VITT nice guidelines 2021

Incidence:

- Incidence after first or unknown dose of COVID-19 vaccine of 14.2 per million doses.
- 405 cases of major thromboembolic events with concurrent thrombocytopenia (MHRA)

Symptoms and signs:

Advise patients to seek urgent medical advice if they experience any of the following symptoms more than 4 days and within 28 days of coronavirus vaccination:

- New onset of severe headache, which is getting worse and does not respond to simple painkillers
- An unusual headache which seems worse when lying down or bending over, or may be accompanied by blurred vision, nausea and vomiting, difficulty with speech, weakness, drowsiness or seizures
- New unexplained pinprick bruising or bleeding
- Shortness of breath, chest pain, leg swelling or persistent abdominal pain

Investigations:

If the full blood count confirms thrombocytopenia, or a strong clinical suspicion of VITT remains, do the following tests in secondary care:

- Coagulation screen, including Clauss fibrinogen assay and D-dimer measurement
- A blood film to confirm true thrombocytopenia and identify potential alternative diagnoses.

Investigations to exclude other causes:

- Cancer, antiphospholipid syndrome, heparin-induced thrombocytopenia, thrombotic thrombocytopenic purpura and paroxysmal nocturnal haemoglobinuria.

	VITT probable	VITT Unlikely
Thrombosis	Present	Maybe present
Thrombocytopenia	Present	Maybe present
D-dimer	>4000	2000-4000
Fibrinogen	<2	2-4

If high suspicion:

- Repeat blood investigations after 2-3 days of if symptoms worsen
- CT imaging is superior to ultrasound, and should be used if there is a clinical suspicion of splanchnic vein thrombosis, consider repeat imaging if initial imaging is normal.
- Enzyme-linked immunosorbent assay (ELISA) for platelet factor 4 antibodies to confirm the diagnosis → if negative think of alternative diagnosis.

Prognosis:

Signs of poor prognosis in people with VITT include any of the following:

- Having CVST
- Having thrombosis at multiple sites
- Developing secondary bleeding
- Having very low platelet levels (less than 30 x 109 /litre)

Management:

Cases should be reported to MHRA and public health of England.

Consider fibrinogen replacement therapy with fibrinogen concentrate or cryoprecipitate to maintain a level of fibrinogen of at least 1.5 g/litre, if bleeding or surgery is needed.

If CSVT consider pre-emptive transfer to a centre with neuroscience services, even if the person is still clinically well.

Ensure patient education: Give patient information leaflet.

Psychological support for patients and their families particularly if ill.

A. VITT with thrombosis:
   Start anticoagulation treatment for people with VITT, including those who have only had arterial thrombosis, as soon as the benefit outweighs the risk of bleeding.
   Use non-heparin drugs for anticoagulation treatment for VITT, for example: direct oral anticoagulants, fondaparinux, danaparoid sodium and argatroban.

- Avoid using heparins, including heparin flushing solution in people with VITT.
- Avoid using warfarin in people with VITT until platelet count has returned to normal.
- Avoid using warfarin and direct oral anticoagulants in pregnant women.
- If surgery to treat the thrombosis is not planned, switch to oral anticoagulation with direct oral anticoagulants as soon as the person's clinical condition and platelet level allows. Continue the same anticoagulation treatment after discharge.
- For people with VITT who have a very low platelet count (under 30 x109 /litre), consider one of the following alternative anticoagulation strategies that may reduce the risk of bleeding:
    - A critical illness dose of argatroban, or
    - A therapeutic dose of argatroban, plus platelet transfusion.

  Take into account the risks and benefits of each option in relation to the person's clinical condition, and the person's preferences.

B. VITT without thrombosis:
   For people with VITT without confirmed thrombosis, but who have thrombocytopenia with very high D-dimer and a positive ELISA for platelet factor 4 antibodies, consider venous thromboembolism (VTE) thromboprophylaxis after taking into account the benefits and risks of treatment.

C. Managing VITT immune response:

- Give intravenous immunoglobulin immediately at a dose of 1 g/kg to people with a clinical diagnosis of probable VITT, spilt in 2 days doses.
- Consider adding corticosteroids if intravenous immunoglobulin treatment is insufficient (that is, if there is progression of thrombosis or the platelet count does not rise to an acceptable level) → methylpred 1g for 3 days or Dex 20-40mg f days
- Consider plasma exchange with fresh frozen plasma (1 volume exchange a day) as an alternative to a second dose of intravenous immunoglobulin → daily for 5 days or until Plt count recover.
- Consider rituximab for people with VITT that has not responded to a second dose of intravenous immunoglobulin or plasma exchange → 375mg/m2 weekly for 4 weeks (off label, not for pregnant patients).

D. Intensive treatment for poor prognosis patients:
For people with VITT who have signs of poor prognosis, consider an intensive treatment strategy of plasma exchange and high-dose steroids.

E. After discharge:
Keep the person under the care of the haematology department, and assess symptoms and monitor as follows:

- Measure D-dimer, fibrinogen and platelet counts every 2 to 3 days for the first 2 weeks.
- Repeat ELISA for platelet factor 4 antibodies weekly for the first 4 weeks
- After the initial periods noted above, repeat monitoring tests monthly for the first 6 months and, if no relapses occur, reduce the frequency of testing to every 3 months.
- When platelet 4 antibodies are no longer detected, review the need for ongoing treatment and monitoring.
- If the person is taking corticosteroids and a decision is made to stop this treatment, ensure that the dose is tapered down
- Continue anticoagulation for at least 3 months, or until platelet factor 4 antibodies are no longer detected. If anticoagulation needs to be stopped sooner, discuss the risks and benefits of stopping treatment with a clinical haematologist and the person with VITT.
- For arterial thrombosis (or IHD): continue anticoagulation for at least 1 month, and consider adding antiplatelet agents, if normal fibrinogen, D-dimer and platelet levels are maintained after 1 month, consider stopping anticoagulation and switching to antiplatelet agents only.
- Retreat if: platelet levels drop substantially from the previous measurement, or new thrombosis occurs despite therapeutic anticoagulation.
- Further vaccination should be deferred until their clotting has completely stabilised, and they should then be considered for a second dose of an alternative product (keep in mind Anti-PF4 can persist for 6 months).