



**Western Cape
Government**

Health

Risk of thrombosis with COVID-19 vaccines

23 April 2021

Acknowledgement: Compiled with support from Dr Z Mohamed,
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Background

- There have been recent reports of blood clots associated with COVID-19 vaccines.
- This presentation will help to clarify what these reports signify
- Initial reports were from Europe and were related only to the Oxford/ AstraZeneca vaccine but more recent reports have included the Johnson and Johnson Janssens vaccine as used in the USA

Are vaccines the cause of these blood clots?

On the 7th of April, the EMA (European Medicines Agency) released a statement asking the manufacturers of the Oxford/ AstraZeneca vaccine to list the combination of unusual blood clots and low platelets as very rare side effects of the vaccine.

<https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood>.

On the same day, the MHRA (the British Medicines Health Regulatory Authority) confirmed that there is a link between the clots and the Oxford/ AstraZeneca vaccination but that more work is needed to investigate it. <https://www.gov.uk/government/news/mhra-issues-new-advice-concluding-a-possible-link-between-covid-19-vaccine-astrazeneca-and-extremely-rare-unlikely-to-occur-blood-clots>.

The WHO also released a statement on the 7th of April about the plausibility of a causal relationship between the Oxford/ AstraZeneca vaccine and the blood clots but asserted that more research is required to confirm this. <https://www.who.int/news/item/07-04-2021-interim-statement-of-the-covid-19-subcommittee-of-the-who-global-advisory-committee-on-vaccine-safety>.

All these organisations have indicated that vaccinations with this vaccine should continue and that the benefits far outweigh the risks.

Blood clots and the Johnson and Johnson COVID-19 vaccine

On 13 April 2021, the FDA and CDC in the USA issued a joint statement pausing the rollout of the Johnson and Johnson COVID-19 vaccine in the USA due to reports of 6 persons (now 8) developing a rare form of blood clot associated with low platelets after 6.8 million vaccinations with this vaccine.

<https://www.cdc.gov/media/releases/2021/s0413-JJ-vaccine.html>

The European Medicines Agency followed suit and so did the South African Government and SAHPRA.

SAHPRA issued a statement on 17 April indicating that the pause will be lifted in South Africa subject to certain conditions. <https://www.sahpra.org.za/news-and-updates/sahpra-statement-update-on-sisonke-phase-3b-implementation-study/>

The EMA issued a statement on 20 April indicating that these clotting events should be listed as rare side effects of this vaccine. <https://www.ema.europa.eu/en/news/covid-19-vaccine-janssen-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood>

The CDC has indicated that they will make a determination about the status of the vaccine on the 23 April 2021 (news reports).

What is Vaccine Induced Thrombosis with Thrombocytopenia (VITT)?

These are blood clots which occur within 3 weeks of vaccination affecting the brain veins (Cerebral Venous Sinus Thrombosis [CVST]) and digestive veins (Splanchnic Venous Thrombosis) and is associated with low platelets.

While thrombotic events such as myocardial infarction and strokes are common, the above combination is highly unusual and has not been seen with the Pfizer and Moderna vaccines.

The most commonly associated condition that manifests in this way is heparin-induced thrombocytopenia with thrombosis (HITT).

The clotting events are similar for the Oxford/ AstraZeneca vaccine and the J&J vaccine.

The mechanism for this condition is that antibodies develop against platelet factor 4 which results in clots and reduced platelet counts. How exactly the vaccines cause this effect is not completely clear.

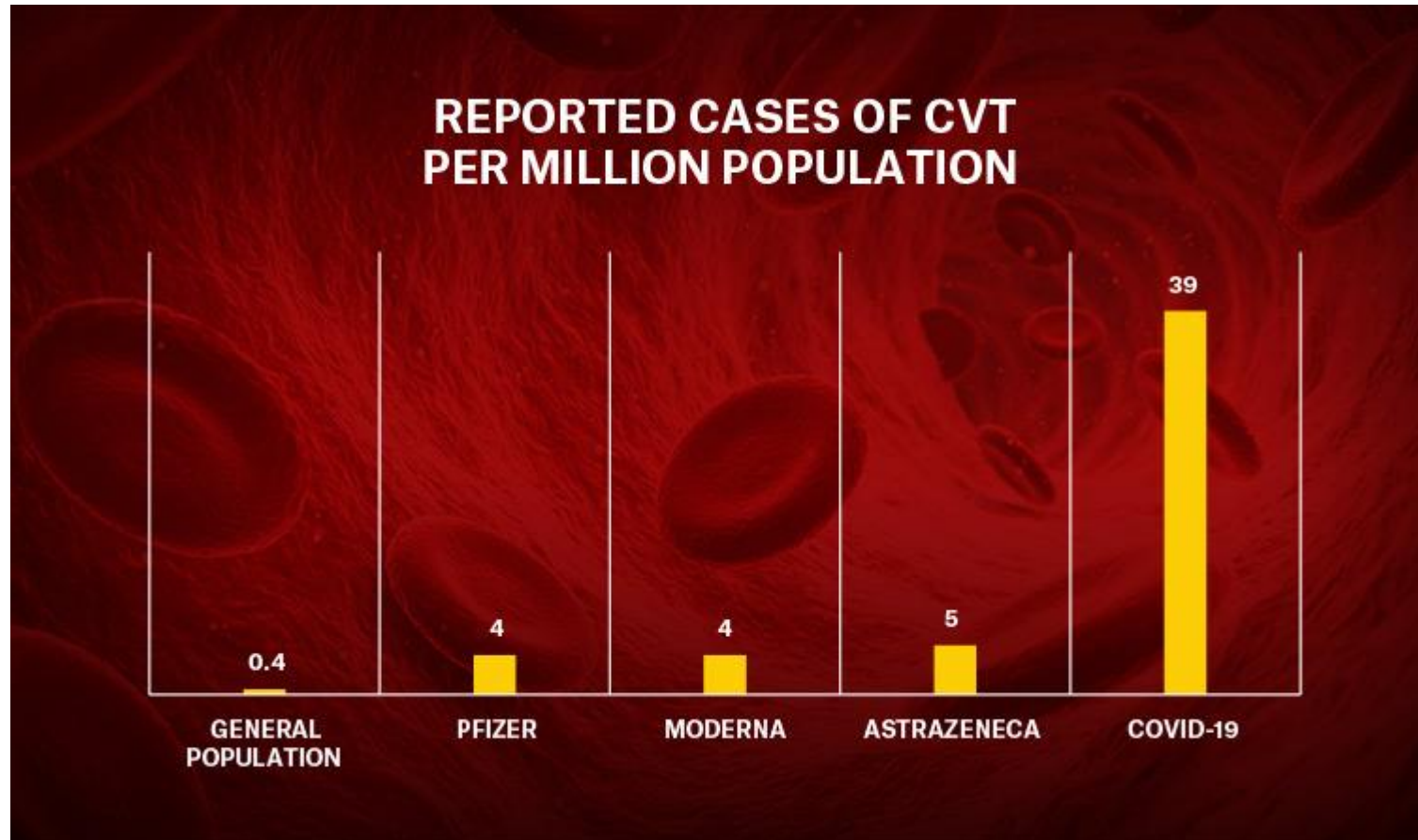
How common does this condition occur with vaccination?

