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# AMPATH LAB UPDATE

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# COVID-19 vaccine side-effects: The essential facts

## SUMMARY

Social media is flooded with false information regarding the risks associated with the COVID-19 vaccination. Patients often turn to doctors for answers. If we are not able to address their concerns, patients may miss out on this potentially life-saving vaccination.

This is not a comprehensive overview of all the side-effects of the COVID-19 vaccines that are currently used in South Africa, but we will try to address the two most common medical concerns: thrombosis and allergic reactions post-vaccination. We aim to answer the following pertinent questions:

- *Can a patient receive a COVID-19 vaccination if they have a history of previous thrombosis?*
- *Can a patient with known allergies receive a COVID-19 vaccination?*

### Blood clots, COVID-19 and COVID-19 vaccination

#### Advice to patients

One in a million patients may develop a new type of blood clot after vaccination for COVID-19, called vaccination-induced thrombocytopenia with thrombosis (VITT), while a small number may develop arterial or venous thrombosis[1] (1.7 events per 100 000 participants in the South African Sisonke clinical trial, of which all had known risk factors for thrombosis)[1]. The risk of developing a blood clot during a COVID-19 infection is far higher (some studies show an incidence of up to 30% in hospitalised patients with COVID-19). The pathogenesis of thrombosis after vaccination is different from that seen in other thrombosis. Given our current knowledge, vaccination for COVID-19 in a patient with a previous history of thrombosis is not contra-indicated.

Bleeding problems occurring after vaccination are equally rare. A very small number of patients may develop immune thrombocytopenia (ITP), which rarely causes bleeding, even with very low platelet counts. There is no evidence of platelet dysfunction post-vaccination.

COVID-19 infection may be associated with venous and arterial thrombosis due to many proposed mechanisms. Anticoagulation is prescribed for all patients admitted to hospital. It has currently not been proven whether ambulant patients in homecare should be offered anticoagulant prophylaxis. Research studies are currently underway to investigate the use of anticoagulants in ambulant high-risk patients. Prof Barry Jacobson at the University of the Witwatersrand is conducting a study on home-based coagulation in patients older than 30 years of age diagnosed with COVID-19 and with any of the following risk factors: diabetes, COPD, previous venous thromboembolism, liver disease, immunocompromised state, including HIV, anaemia of chronic disease or sickle cell disease, BMI > 25 kg/m$^2$, hypertension or any cardiovascular disease. Please contact Dr Farzanah Laher (cell 082 837 1568) or Prof Jacobson (cell 083 625 6444) should you wish to enrol patients.

Post-discharge prophylaxis is also still being investigated, but the current practice is to continue with prophylactic anticoagulation while high D-dimer values are present. Patients who have had a venous thromboembolic event (VTE) should continue with the normal duration of full anticoagulation for the VTE treatment[2].

Vaccination with COVID-19 vaccines may rarely lead to the development of an antibody directed to a protein present in blood platelets called platelet factor 4 (PF4). This usually develops between 4 and 28 days after vaccination. These antibodies can activate platelets and a serious and potentially fatal thromboembolic state may develop, called vaccine-

induced thrombocytopenia with thrombosis (VITT). Treatment of this type of thrombosis is different to normal VTEs, as no heparin or warfarin should be given. If low platelet counts are present, platelet transfusion should also be avoided. Should the diagnosis of VITT be considered, immediate action is required. Patients should preferably be managed in a unit experienced in managing heparin-induced thrombocytopenia (HITT) cases. A small number of patients (with risk factors for thrombosis) may also develop arterial and venous events (not VITT) and be treated with the standard care, after excluding VITT. No cases of VITT have been reported in South Africa to date.

