PHAC: COVID-19 Vaccine Emerging Issues Webinar: Vaccine-induced Immune Thrombotic Thrombocytopenia (VITT)

Speaker: Dr. Menaka Pai
Moderator: Dr. Marina Salvadori, PHAC

Zoom

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Public Health Agency of Canada | Agence de la santé publique du Canada

Thrombosis Canada | Thrombose Canada

Vaccine-induced Immune Thrombotic Thrombocytopenia (VITT) following ChAdOx1 nCov-19 Vaccination

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Declaration of interest

- I have no financial conflicts of interest to declare
- I have no intellectual conflicts of interest to declare

What we'll cover today

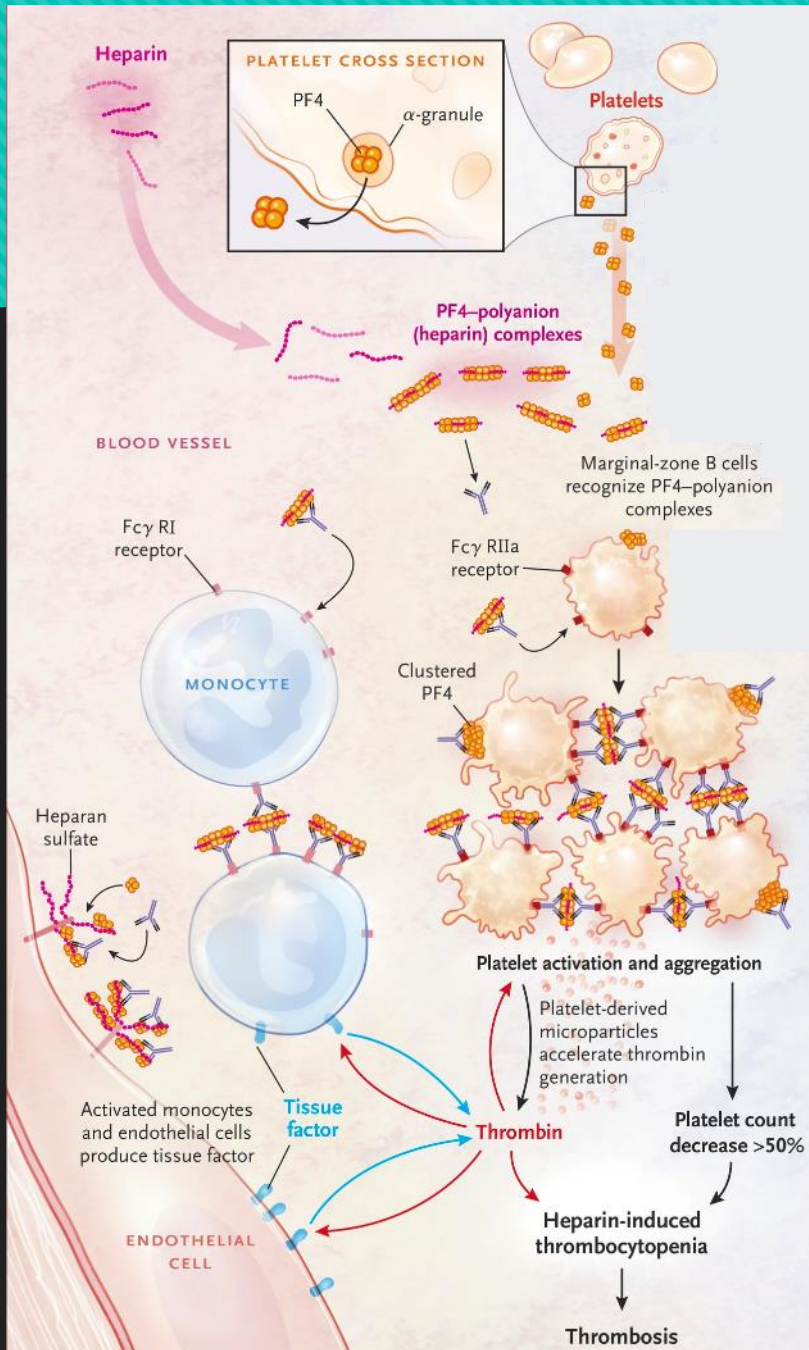
- What is VITT?
- How do I rapidly identify VITT?
- How do I treat VITT?
- Next steps and unanswered questions

A “typical” case

- 56 year old woman who received COVISHIELD (ChAdOx1 nCov-19) vaccine 12 days ago at her local pharmacy
- Presents to her family physician with severe headache, diplopia
- No medical history, no family history, no medications
- Presenting platelet count: 31 x 10^9/L (normal 150 – 400 x 10^9/L)
- **What’s going on? And does the vaccine she received have anything to do with it?**

What is VITT?

