

# Heparin-induced thrombocytopenia

Stefan D. Jevtic MD, Andrew M. Morris MD SM(Epi), Theodore E. Warkentin MD, Menaka Pai MD MSC

■ Cite as: *CMAJ* 2021 May 17;193:E736. doi: 10.1503/cmaj.210637; early-released April 27, 2021

## 1 About 0.2% of patients exposed to heparin develop heparin-induced thrombocytopenia (HIT)

Heparin-induced thrombocytopenia is an uncommon condition mediated by anti-PF4 platelet-activating antibodies that typically begins 5–14 days after heparin initiation. Overall, greater risk is associated with unfractionated heparin than with low-molecular-weight heparin.<sup>1</sup>

## 2 This acquired hypercoagulable state carries a high risk of venous and arterial thrombosis

The platelet count nadir ranges from 10 to 150 (median: about 60)  $\times 10^9/L$ , or a drop of 50% or more.<sup>1</sup> As many as 70% of patients with HIT experience thrombosis, most often deep-vein thrombosis, pulmonary embolism or both, but also arterial thrombosis.<sup>1</sup>

## 3 A 4Ts score > 3 should prompt antibody screening and, if positive, a platelet activation assay

A 4Ts score estimates pretest probability of HIT compared with other causes of thrombocytopenia, assessing platelet count, timing, sequelae and causes.<sup>2</sup> Screening is usually performed by immunologic assays (e.g., enzyme-linked immunosorbent assay [ELISA]). If positive, a confirmatory platelet activation test (e.g., serotonin-release assay) is required as many patients with a positive ELISA result do not have HIT.

## 4 If HIT is suspected, heparin should be stopped and alternative anticoagulation started

Warfarin should be avoided and vitamin K administered if warfarin has already been given, because of the risk of warfarin-associated microthrombosis.<sup>3</sup> Factor Xa inhibitors (fondaparinux, apixaban, rivaroxaban) and thrombin inhibitors (argatroban, bivalirudin, dabigatran) should be considered if the patient needs anticoagulation. Intravenous immunoglobulin may be beneficial in atypical, severe HIT.<sup>4</sup> Patients should be referred to a hematologist if possible.

## 5 Vaccine-induced immune thrombotic thrombocytopenia (VITT) is an uncommon complication of the SARS-CoV-2 vaccine produced by AstraZeneca (ChAdOx1 nCoV-19) that mimics severe HIT in patients without exposure to heparin

Clinical features of VITT include thrombocytopenia and unusual thrombi, including cerebral venous sinus thrombosis and splanchnic vein thrombosis.<sup>5</sup> A 4Ts score, substituting “vaccine” for “heparin,” can be used. Treatment for VITT is similar to that for HIT but emphasizes high-dose intravenous immunoglobulin. Diagnostic testing for VITT antibodies is available in Canada (McMaster Platelet Immunology Laboratory, in Hamilton, Ont.).

## References

1. Warkentin TE, Roberts RS, Hirsh J, et al. An improved definition of immune heparin-induced thrombocytopenia in postoperative orthopedic patients. *Arch Intern Med* 2003;163:2518-24.
2. Cuker A, Gimotty PA, Crowther MA, et al. Predictive value of the 4Ts scoring system for heparin-induced thrombocytopenia: a systematic review and meta-analysis. *Blood* 2012;120:4160-7.
3. Warkentin TE, Elavathil LJ, Hayward CPM, et al. The pathogenesis of venous limb gangrene associated with heparin-induced thrombocytopenia. *Ann Intern Med* 1997;127:804-12.
4. Warkentin TE. High-dose intravenous immunoglobulin for the treatment and prevention of heparin-induced thrombocytopenia: a review. *Expert Rev Hematol* 2019;12:685-98.
5. Greinacher A, Thiele T, Warkentin TE, et al. Thrombotic thrombocytopenia after ChAdOx1 nCoV-19 vaccination. *N Engl J Med* 2021 Apr. 9 [online release]. Available: <https://doi.org/10.1056/NEJMoa21048402021> (accessed 2021 Apr. 15).

**Competing interests:** Theodore Warkentin reports receiving grants from Instrumentation Laboratory, royalties from Informa (Taylor & Francis), consulting fees from Aspen Global and Ergomed, lecture honoraria from Alexion Canada and Instrumentation Laboratory, and payment for providing expert witness testimony relating to heparin-induced thrombocytopenia (HIT) and non-HIT thrombocytopenic and coagulopathic disorders. Dr. Warkentin has participated on advisory boards for CSL Behring and Octapharma and been a member of a committee on disseminated intravascular coagulation for the International Society on Thrombosis and Haemostasis. Menaka Pai reports receiving royalties from UpToDate and support for attending a conference from Scripps. No other competing interests were declared.

This article has been peer reviewed.

**Affiliations:** Departments of Medicine (Jevtic, Warkentin, Pai) and Pathology and Molecular Medicine (Warkentin), McMaster University, Hamilton, Ont.; Department of Medicine (Morris), Sinai Health, University Health Network; Faculty of Medicine (Morris), University of Toronto, Toronto, Ont.

**Content licence:** This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY-NC-ND 4.0) licence, which permits use, distribution and reproduction in any medium, provided that the original publication is properly cited, the use is noncommercial (i.e., research or educational use), and no modifications or adaptations are made. See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>

**Correspondence to:** Menaka Pai, [mpai@mcmaster.ca](mailto:mpai@mcmaster.ca)