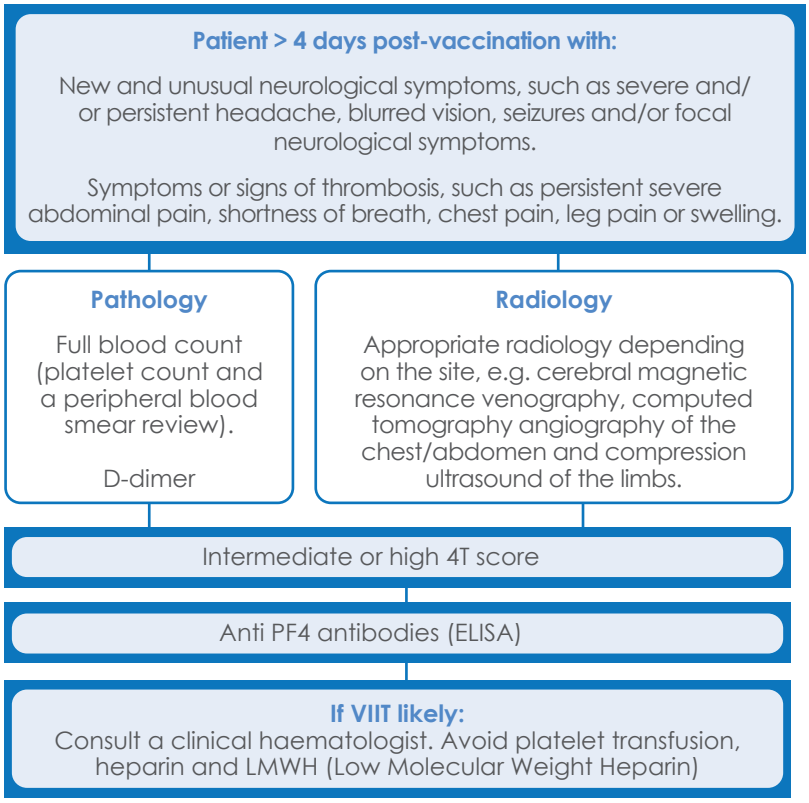
Awareness of the complications of VITT is extremely important. As VITT may be difficult to diagnose, a scoring system is available to guide us. It is called the 4T score (see below) and evaluates time since vaccination, thrombosis present, thrombocytopenia, and whether other reasons are more likely for the thrombosis and thrombocytopenia. Even though this scoring system was initially developed for HITT, it has been adapted for VITT. If the scoring system is positive or clinical indication exists, an anti-PF4 antibody test should be requested. Additional details can be obtained from the South African Society of Thrombosis and Hemostasis (SASTH)'s suggested guideline at http://www.samj.org.za/index.php/samj/article/view/13273.

### 4T scoring system to identify the probability of VITT:

| Variable | Score |
|---|---|
| **Thrombocytopenia** | |
| Platelet count fall >50% | 2 |
| Platelet count fall 30–50% | 1 |
| Platelet count fall <30% | 0 |
| **Timing of onset** | |
| Within 4–16 days | 2 |
| >2 weeks after vaccination or unclear exposure | 1 |
| No history of vaccination | 0 |
| **Thrombosis** | |
| New thrombosis post-vaccination | 2 |
| Progressive of recurrent thrombosis | 1 |
| No thrombosis | 0 |
| Other causes of thrombocytopenia | |
| None | 2 |
| Possible | 1 |
| Definite | 0 |
| **TOTAL SCORE** | |
| **0–3** | **Low probability of VITT** |
| **4–5** | **Intermediate probability of VITT** |
| **6–8** | **High probability of VITT** |

A suggested flow diagram follows that may guide the management of this extremely rare post-vaccination complication.

### Vaccine-induced thrombosis/thrombocytopenia




### Severe allergic reactions to COVID-19 vaccines

#### Advice to patients

Anaphylaxis is a severe, immediate, life-threatening reaction that occurs rarely following vaccination.

Between **2.4 and 4.7 in one million patients** may develop a severe allergic reaction after receiving an mRNA vaccine (e.g. Pfizer/BioNTech) and **less than 1 in a million** patients may develop such a reaction after receiving an adenoviral vector vaccine (e.g. Johnson & Johnson) for COVID-19.

The risk of developing a severe allergic reaction to adenoviral vector vaccines is similar to that of common vaccines in use today, e.g. influenza, Hepatitis B and tetanus.

