Interim Guidelines: Diagnosis and Management of Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT) following AstraZeneca COVID-19 Vaccinations

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Introduction

Rare cases of blood clots with low platelets after receipt of AstraZeneca (AZ) COVID-19 vaccine have been reported. This document provides guidance to UN medical staff globally on the diagnosis, management and reporting of vaccine-induced prothrombotic immune thrombocytopenia (VIPIT) cases.

For any questions, contact DHMOSH Public Health at dos-dhmosh-public-health@un.org **Note that this is a living document which will be updated as more information emerges.**

Current Situation Update

At the time of writing, the AstraZeneca vaccine is currently being authorized for use in the EU and several other countries, including the UK, Canada and India. Based on a multinational Phase 3 trial, the vaccine had 70.4% efficacy in preventing symptomatic COVID-19 at/after 14 days post second dose. Although there is some concern about vaccine efficacy against certain "variants", the WHO continues to recommend use of this vaccine even if those variants are circulating in a country[1,2].

"Vaccine induced prothrombotic immune thrombocytopenia", or VIPIT, is a condition of blood clots associated with low platelet counts, that occurs following receipt of the vaccine. The likely mechanism is antibodies that induce massive platelet activation, reducing platelet count and causing thrombosis although the full mechanism remains to be elucidated. This syndrome is thought to mimic "heparin-induced thrombocytopenia" (HIT) but does not require heparin itself as a trigger. Most cases occurred 5 to 28 days[3] after receipt of the AZ vaccine, and in women[4] under 60 years old[5].

Available evidence so far, at the time of writing, continues to suggest that **this syndrome is extremely rare**[6] though information continues to evolve.

Because of the rarity of events and potential severity of COVID-19, the European Medicines Agency (EMA) concluded that the overall benefits of the vaccine continue to outweigh the risk. The WHO has also stated that the very rare incidence should be weighed against the risk of morbidity from COVID-19. See WHO statement here. The WHO has stated that a causal relationship, while plausible, has still yet to be confirmed.

[1] https://www.who.int/news-room/feature-stories/detail/the-effects-of-virus-variants-on-covid-19-vaccines
[2] AstraZeneca ChAdOx1-S/nCoV-19 [recombinant]. COVID-19 vaccine (who.int)
[3] https://b-s-h.org.uk/media/19530/guidance-version-13-on-mngmt-of-thrombosis-with-thrombocytopenia-occurring-after-c-19-vaccine_20210407.pdf
[4] Note that additional studies needed on this since many vaccine recipients are women as they fall under the high priority first responders groups such as teachers and healthcare workers being prioritized early for vaccination.
[5] https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood
[6] At the time of writing, Norway has reported a rate of 1 in every 25,000 doses, Germany reported 1 in 100,000 doses, while Europe's overall figures are 1 in 210,000. The UK has reported about 1 in 500,000 doses. Specifically, 169 reported cases of cerebral venous sinus thrombosis (CVST) and 53 cases of splanchnic vein thrombosis were reported in 34 million vaccine recipients in the UK and European Economic Area as of time of writing this document.

Clinical Presentation of VIPIT

Patients with VIPIT may present with cerebral sinus vein thrombosis (CSVT), or with other arterial or venous clots.

Symptoms that make you suspect VIPIT include:

- **persistent and severe headache**
- **focal neurological symptoms**
- **seizures, or blurred or double vision (suggesting CSVT or arterial stroke)**
- **shortness of breath or chest pain (suggesting pulmonary embolism or acute coronary syndrome)**
- **abdominal pain (suggesting portal vein thrombosis) or limb swelling, redness, pallor, or coldness (suggesting deep vein thrombosis or acute limb ischemia).**

VIPIT cases usually present 5 to 28 days[7] after vaccination, so the above symptoms occurring within this time frame should raise clinical suspicion of VIPIT.

What To Do When An Individual Presents with the Above Symptoms

1. Ask patient about their COVID-19 vaccine history and note the date that they received the doses, if any
2. Draw a complete blood count (CBC) from the patient
3. If platelet count is equal or less than 150 x 10^9 /L, **AND** their symptoms occur within 28 days after COVID-19 vaccination, such patients are considered a **suspected case of VIPIT**.
4. **Suspect VIPIT patients need to be further evaluated for VIPIT through D-dimer level and blood films drawn, and imaging (e.g. CT or MRI) to rule out CSVT.**
5. **If such services are not available in your clinic, you need to organize a referral to a local hospital with such services, or medically evacuate for evaluation to rule out VIPIT.**

A summary of these steps is found in Annex 1.

Treatment of VIPIT

Treatment of suspect or confirmed VIPIT requires consultation with a specialist hematologist. However, please bear in mind the following principles for treating such patients:

1. DO NOT give heparin
2. No platelet transfusions
3. Consult a hematologist (in person, virtually, by phone)
4. Give intravenous immunoglobulin 1 g/kg daily for 2 days for severe or life-threatening clots, if available.
5. Use first line anticoagulants: direct oral anti-Xa inhibitors (e.g. rivaroxaban, apixaban, edoxaban)

Until VIPIT has been ruled out, anticoagulation with heparin (both unfractionated heparin and low molecular weight heparins) should **not** be given. Platelet transfusions should **not** be given.

[7] https://b-s-h.org.uk/media/19530/guidance-version-13-on-mngmt-of-thrombosis-with-thrombocytopenia-occurring-after-c-19-vaccine_20210407.pdf

Further information concerning specialized guidance on how to confirm VIPIT diagnosis and its clinical management is available at UK: Guidance Produced from the Expert Haematology Panel (EHP) focused on Covid-19 Vaccine induced Thrombosis and Thrombocytopenia (VITT)

Treatment of VIPIT With Life Threatening Blood Clots

In patients with confirmed VIPIT and severe or life-threatening blood clots (e.g., CSVT, splanchnic vein thrombosis), it is important to administer **high dose intravenous immunoglobulin (IVIG) at 1g/kg of body weight daily for two days** urgently, if available. This treatment should be guided by a consulting hematologist and can be given whilst awaiting confirmatory diagnosis.

Reporting VIPIT

Prompt reporting of such cases amongst UN personnel is essential to learn more about this rare but serious thrombotic phenomenon.

All cases of thrombosis, thrombocytopenia occurring within 28 days of COVID-19 vaccine must be reported immediately to DHMOSH Public Health at dos-dhmosh-public-health@un.org

References

- UK: Guidance Produced from the Expert Haematlogy Panel (EHP) focused on Covid-19 Vaccine induced Thrombosis and Thrombocytopenia (VITT)
- Ontario: Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT) Following AstraZeneca COVID-19 Vaccination
- Interim statement of the COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety on AstraZeneca COVID-19 vaccine
- https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood

Annex 1: Summary of Algorithm for VIPIT