DC HEALTH
GOVERNMENT OF THE DISTRICT OF COLUMBIA

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May 28, 2021

Health Alert Notice for District of Columbia Health Care Providers
COVID-19 Vaccine Side Effects

SUMMARY:

This health notice discusses the side effects of the three COVID-19 vaccines authorized for use in the United States: the two mRNA vaccines (Pfizer/BioNTech and Moderna), and the adenovirus vaccine (Janssen/Ad26.COV2.S). The majority of side effects are mild to moderate and self-limited, but the Janssen COVID-19 vaccine has recently been associated with a serious clinical syndrome called thrombotic thrombocytopenic syndrome (TTS). This health alert notice provides information for health care providers on common side effects and their management, as well as an in-depth discussion about TTS: counseling patients about risks, recognizing symptoms, and evaluation and management considerations.

BACKGROUND:

There are currently 3 COVID-19 vaccines available for use in the U.S. under Emergency Use Authorizations (EUA). The COVID-19 vaccines are known to be reactogenic vaccines, and local and systemic side effects are common post-vaccination. Most side effects are self-limited and not harmful to patients. Recently, a serious clinical syndrome, termed thrombotic thrombocytopenic syndrome (TTS) has been plausibly associated with the Janssen COVID-19 vaccine. This newly identified syndrome is similar to heparin-induced thrombocytopenia (HIT). TTS has not been associated to date with either of the two mRNA COVID-19 vaccines approved for emergency use in the United States (Pifzer-BioNTech and Moderna). **It is important for HCPs to consider recent COVID-19 vaccination as part of their clinical histories, and to continue to report adverse events that occur in a recipient following COVID-19 vaccination to VAERS.**

SIDE EFFECTS OF THE MRNA COVID-19 VACCINES:

Before vaccination, providers should counsel mRNA COVID-19 vaccine recipients about possible post-vaccination symptoms, local (e.g., pain, swelling, erythema at the injection site, localized axillary lymphadenopathy on the same side as the vaccinated arm) and systemic (e.g., fever, fatigue, headache, chills, myalgia, arthralgia). For the Pfizer vaccine, post-vaccination symptoms are similar in adults and children 12-15.

- Most systemic post-vaccination symptoms are mild to moderate in severity, occur within the first three days of vaccination, and resolve within 1–3 days of onset.
- Symptoms are more frequent and severe following the second dose and among younger persons compared to older persons[1]
    - Frequency of post-vaccination symptoms in adults aged 18 and older:
        - 80-89% experience at least one local symptom.
        - 55-83% experience at least one systemic symptom.
    - Frequency of post-vaccination symptoms is higher in children 12-15.
        - 90.9% experience at least one local symptom.
        - 90.7% experience at least one systemic symptom.
        - Adolescents are more likely to experience syncope shortly after vaccination compared to adults. This is not specific to the COVID-19 vaccine. Healthcare providers administering the COVID-19 vaccine are advised to be aware of this and to plan accordingly (e.g., have young patients sit or lie down during their observation period, have procedures in place to manage syncopal reactions).

[1] In this context, “older persons” refers to: older than 55 (for the Pfizer vaccine) and 65 and older (for the Moderna vaccine)

- Patients with a history of COVID-19 infection are more likely to have systemic symptoms after the first mRNA vaccine dose.
- Unless patients develop a contraindication to vaccination, they should be encouraged to complete the series even if they develop local or systemic symptoms following the first dose.
- In May 2021, the ACIP COVID-19 Vaccine Safety Technical (VaST) Work Group indicated that reports of **myocarditis** and **pericarditis** that occurred following mRNA vaccine administration were being investigated. There were relatively few reports that were identified predominantly in adolescents and young adults, more in males than females, more often after the 2nd dose, and typically 4 days after vaccination. Most cases were mild and treated with standard clinical care. At this time the reports of myocarditis have not differed from expected baseline rates but are continuing to be monitored.
    - For more information about this subject, please see the CDC website at cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html.
- Thrombotic thrombocytopenic syndrome (TTS) has not been reported with either of the mRNA vaccines.