The most likely offending agents in the Pfizer/BioNtech vaccine are Polyethylene glycol (PEG) 2000 and Polysorbate 80 in the Johnson & Johnson vaccine. COVID-19 vaccines do not contain other known agents associated with vaccine-induced anaphylaxis, such as gelatins or egg proteins.

Anaphylaxis or severe vaccine allergies usually occur soon after vaccination (within five to 30 minutes), and can be successfully treated on site. Patients will be questioned before vaccination regarding previous episodes of anaphylaxis or severe allergy to other vaccines and injectable drugs. If patients are considered to be at risk of a severe allergic reaction post-vaccination, they should be sent for testing to determine whether they could safely receive the vaccine.

High-risk patients will be observed for at least 30 minutes after vaccination to monitor the development of potential allergic reactions. Well-controlled asthma, hay fever and other mild allergies are not risk factors for COVID-19 vaccination and are therefore not contra-indications to vaccination.

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Please contact your local Ampath pathologist for more information.

Patients with the potential risk of a severe allergic reaction or anaphylaxis to a COVID-19 vaccine should be identified and sent for workup before vaccination. The following questions can assist in identifying patients at risk and direct appropriate management and vaccination:

1. Have you had an immediate (<4 hours) or severe allergic reaction (anaphylaxis) to Polyethylene glycol (PEG) or Polysorbate 80?
2. Have you had a severe allergic reaction (anaphylaxis) to any injectable medication or a vaccine?
3. Have you had a severe reaction (anaphylaxis) to any allergen (e.g. food, venom, etc.)?
4. Do you suffer from mastocytosis or mast cell activation syndrome?
5. Do you suffer from any other allergies like asthma or hay fever?

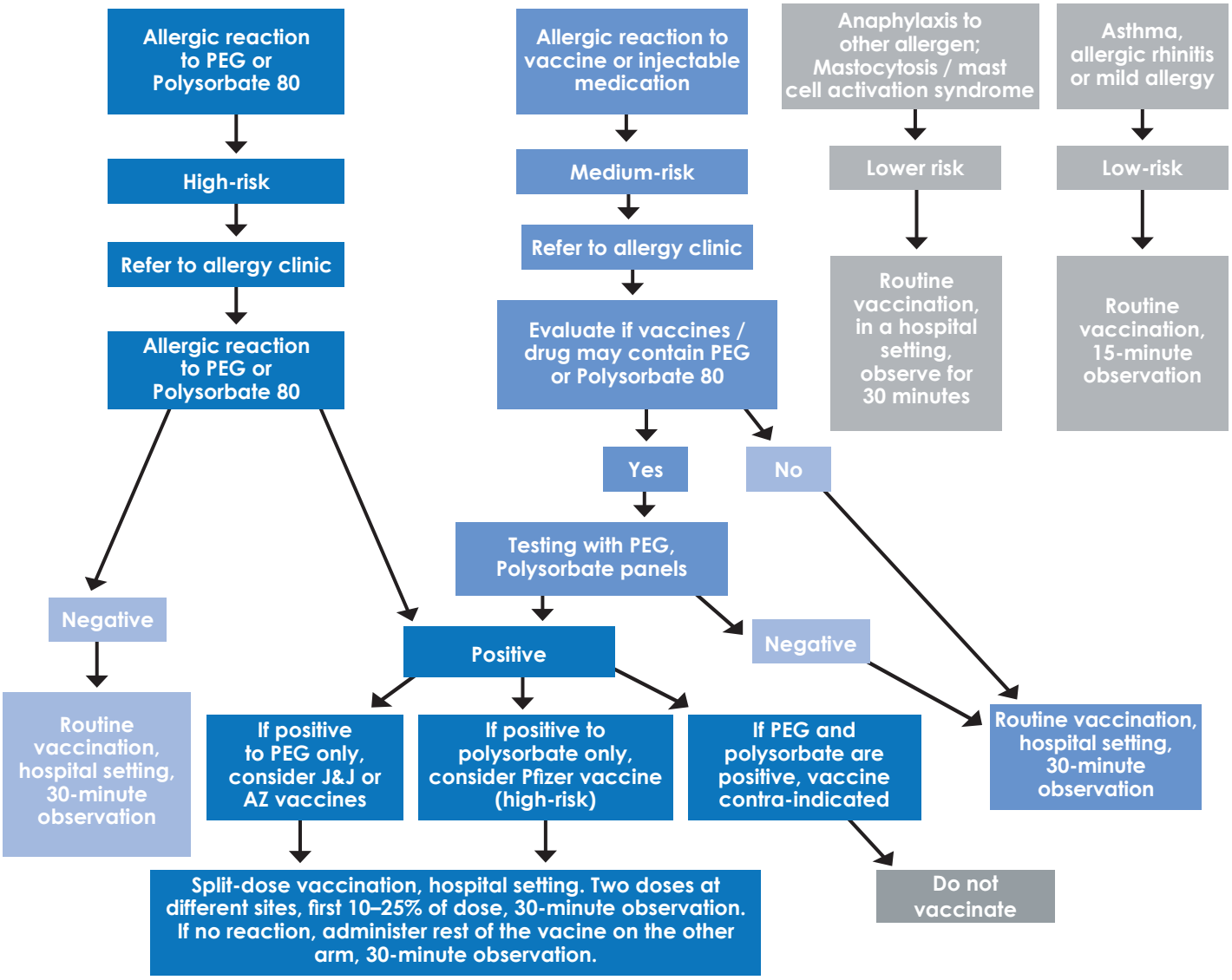
The answers to these questions can help guide clinicians on which patients need to be considered for referral to an allergy clinic or other appropriate testing facility.