- Newly described syndrome: **thrombosis** and **thrombocytopenia**, in a typical **timeframe** after vaccination
  - Thromboses generally in unusual sites
  - Thrombocytopenia generally dramatic
  - Patients generally healthy before presentation
- Case fatality high (40%) in reported cases
- Pathophysiology?
  - Antibodies to platelet factor 4-polyanion complexes



Greinacher A. NEJM 2015; 373:252-261

If your jurisdiction uses the ChAdOx1 nCov-19 vaccine, be aware of VITT

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SCIENCE TABLE
COVID-19 ADVISORY FOR ONTARIO

SCIENCE BRIEFS

Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT) Following AstraZeneca COVID-19 Vaccination

Menaka Pai, Allan Grill, Noah Ivers, Antonina Maltsev, Katherine J. Miller, Fahad Razak, Michael Schull, Brian Schwartz, Nathan M. Stall, Robert Steiner, Sarah Wilson, Ullanda Niel Zax, Peter Jüni, Andrew M. Morris on behalf of the Drugs & Biologics Clinical Practice Guidelines Working Group and the Ontario COVID-19 Science Advisory Table

Version 1.0

Published: March 26, 2021

Citation: Pai M, Grill A, Ivers N, et al. Vaccine-induced prothrombotic immune thrombocytopenia VIPIT following AstraZeneca COVID-19 vaccination. *Science Briefs of the Ontario COVID-19 Science Advisory Table*. 2021;1(17). https://doi.org/10.47326/ocsat.2021.02.17.1.0

Key Message

This Science Brief provides information for health care professionals about Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT), a rare adverse event following the AstraZeneca COVID-19 vaccine.

This brief describes the pathophysiology, presentation, diagnostic work-up and treatment of VIPIT. Figure 1 presents a decision tree for diagnosing and ruling out VIPIT.

Review Article

Diagnosis and Management of Vaccine-Related Thrombosis following AstraZeneca COVID-19 Vaccination: Guidance Statement from the GTH

Johannes Oldenburg[1] Robert Klamroth[2] Florian Langer[3] Manuela Albisetti[4] Charis von Auer[5] Cihan Ay[6] Wolfgang Korte[7] Rüdiger E. Scharf[8] Bernd Pötzsch[1] Andreas Greinacher[9]

The Royal College of Emergency Medicine

sam THE SOCIETY FOR ACUTE MEDICINE

Royal College of Physicians

Guidance agreed with Expert Haematology Panel (EHP) April 10th 2021
Guidance agreed with British Society of Neuroradiologists (BSNR) and RCR April 11th 2021

