Thrombosis with Thrombocytopenia Syndrome following COVID-19 vaccination

Assessment of patients presenting to the Emergency Department with TTS symptoms

June 2021 v2.0
About

This guide
This guide addresses the recognition, diagnosis and management of suspected Thrombosis with Thrombocytopenia Syndrome (TTS) following COVID-19 vaccination. To date this complication has only been described with the Astra Zeneca vaccine and Johnson & Johnson’s Janssen vaccine.

Synonyms for TTS

- VIPIT “vaccine induced prothrombotic immune thrombocytopenia”
- VATT “vaccine associated thrombosis and thrombocytopenia”
- VITT “vaccine induced immune thrombotic thrombocytopenia”

Rapid Reference Summary

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Basic Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient has <strong>not</strong> received Astra Zeneca (AZ) vaccine or Johnson &amp; Johnson’s Janssen (JJ) vaccine</td>
<td>Exit pathway</td>
</tr>
<tr>
<td>Patient received AZ or JJ vaccine but time window <strong>not</strong> within 4-42 days</td>
<td>Exit pathway</td>
</tr>
<tr>
<td>Patient received AZ or JJ vaccine within the past 4-42 days <strong>and</strong> platelets greater than 150 x 10⁹ <strong>and</strong> D-dimer less than 5 x upper limit of normal</td>
<td>TTS unlikely; exit pathway</td>
</tr>
<tr>
<td>Patient received AZ or JJ vaccine within the past 4-42 days <strong>and</strong> platelets less than 150 x 10⁹ <strong>and / or</strong> D-dimer greater than 5 x upper limit of normal</td>
<td>TTS likely; Further investigation, Obtain urgent haematology advice</td>
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</tbody>
</table>

The Australasian College for Emergency Medicine

The Australasian College for Emergency Medicine (ACEM) is the not-for-profit organisation responsible for training emergency physicians and advancement of professional standards in emergency medicine in Australia and New Zealand.

**Our vision** is to be the trusted authority for ensuring clinical, professional and training standards in the provision of quality, patient-focused emergency care.

**Our mission** is to promote excellence in the delivery of quality emergency care to all of our communities through our committed and expert members.

As this is an emerging area of practice, please continue to check back for updates: https://acem.org.au/Content-Sources/Advancing-Emergency-Medicine/COVID-19/Resources
Guideline for Suspected TTS in the Emergency Department

**Do this patient’s symptoms raise any concern for TTS?**

- **YES**: Manage as per routine practice for specific presentation
- **NO**: TTS unlikely; consider other causes

**Did the patient develop symptoms within 4-42 days since AZ or JJ vaccine?**

- **YES**: TTS unlikely; consider other causes
- **NO**: Obtain Full Blood Count and D-dimer test

**Obtain Full Blood Count and D-dimer test**

**Blood test results**

<table>
<thead>
<tr>
<th></th>
<th>platelet count &lt; 150 x 10⁹</th>
<th>platelet count normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-dimer</td>
<td>TTS suspected</td>
<td>TTS unlikely - exit pathway</td>
</tr>
<tr>
<td>&lt; 5 x ULN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D-dimer</td>
<td>TTS likely</td>
<td>TTS possible, consider symptoms, alternative diagnoses and repeat testing</td>
</tr>
<tr>
<td>&gt; 5 x ULN</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*ULN = upper limit of normal (not age-adjusted)*

**If TTS suspected or likely obtain urgent haematology advice**

- Treat as per guidance from [Expert Haematology Panel](#)
- Do not use heparin anticoagulant

**Appropriate imaging and other specialty referral as indicated based on clinical presentation**

- e.g. Cerebral venous sinus thrombosis (CVST) → Neurology
TTS Symptoms

Symptoms of TTS include, but not limited to, **new onset**:

1. Persistent headaches +/- vision change, other focal neurology, seizure-like activity
2. Persistent abdominal pain
3. Leg swelling or pain +/- colour change
4. Chest pain and/or shortness of breath (without a clear alternative cause)

Cases usually present with progressive thrombosis, with a high preponderance of cerebral venous sinus thrombosis. Splanchnic vein thrombosis is common and pulmonary embolism and arterial ischaemia are also seen. Bleeding can be significant and unexpected.

Investigation recommendations

- Note that in greater than 5% of TTS cases, the platelet count is normal at presentation and drops later. Therefore, if there is a high index of suspicion in a patient with normal platelets, check D-dimer and fibrinogen, and/or consider repeating the platelet count the following day. Current evidence suggesting the need for a ‘high index of suspicion’ in this context is in days 5-28 post AZ vaccine with new onset headache or abdominal pain which is atypical and severe in nature.
- Patients who have mildly elevated D-dimer but no other suspicion of clotting disorder should exit the above algorithm.
- Deep vein thrombosis (DVT) and pulmonary embolism (PE) due to TTS have presented clinically as late as day 42.
- Patients who represent (within the 4-42 day window) with persistent or ongoing significant symptoms having previously been ruled out and exited this pathway should be re-tested.

Neuroimaging recommendations

- If no clinical or haematological features of TTS are present, headache symptoms should be managed via usual headache pathways, with neuro-imaging only if clinically appropriate. Cerebral venography is not generally indicated.
- For patients with TTS and headache symptoms, dedicated cerebral venous imaging is appropriate.
  - Non-contrast CT brain combined with contrast enhanced CT cerebral venography is rapid, accessible and has very high diagnostic accuracy.
  - MRI/MRI venography is an equally accurate alternative and may be preferred in some centres.

The need for other imaging investigations (e.g. CT pulmonary angiography or CT abdomen / pelvis) should be determined on the basis of clinical suspicion and in discussion with radiology.

Role of D-dimer testing

D-dimer is a highly sensitive and non-specific test. Elevated D-dimer levels may indicate a clotting disorder such as DVT, PE or Disseminated Intravascular Coagulation (DIC). D-dimer may also be elevated for a range of other reasons including pregnancy, heart disease, recent surgery, injury, or non-specific inflammation. D-dimer levels increase with advancing age.

Patients who have mildly elevated D-dimer but no other suspicion of clotting disorder may not require further investigation unless there are concerns about other significant pathology.

*This guideline has been adapted with permission from The Royal College of Emergency Medicine, The Society for Acute Medicine, and the Royal College of Physicians in the UK.*