SIDE EFFECTS OF THE JANSSEN COVID-19 VACCINE

Before vaccination, providers should counsel vaccine recipients about possible post-vaccination symptoms, local (e.g., pain, swelling, erythema at the injection site, localized axillary lymphadenopathy on the same side as the vaccinated arm) and systemic (e.g., fever, fatigue, headache, chills, myalgia, arthralgia). **Healthcare providers must also counsel patients, especially women age 18-49, about the risk of TTS and inform patients of the option to receive one of the two other vaccine products available.**

- 50% of vaccinated individuals experience at least one local symptom and 55% experience at least one systemic symptom.
- Post-vaccination symptoms can occur within 7-8 days. Symptoms are usually mild to moderate in severity, most commonly occurring within the first 2 days after vaccination and resolving within 1–2 days of onset.

Thrombosis Thrombocytopenia Syndrome

TTS is a syndrome characterized by venous or arterial thrombosis at unusual sites including cerebral venous sinus thrombosis (CVST) and splanchnic thrombosis, in association with mild to severe thrombocytopenia and a positive platelet factor-4 (PF-4) enzyme-linked immunosorbent assay (ELISA) test. TTS is also similar to a post-vaccination syndrome identified in Europe associated with the AstraZeneca vaccine (CHaDOx1 nCov-19), which like the Janssen vaccine is an adenovirus vaccine. On April 13, 2021, after 6 cases of CVST with thrombocytopenia in women younger than 50 were reported to the Vaccine Adverse Event Reporting System (VAERS), the U.S. Food and Drug Administration (FDA) and the U.S. Centers for Disease Control and Prevention (CDC) initiated a pause on the use of the Janssen vaccine. On April 23, 2021, after a thorough review of the data, the Advisory Committee on Immunization Practices (ACIP), determined that the benefits of the Janssen COVID-19 vaccine outweigh the risks of this rare side effect and re-affirmed the vaccine's use in adults aged 18 and older under the EUA. A warning has been added to the EUA about the risk of TTS, especially in women younger than 50. Healthcare providers (HCP) must counsel patients, especially women aged 18-49, about this risk and inform them of the option to receive one of the two other vaccine products available. HCP must be aware of the symptoms of TTS, so that it can be recognized and managed appropriately. Health authorities will continue to monitor this issue closely.

Additional Facts learned during the Janssen COVID-19 pause:

- By the end of the April 2021 10 day long pause period, the number of cases of TTS reported through VAERS had grown from 6 to 15.
    - All 15 cases occurred in women

  - 13 of 15 cases were women age 18-49 (rate of 7 cases/million doses)
  - 2 of 15 cases were in women age 50 or older (rate of 0.9 cases/million doses)
  - Median age: 37
  - Median time to onset of TTS symptoms after vaccination: 8 days (range 6-15 days)
  - 3 of the 15 cases died.
  - None had exposure to heparin
  - Overall rate of TTS occurrence: 2 cases/million doses given (as of 4/21/21)
- Review of data showed one case of TTS had occurred in a man (between the ages of 18-49) in the Phase III Clinical Trial of the Janssen COVID-19 vaccine.
- As of May 18, 2021, there have been 30 confirmed cases of TTS reported with more than 9.6 million doses of the Janssen COVID-19 vaccine administered.
- There is no increased risk of TTS in people with a history of DVT/PE, traditional risk factors for thrombosis, or autoimmune disorders.