The challenge: quickly rule VITT in (or out) and initiate life saving treatment

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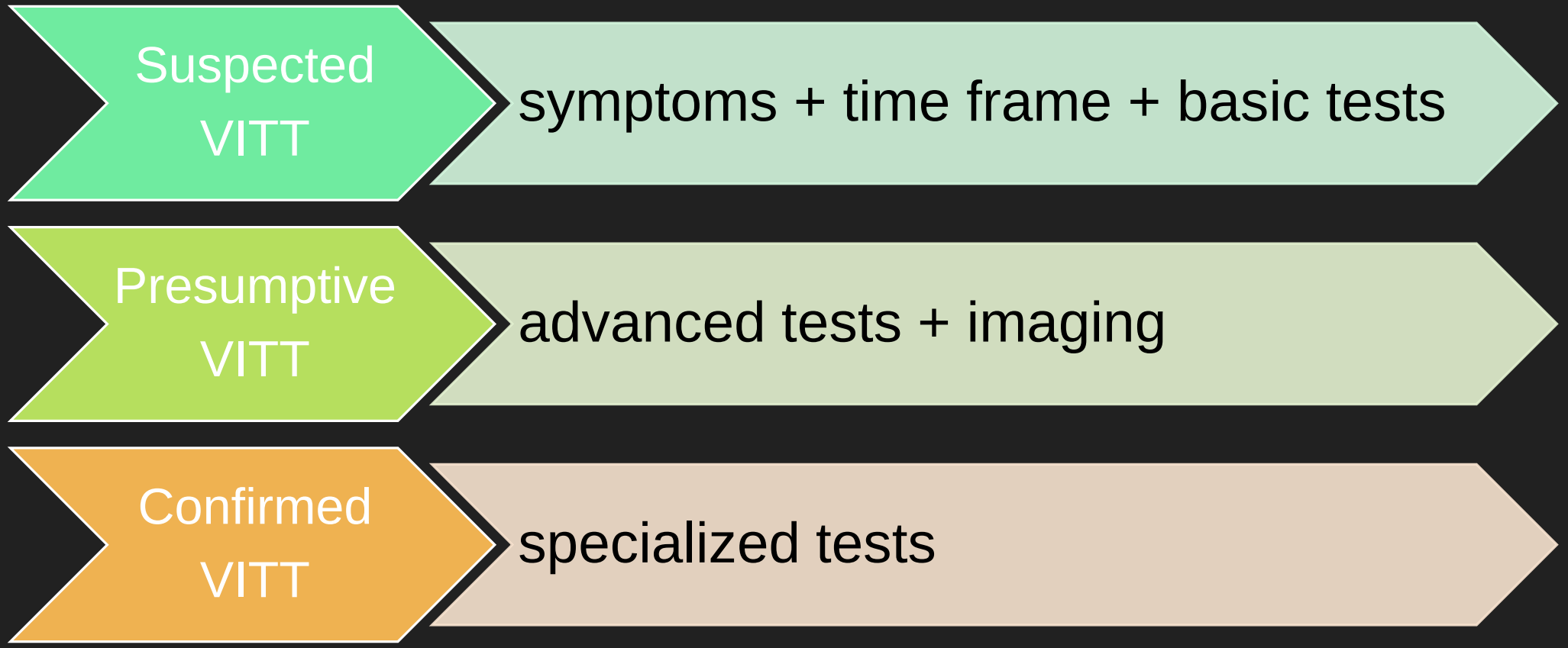

Pai M, Grill A, Ivers N, et al. Vaccine induced prothrombotic immune thrombocytopenia VIPIT following AstraZeneca COVID-19 vaccination. *Science Briefs of the Ontario COVID-19 Science Advisory Table*. 2021;1(17). https://doi.org/10.47326/ocsat.2021.02.17.1.0

