna).

These reports following the J&J COVID-19 vaccine are similar to reports of thrombotic events with thrombocytopenia after receipt of the AstraZeneca COVID-19 vaccine in Europe. Both vaccines contain replication-incompetent adenoviral vectors (human [Ad26.COV2.S] for J&J and chimpanzee [ChAdOx1] for AstraZeneca) that encode the spike glycoprotein of SARS-CoV-2, the virus that causes COVID-19. Based on studies conducted among the patients diagnosed with immune thrombotic thrombocytopenia after the AstraZeneca COVID-19 vaccine in Europe, the pathogenesis of these rare and unusual adverse events may be associated with platelet-activating antibodies against platelet factor 4 (PF4). Anti-PF4, also known as heparin-PF4 antibody, can induce thrombotic thrombocytopenia in a small percentage of persons exposed to heparin. However, none of the cases reported from Europe had recent heparin exposure. As with heparin-induced thrombocytopenia, the administration of the anticoagulant heparin should be avoided in patients with potential vaccine-associated immune thrombotic thrombocytopenia (VITT), unless heparin-induced thrombocytopenia (HIT) testing is negative. Non-heparin anticoagulants and high-dose intravenous immune globulin should be considered in treatment of patients who present with immune-mediated thrombotic events with thrombocytopenia after J&J COVID-19 vaccination. Consultation with hematology specialists is strongly recommended.

** The term 'splanchnic circulation' describes the blood flow to the abdominal gastrointestinal organs including the stomach, liver, spleen, pancreas, small intestine, and large intestine.*

For More Information

- Resources on thrombotic thrombocytopenia after AstraZeneca COVID-19 vaccine https://www.nejm.org/doi/full/10.1056/NEJMoa2104840 , https://www.nejm.org/doi/full/10.1056/NEJMoa2104882
- Frequently asked questions about VAERS reporting for COVID-19 vaccines VAERS - FAQs (hhs.gov)
- How to report to VAERS
- How to report to V-Safe
- CDC materials on stroke and NIH materials on thrombocytopenia