Clinical Considerations for TTS:

- Healthcare providers must maintain a high index of suspicion for TTS. The presence of any of these symptoms occurring in patients 4-30 days after receipt of the Janssen COVID-19 vaccine warrants urgent evaluation for TTS:
  - Severe headache
  - Changes in mental status
  - Visual changes
  - Abdominal pain
  - Nausea and/or vomiting
  - Back pain
  - Shortness of breath
  - Leg pain or swelling
  - Petechiae, easy bruising, or bleeding
- **Diagnostic criteria for TTS:**
  The American Society of Hematology ASM) have developed diagnostic criteria for TTS. Patients must have all 4 of the following elements:
  - **History of receipt of the Janssen COVID-19 vaccine in the past 4-30 days**
  - **Venous or arterial thrombosis**
  - **Thrombocytopenia**
  - **Positive Platelet-factor 4 (PF4) ELISA test**
- **Initial Evaluation and Management of TTS**
  - First tests to order: CBC with platelets, PF4 ELISA, and imaging guided by signs and symptoms (e.g. CT or MRI venogram to evaluate for CVST, imaging for PE/DVT)
  - Additional tests for workup: peripheral blood smear, D-dimer (elevated in majority of cases), fibrinogen (sometimes low).
  - Avoid giving heparin until TTS is ruled out.
  - **Consultation with a Hematology specialist is strongly recommended if TTS is suspected.**
  - Initial therapy for TTS: intravenous immunoglobulin (IVIG) **PLUS** a non-heparin anticoagulant (e.g., argatroban, bivalrudin, fondaparinux, danaparoid)
    - No strong evidence that heparin is harmful to patients with TTS currently exists, but the similarity of TTS to HIT warrants this approach.

For detailed information see the American Society of Hematology TTS guidelines at hematology.org/covid-19/vaccine-induced-immune-thrombotic-thrombocytopenia.

MANAGEMENT OF GENERAL COVID-19 VACCINE SIDE EFFECTS

Antipyretics (e.g., acetaminophen, non-steroidal anti-inflammatory drugs) may be taken for the treatment of post-vaccination local or systemic symptoms, if medically appropriate. However, routine prophylactic administration is not currently recommended at this time, as information on the impact on COVID-19 vaccine-induced antibody response is unknown.

- Cool compresses may be applied to reduce pain or discomfort at the injection site.

SAFETY AND REPORTING

- **Vaccine Administration Reporting**
  - Vaccine administration must be reported to the District of Columbia Immunization Information System, (DOCIIS) **within 24 hours of administration**.
  - DOCIIS is the Immunization Program's key tool for tracking individual- and population-level immunization data in DC. Health care providers should use DOCIIS to check immunization history to ensure their patients receive recommended vaccines as prescribed, and schools and LCDCs use DOCIIS to track compliance with immunization laws and regulations (e.g., DC Law 3-20). For more information on DOCIIS please visit dchealth.dc.gov/dociis.
  - **ALL** vaccine administration errors should be reported to the Vaccine Adverse Event Reporting System (VAERS) as described below.
- **Encourage patients to utilize *V-Safe.*** This is very important to allow for more real-world data to be gathered on vaccine side effects.
  - *V-Safe* is a voluntary, smartphone-based tool developed by the CDC that uses text messaging and web surveys to provide patients with near real-time health check-ins after they receive a COVID-19 vaccination.
  - CDC/*v-safe* call center representatives will follow up on reports of medically significant health impacts to collect additional information to enter in VAERS. More information on VAERS can be found in the reporting section of this document.
- **Adverse Event Reporting:** Adverse events that occur in a recipient following COVID-19 vaccination should be reported to VAERS. Vaccination providers are required by the Food and Drug Administration to report the following that occur after COVID-19 vaccination under Emergency Use Authorization:
  - Vaccine administration errors
  - Serious adverse events
  - Cases of Multisystem Inflammatory Syndrome
  - Cases of COVID-19 that result in hospitalization or death

Reporting is encouraged for any other clinically significant adverse event even if it is uncertain whether the vaccine caused the event. Information on how to submit a report to VAERS is available at vaers.hhs.gov or by calling 1-800-822-7967

Please contact DC Health regarding COVID-19 at:
Phone: 202-576-1117 Fax: 202-442-8060 | Email: coronavirus@dc.gov