Be aware of TYPICAL symptoms in a TYPICAL time frame after vaccination

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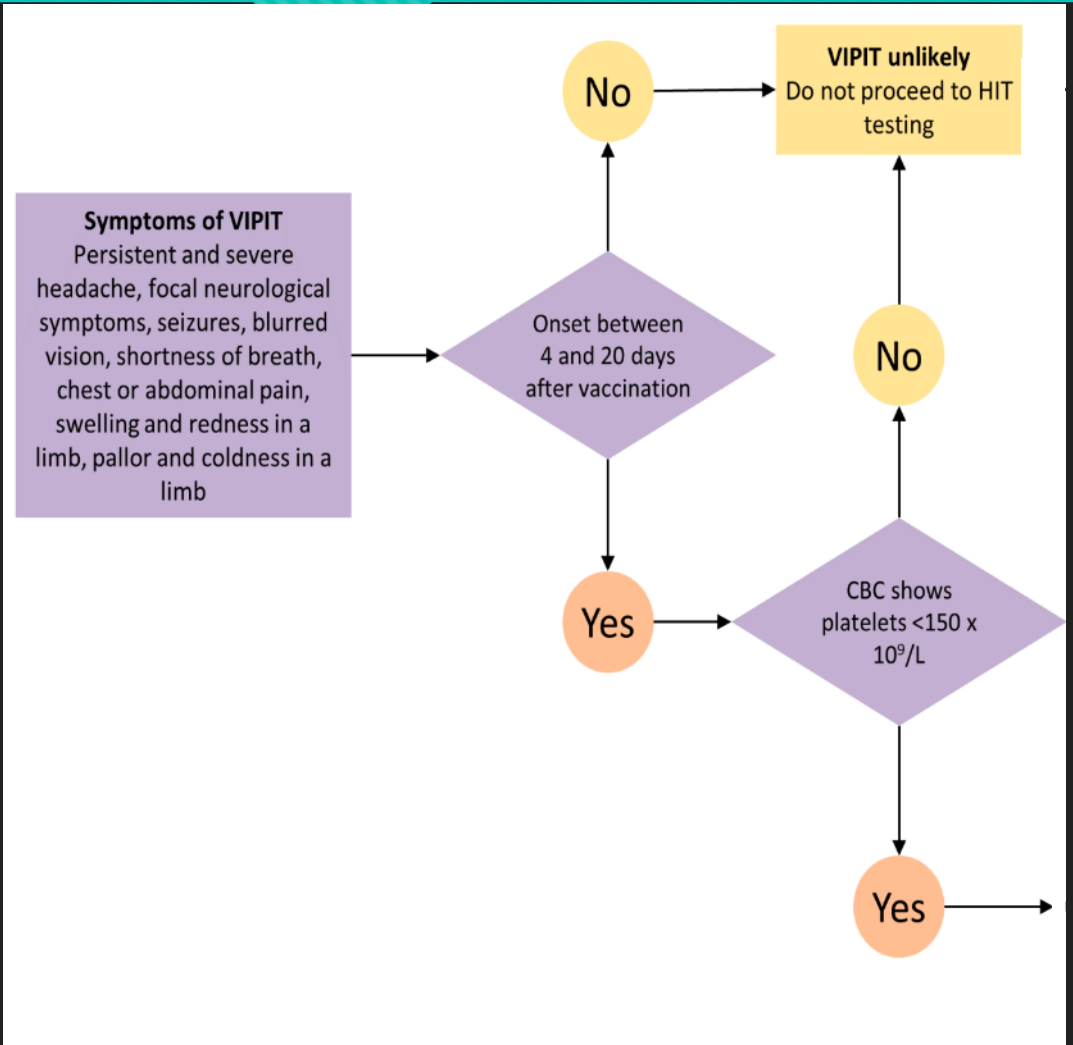
- Typical symptoms of arterial or venous clots
  - Persistent and severe headache, focal neurological symptoms, seizures, blurred or double vision (suggesting cerebral vein thrombosis or arterial stroke)
  - Shortness of breath or chest pain (suggesting pulmonary embolism or acute coronary syndrome)
  - Abdominal pain (suggesting splanchnic thrombosis)
  - Limb swelling, redness, pallor, or coldness (suggesting deep vein thrombosis or acute limb ischemia)
- Typical time frame is 4 to 28 days post-vaccination

