



# Clinical Pharmacology & Toxicology Pearl of the Week

## Heparin-Induced Thrombocytopenia and Thrombosis (HITT)

- ✓ Heparin-induced thrombocytopenia (HIT) is a transient condition resulting in a decrease of platelet count after several days of heparin therapy due to immune-mediated platelet aggregation. It occurs in up to 5% of patients.
- ✓ HITT, the more severe form of the syndrome, occurs in 1-5% of patients on heparin. Its hallmark is thrombotic events in the setting of thrombocytopenia.
- ✓ HIT/HITT occurs more commonly with unfractionated heparin compared to low molecular weight heparin
- ✓ Treatment is avoidance of heparin-based medications.

### Mechanism of HITT

- ✓ Heparin stimulates the release of platelet factor 4 (PF4) from platelets, which forms a complex with heparin
- ✓ IgG antibodies against the heparin-PF4 complex can develop, leading to activation of platelets and prothrombotic cascades that lead to development of platelet-fibrin-mediated thrombotic events.
- ✓ This IgG-mediated response is what causes platelet aggregation and the hallmark of HITT → thrombocytopenia
- ✓ Left untreated, up to 55% of patients with HIT go on to develop the second 'T' and develop Thrombosis.

### Signs and Symptoms of HITT

- ✓ Presents at least five days after heparin administration, but can present earlier with recent exposure to heparin.
- ✓ Mild symptoms include rash or discomfort at site of injection, which can worsen into necrotic tissue
- ✓ Patients can present with hemorrhagic or thromboembolic features (venous more common than arterial)
  - Hemorrhagic: epistaxis, bleeding gums, hematemesis, hematochezia, melena
  - Thromboembolic: pain/redness/swelling of an extremity, weakness/numbness/decreased mobility of an arm or leg, chest pain, shortness of breath, ischemic necrosis of digits
  - Enlargement or extension of a previously diagnosed thrombus, or development of a new blood clot elsewhere

### Diagnosis and investigations

- ✓ 4T score – prediction tool (see table)
  - 0-3: HITT **unlikely**
  - 4-5: **intermediate** probability
  - 6-8: **high likelihood** of HITT
- ✓ HITT Immunoassay for Anti-PF4-heparin antibodies
- ✓ Confirmatory Serotonin Release assay if HITT test is +
- ✓ Consider assessing for DVT/VTE in asymptomatic patients at high probability as this affects duration of anticoagulation.
- ✓ Assess for OTHER causes of low platelets

Element	2 Points	1 Point	0 Points
Thrombocytopenia	Platelet count decreased >50% AND nadir $\geq 20 \times 10^9/L$	Platelet count 30-50% decreased OR nadir 10-19 $\times 10^9/L$	Platelet count decreased <30% or nadir <10 $\times 10^9/L$
Timing	Count dropped 5-10 days after starting heparin (or exposed to heparin <30 days ago and count dropped <1 day after re-exposure)	Count dropped >10d after starting heparin (or previous heparin exposure 30-100 days ago and count dropped <1 day after re-exposure)	Count dropped within <4 days without recent exposure to heparin
Thrombosis	New proven thrombosis, skin necrosis, or systemic reaction	Progressive or recurrent thrombosis, silent thrombosis, or red skin lesions	No thrombotic symptoms
Other Cause	None	Possible	Definite
Low 4Ts score = negative predictive value 99.8%			
High 4Ts score = positive predictive value 64%			

### Treatment and Management

- ✓ All patients on heparin should have a CBC every 2-3 days.
- ✓ Consult Hematology for guidance with management
- ✓ STOP heparin immediately if intermediate or high probability of HITT
- ✓ Immediately start NON-heparin anticoagulant (ex: argatroban infusion, fondaparinux injection; DOAC use is not currently recommended and is an off-label use.)
- ✓ Treat thrombocytopenia only if bleeding complication occurs
- ✓ Patients will need to transition to Warfarin (once platelets are above 150) for a minimum of 1-month, and 3–6 months if proven to have VTE.



The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click [HERE](#) for clinical issues the CP service can assist with.



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