- The latest figures from 04/04/2021, the EMA had recorded 169 cases of central venous sinus thrombosis and 53 cases of splanchnic vein thrombosis out of approximately 34 million vaccinated people = 6.5 cases per million.
- 8 cases so far have been reported amongst 6.8 million vaccinated persons in the US with the Johnson and Johnson vaccine = 1.2 cases per million vaccinated.

“Clotting occurs 30 to 100 times more often with COVID-19 than with these vaccines” – Prof Barry Jacobson, President of the South African Society of Thrombosis and Haemostasis and Wits University

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

Maxime Taquet et al (pre print – still to be peer reviewed)



What symptoms occurs with these clotting conditions?

“Clinical presentation of VITT

The following side-effects that persist or recur >4 days after vaccination should raise clinical suspicion of VITT:

- new and unusual neurological symptoms, such as severe and/ or persistent headache, blurred vision, seizures and/or focal neurological symptoms
- symptoms or signs of thrombosis, such as persistent severe abdominal pain, shortness of breath, chest pain, leg pain or swelling.”

*Recommendations for the diagnosis and management of vaccine-induced immune thrombotic thrombocytopenia. B F Jacobson et al, S Afr Med J. Published online 20 April 2021.
<https://doi.org/10.7196/SAMJ.2021.v111i7>.*

Diagnosis

(Recommendations for the diagnosis and management of vaccine-induced immune thrombotic thrombocytopenia. B F Jacobson et al, S Afr Med J. Published online 20 April 2021. <https://doi.org/10.7196/SAMJ.2021.v111i7>.)

A diagnosis of VITT should only be considered in a patient:

- with a platelet count $<150 \times 10^9/L$, or a decrease in the platelet count of 50%,
- in the presence of symptoms 4 - 16 days after COVID-19 vaccination with adenoviral vector vaccines, namely AstraZeneca and Johnson & Johnson/Janssen.

Other important causes of thrombocytopenia that should be considered include malaria, HIV or immune thrombocytopenia.

In patients with thrombocytopenia and thrombosis, the following differential diagnoses should be considered:

- disseminated intravascular coagulation
- sepsis
- malignancy
- thrombotic microangiopathy
- systemic lupus erythematosus and/or antiphospholipid syndrome
- paroxysmal nocturnal haemoglobinuria
- sickle cell anaemia.

How is it treated?

“Management principles of VITT

The treatment principles are similar to severe HIT. Treatment of suspected or confirmed VITT requires urgent consultation with a clinical haematologist or facility with expertise in thrombosis.

- Platelet transfusions must be avoided.
- Anticoagulation with heparins (including heparin flushes) should be avoided.
- Warfarin should be avoided in the acute period.
- Treatment with high-dose intravenous immunoglobulin (1 g/ kg daily for 2 days) has been recommended. However, its limited availability together with limited data preclude its routine recommended use.
- The platelet count should be closely monitored. Platelet recovery is defined as a platelet count $>150 \times 10^9/L$.
- In the setting of vaccines requiring a second dose, the culprit vaccine should not be re-administered.”

Drug treatment

First-line anticoagulants according to the clinical picture include direct oral anticoagulants (e.g. rivaroxaban, apixaban, dabigatran) or fondaparinux. Most experience in HIT is with rivaroxaban.

For details, please consult:

Recommendations for the diagnosis and management of vaccine-induced immune thrombotic thrombocytopenia. B F Jacobson et al, S Afr Med J. Published online 20 April 2021.

<https://doi.org/10.7196/SAMJ.2021.v111i7>.

What is the way forward?

- Vaccination with these vaccines will continue
- Vaccinees will be informed of these rare side effects prior to vaccination
- There will be enhanced surveillance to detect such cases
- There are recommended clear treatment guidelines for this condition.

The benefits of these vaccines far outweigh the risks of this rare condition.

Thank You & Questions?