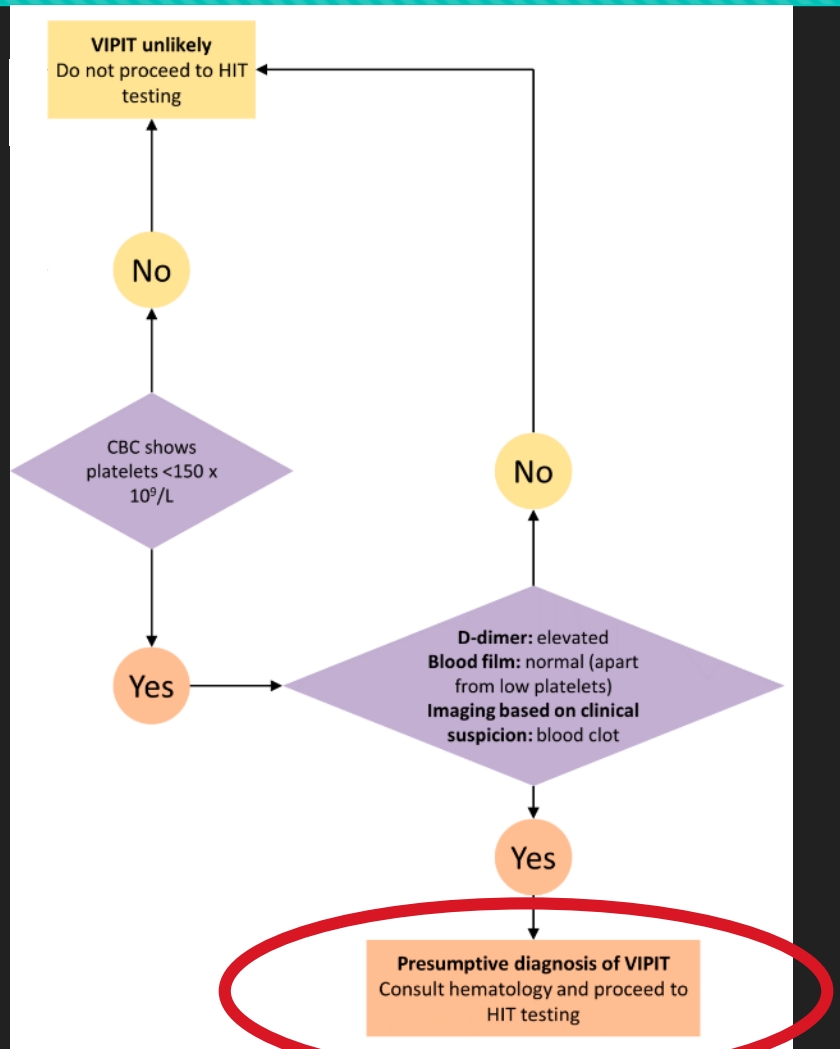
Pai M, Grill A, Ivers N, et al. Vaccine induced prothrombotic immune thrombocytopenia VIPIT following AstraZeneca COVID-19 vaccination. *Science Briefs of the Ontario COVID-19 Science Advisory Table*. 2021;1(17). https://doi.org/10.47326/ocsat.2021.02.17.1.0

Suspected diagnosis?
Focus on basic testing with high NPV



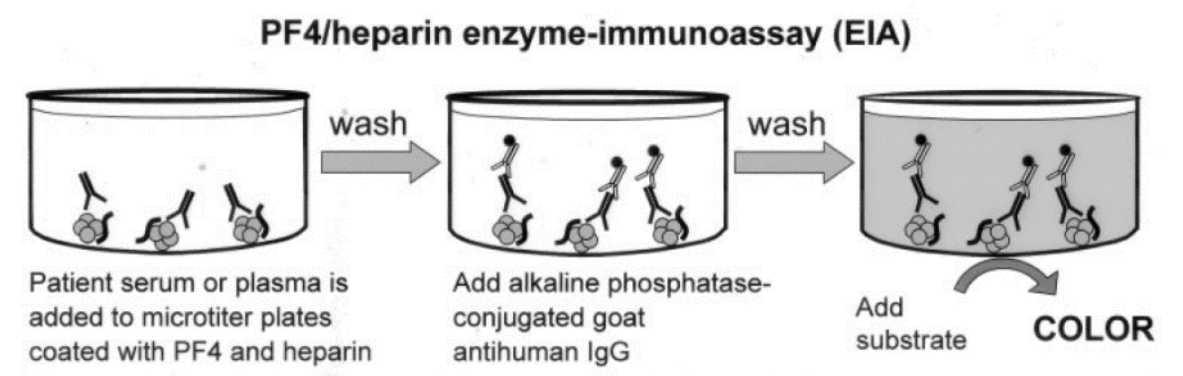
- Key questions:
  - Symptoms?
  - Date of the vaccine?
- Key diagnostics:
  - Complete blood count (CBC)

