

## Clinical Guidance on Vaccine-induced Immune Thrombotic Thrombocytopenia (VITT)

VITT is a syndrome currently characterized by 1) thrombosis, often at unusual sites including cerebral sinus venous thrombosis (CSVT)/splanchnic thrombosis; 2) mild to severe thrombocytopenia; 3) elevated D-dimers, and 4) positive PF4-heparin ELISA and platelet activation assays.

Incidence so far is extremely rare. Risk of death and serious outcome of COVID-19, including thrombosis, may outweigh risk of VITT possibly associated with highly efficacious vaccines.

Clinical Presentation
<p>Urgent medical evaluation for suspected VITT is indicated if any of the following develop 4 to 30 days after receiving COVID vaccine (Johnson &amp; Johnson/AstraZeneca <i>only</i> to date):</p> <ul style="list-style-type: none"> <li>• Severe headache</li> <li>• Visual changes</li> <li>• Abdominal pain</li> <li>• Nausea and vomiting</li> <li>• Backache</li> <li>• Shortness of breath</li> <li>• Leg pain or swelling</li> <li>• Petechiae or easy bruising</li> </ul>
Initial Evaluation
<ul style="list-style-type: none"> <li>• CBC with differential, PT, PTT, fibrinogen and D-dimer</li> <li>• Imaging for thrombosis is a clinical decision based on history, exam, lab results <ul style="list-style-type: none"> <li>○ CNS or abdominal evaluation: CT arteriography / venography; MRA / MRV with gadolinium if unable to use contrast or for complicated picture</li> <li>○ Chest: PE protocol CT</li> <li>○ Extremity: ultrasound with doppler</li> </ul> </li> <li>• If labs or imaging are abnormal, send PF4-ELISA (HIT assay); <b>draw blood prior to any therapies</b></li> <li>• If thrombocytopenia* (platelets &lt; 150 x 10<sup>9</sup>/L) or thrombosis are present, recommend urgent consultation for hematologist with expertise in hemostasis</li> <li>• If initial evaluation is unremarkable, consider re-evaluation (exam, labs, etc) in 2-3 days based on clinical suspicion</li> </ul> <p><b>*A patient who presents with thrombosis and a normal platelet count post-vaccination might be in an early stage of VITT.</b> Continued assessment for development of thrombocytopenia/VITT required. A non-heparin anticoagulant may be indicated if patient is 4 to 30 days post-Johnson &amp; Johnson – Janssen vaccine.</p>
Initial Management
<p><b>Initiate therapy</b> if signs/symptoms of thrombosis are present with any of the following findings:</p> <ul style="list-style-type: none"> <li>• Positive imaging <i>AND/OR</i></li> <li>• Low platelets*</li> </ul>

**Admission is typically required** for patients meeting these criteria in the setting of recent Johnson & Johnson/AstraZeneca vaccine. Patients who have a non-life-threatening thrombosis (such as DVT) with another inciting factor, and normal laboratory evaluation, may be candidates for home monitoring provided that close follow-up can occur.

**Treat as severe HIT.** Avoidance of heparin in patients presenting with any venous thromboembolism in the post-vaccine window is reasonable while awaiting other lab results and following the platelet count. If VITT diagnosis is suspected, start treatment before PF4-ELISA results:

- IVIG 1 gram/kg daily X 2 days; *AND*
- Non-heparin anticoagulation, chosen based on the clinical status and organ function of the patient:
  - Parenteral direct thrombin inhibitors (argatroban or bivalirudin provided the baseline aPTT is normal); *OR*
  - Direct oral anticoagulants without lead-in heparin phase; *OR*
  - Fondaparinux
- Low fibrinogen or bleeding are associated with VITT, and should not absolutely preclude anticoagulation, particularly if platelets are  $>20,000/\mu\text{L}$  or rising following IVIG initiation. Correct fibrinogen with cryoprecipitate prior to starting anticoagulant. Recommend hematology consult for guidance.
- Based on similarities to HIT, avoid platelet transfusions. However, risk/benefit assessment in individual patients with serious bleeding and/or need for surgical intervention may favor platelet transfusion, following initiation of IVIG, non-heparin anti-coagulation, and fibrinogen replacement (if deficient).

**Note:** Patients may present with a typical lower extremity venous thromboembolism (VTE) following vaccination in the presence of mild thrombocytopenia or a single low normal value

- Consider avoiding heparin while awaiting PF4 ELISA results and following the platelet count

**Note:** Patients with thrombocytopenia and elevated D-dimers, even in the absence of documented thrombosis or suggestive symptoms, should be treated with IVIG and close monitoring. PF4 antibody testing should be sent prior to treatment initiation.

- Very high or rising D-dimers or development of symptoms of thrombosis should also trigger admission and institution of anticoagulation

### Reporting

COVID vaccine reactions identified by clinicians, including thrombosis with thrombocytopenia syndrome or other severe reactions, should be submitted in UCSF [Incident Reporting](#) (IR) system, available on the Carelinks homepage.

For VITT events, please email [MedSafety@ucsf.edu](mailto:MedSafety@ucsf.edu) with the IR report number, to ensure prompt review and reporting. Events will then be submitted to the Vaccine Adverse Event Reporting System (VAERS) and reported to SFDPH by the Medication Safety Team, when appropriate.

If you have any questions about what should be reported or how to report, contact [MedSafety@ucsf.edu](mailto:MedSafety@ucsf.edu).

**References**

Basis for guidelines:

<https://www.hematology.org/covid-19/vaccine-induced-immune-thrombotic-thrombocytopenia>

Other references:

- Greinacher A et al. [Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination](#). DOI: 10.1056/NEJMoa2104840
- Schultz NH et al. [Thrombosis and thrombocytopenia after ChAdOx1 nCoV-19 vaccination](#). DOI: 10.1056/NEJMoa2104882
- Muir KL et al. [Thrombotic thrombocytopenia after Ad26.COV2.S vaccination](#). DOI: 10.1056/NEJMc2105869
- Tacquet et al. Cerebral venous thrombosis: a retrospective cohort study of 513,284 confirmed COVID-19 cases and a comparison with 489,871 people receiving a COVID-19 mRNA vaccine, preprint available at <https://osf.io/a9jdq/>
- Cines DB, Bussell JB. [SAR-CoV-2 vaccine-induced immune thrombotic thrombocytopenia](#). DOI: 10.1056/NEJMe2106315
- Van Dam, LF et al. [Current imaging modalities for diagnosing cerebral vein thrombosis – A critical review](#). DOI: 10.1016/j.thromres.2020.03.011
- Simabukuro T. [Thrombosis with thrombocytopenia syndrome \(TTS\) following Janssen COVID-19 vaccine](#). Advisory Committee on Immunization Practices (ACIP) April 23, 2021