Patients who answer in the affirmative to question 1 or 2 should be referred for allergy workup. Patients who answer in the affirmative to questions 3 or 4 can be vaccinated in hospital-based centres with observation for at least 30 minutes after vaccination. However, patients with well-controlled asthma, hay fever and minor allergies (answered yes to question 5 only) can be vaccinated in any other setting, including pharmacies, with 15-minute observations.

Patients referred for testing should receive appropriate allergy testing to PEG or Polysorbate 80-containing vaccines or compounds. Skin prick testing panels are currently used, which consist of other vaccines or drugs containing similar excipients. Specific commercial allergy tests to these excipients should become available in the near future and will be incorporated into testing protocols.

Please refer to the flow diagram below for guidance on the appropriate management of a patient suspected to be at risk of a severe allergic reaction or anaphylaxis post-COVID-19 vaccination[3&4]:

## Approach to COVID-19 vaccine allergy

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If a patient should develop a severe allergic reaction or anaphylaxis after receiving a dose of COVID-19 vaccine, a clotted blood sample (SST tube) should always be taken between 30 minutes and four hours after the reaction for mast cell tryptase measurement. Tryptase is maintained at a baseline level in all healthy individuals. A baseline mast cell tryptase should also be requested at least 24 hours after the anaphylaxis, as a fourfold increase above baseline is diagnostic for anaphylaxis.

## CONCLUSION

**It is essential that COVID-19 vaccination proceeds safely, but with as few barriers as possible, as widespread vaccination is a key intervention in the control of this pandemic. Both doctors and patients need access to reliable information and reassurance to enable us to achieve this aim.**

***References***


1. Simbarashe Takuva, Azwidhwi Takalan, Nigel Garrett et al. Thromboembolic events in the South African Ad26.COV2.S Vaccine Study. *The New England Journal of Medicine* published online, accessed June 3, 2021.
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3. Turner P J, Ansotegui I J, Campbell D E et al. COVID-19 vaccine-associated anaphylaxis: A statement of the World Allergy Organization Anaphylaxis Committee. Feb 2021. *WAO Journal* 14(2). (https://doi.org/10.1016/j.waojou.2021.100517).
4. Banjeri A, Wickner P G, Staff R et al. mRNA vaccine to prevent COVID-19 disease and reported allergic reactions: current evidence and suggested approach. December 30, 2020. *JACI: In Practice*. (https://doi.org/10.1016/j.jaip.2020.12.047).


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