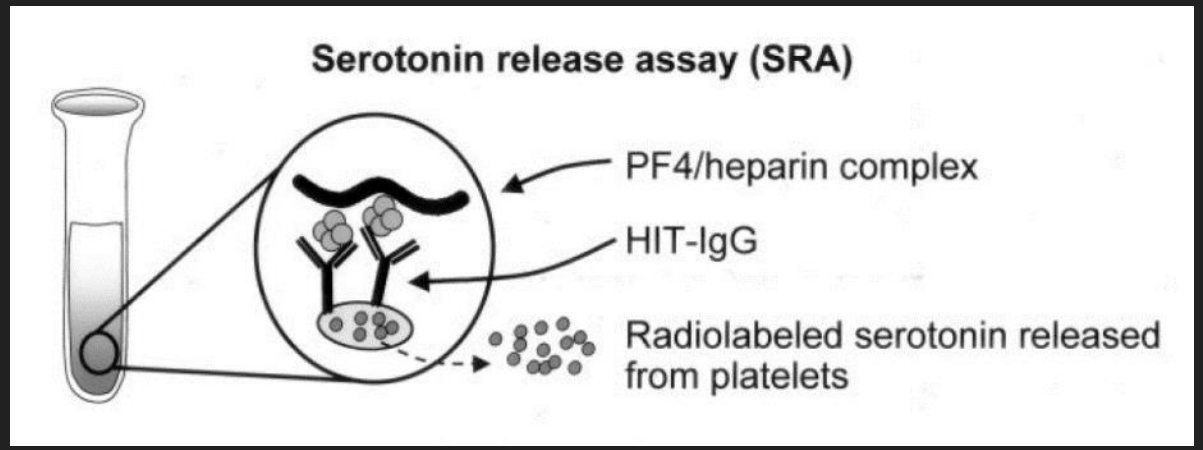
Presumptive diagnosis?
Focus on advanced tests and imaging



- Key diagnostics:
  - D-dimer (> 2000 mcg/mL FEU or DDU)
  - Blood film should show only thrombocytopenia
    - Mimickers may have other abnormalities
  - Imaging
    - Non-contrast CT brain not sensitive enough to rule out CSVT in setting of hematologic findings and suggestive symptoms
    - CT venogram is rapid, accessible, and accurate
    - MR/MR venography may be a practical alternative

HIT testing: immunobinding and functional assays





Enzyme-immunoassay is required as rapid assays seem to be insensitive

IVIG may inhibit reaction, so draw samples before infusion

National Platelet Immunology Lab at McMaster University:
https://fhs.mcmaster.ca/plateletimmunology/documents/VIPIT_test_requisition.pdf

Warkentin TE, Sheppard J. Transfus Med Rev. 2006 Oct;20(4):259-72.

Initial management: anticoagulation and managing the immune reaction

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Hematology consultation + HIT ELISA

- NO heparin
- NO platelet transfusions
- First line anticoagulation:
  - Direct oral anti-Xa inhibitors
  - If patient unstable, or renal function is impaired, consider parenteral anticoagulants
- IVIG 1 g/kg daily for 2 days for severe or life-threatening blood clots
- **Report to Public Health and Health Canada**

Pai M, Grill A, Ivers N, et al. Vaccine induced prothrombotic immune thrombocytopenia VIPIT following AstraZeneca COVID-19 vaccination. *Science Briefs of the Ontario COVID-19 Science Advisory Table*. 2021;1(17). https://doi.org/10.47326/ocsat.2021.02.17.1.0

Many questions remain – for clinicians, regulators, and the public

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- When do we use second line treatment (steroids, plasma exchange)?
- Do these antibodies persist?
- How do we monitor patients at discharge?
- What are the implications for the second dose of AZ and other vaccinations?
- Is this the same as the adverse events reported after the J&J vaccine?

https://covid19-sciencetable.ca/

Evidence based scientific and lay summaries, and focused clinical guidance

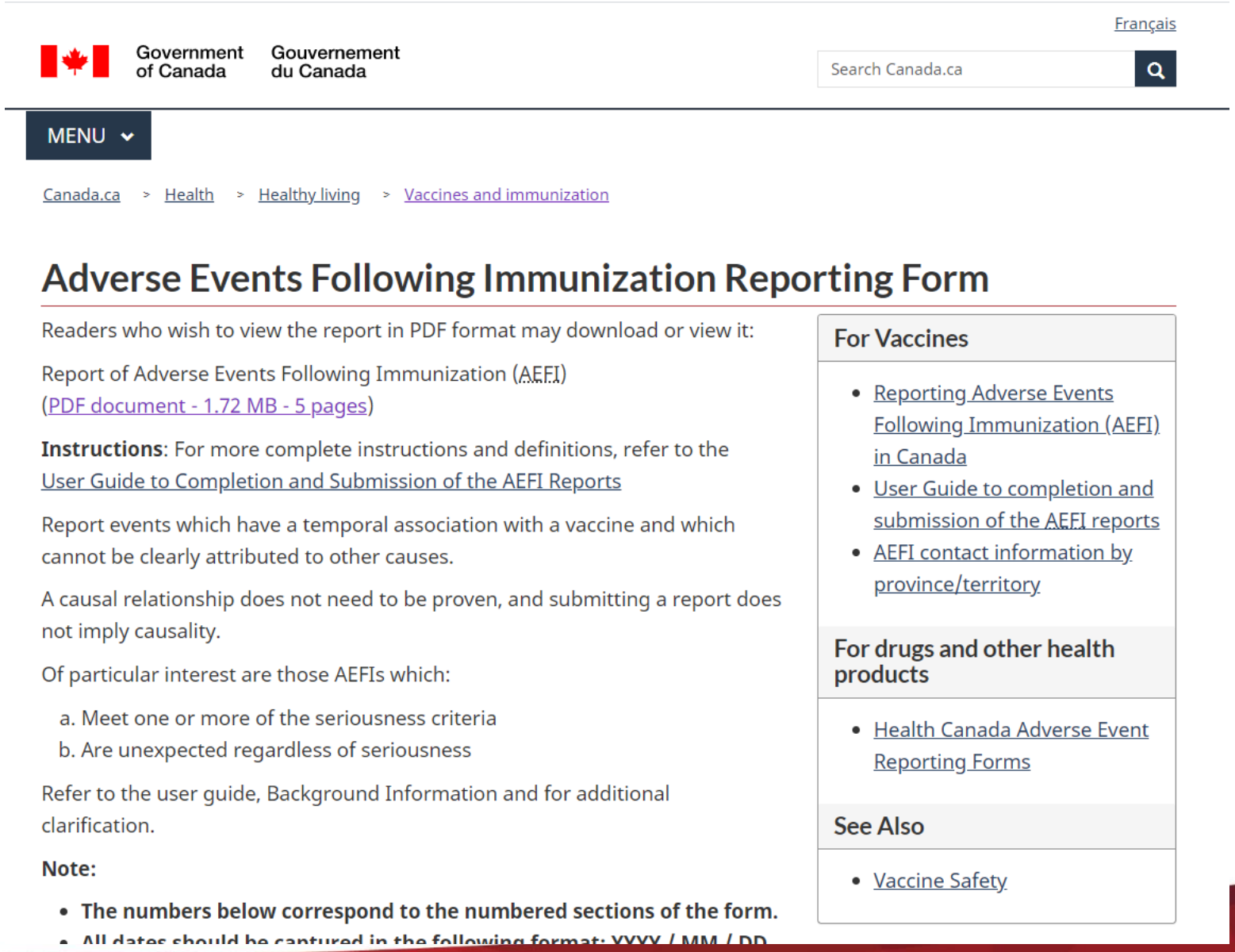
Thank you for your attention, and for your continued efforts during the pandemic

Reporting and Adverse Event Following Immunization (AEFI):

- How to report an AEFI: https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization.html

- AEFI report form: Reporting Adverse Events Following Immunization (AEFI) in Canada

- Submission of AEFI reports: User guide to completion and submission of the AEFI reports



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Adverse Events Following Immunization Reporting Form

Readers who wish to view the report in PDF format may download or view it:

Report of Adverse Events Following Immunization (AEFI)
(PDF document - 1.72 MB - 5 pages)

Instructions: For more complete instructions and definitions, refer to the User Guide to Completion and Submission of the AEFI Reports

Report events which have a temporal association with a vaccine and which cannot be clearly attributed to other causes.

A causal relationship does not need to be proven, and submitting a report does not imply causality.

Of particular interest are those AEFIs which:

a. Meet one or more of the seriousness criteria
b. Are unexpected regardless of seriousness

Refer to the user guide, Background Information and for additional clarification.

Note:

- **The numbers below correspond to the numbered sections of the form.**
- **All dates should be captured in the following format: YYYY / MM / DD**

For Vaccines

- Reporting Adverse Events Following Immunization (AEFI) in Canada
- User Guide to completion and submission of the AEFI reports
- AEFI contact information by province/territory

For drugs and other health products

- Health Canada Adverse Event Reporting Forms

See Also

- Vaccine Safety

NACI Statement on COVID-19 Vaccines

- Refer to NACI recommendations on the use of COVID-19 vaccines for guidance on COVID-19 vaccines.

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> National Advisory Committee on Immunization (NACI): Statements and publications

Recommendations on the use of COVID-19 vaccines

Publication date: January 12, 2021

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  - Vaccine safety and adverse events following immunization (AEFI)
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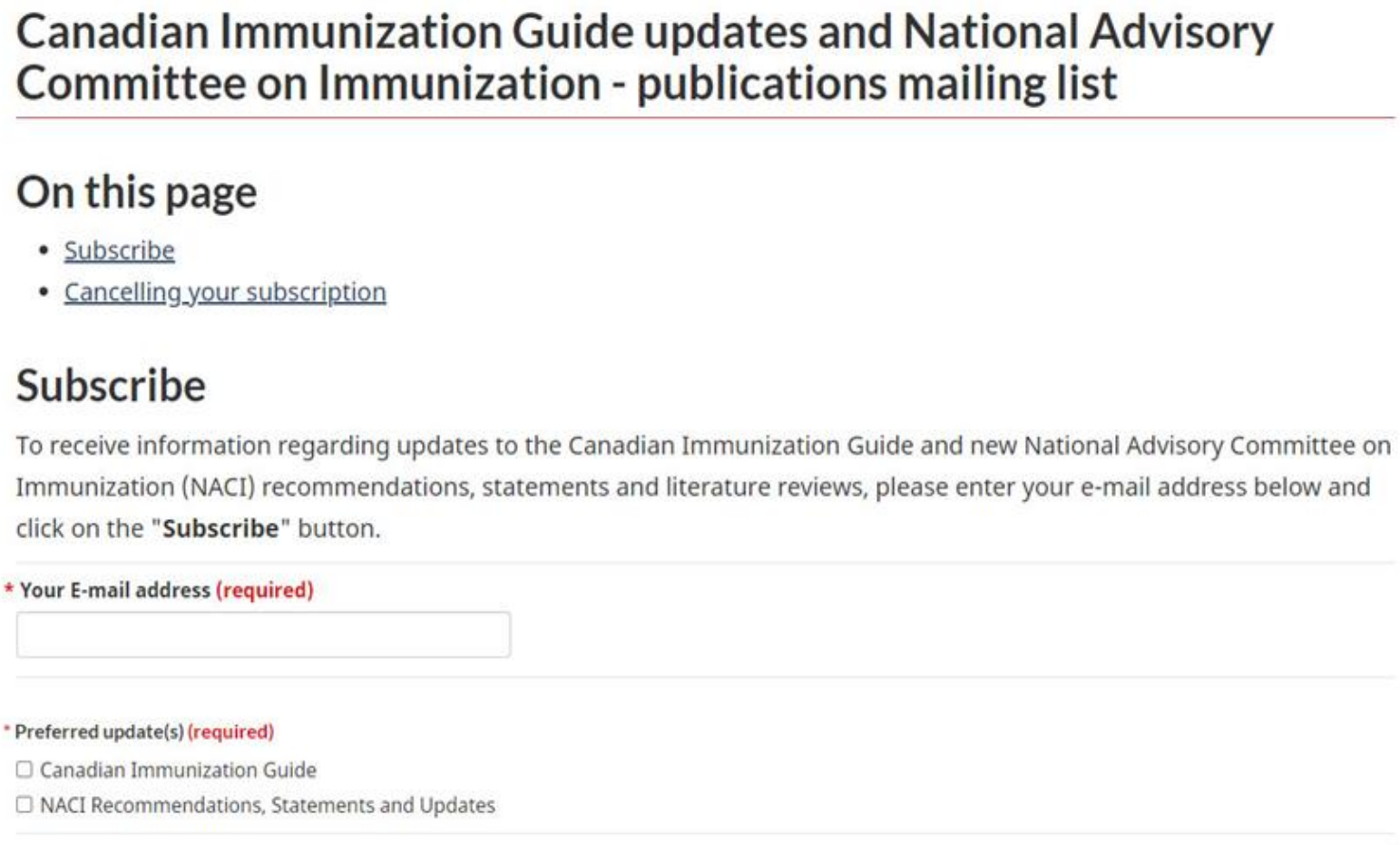

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