

# Heparin-Induced Thrombocytopenia

## General

HIT is an immune-mediated hypersensitivity reaction to the platelet factor 4 / heparin complex characterised by immune complex formation, platelet activation and hypercoagulability

## Differential Diagnosis of Thrombocytopenia

Sepsis  
Post-resuscitation dilution  
Drug-Induced (including HIT)  
Hypersplenism  
Platelet Consumption or Destruction  
DIC  
Massive Transfusion  
Primary Marrow disorders  
Immune Thrombocytopenia (ITP, TTP)  
Antiphospholipid syndrome  
Intravascular devices (IABP, PA catheter, ECMO)

## Individuals at risk of HIT

High risk (>1%)  
- post-operative patients (especially cardiac, vascular or orthopaedic patients receiving unfractionated heparin)

Intermediate risk (0.1-1%)  
- postoperative patients receiving UFH flushes  
- postoperative patients receiving LMWH  
- medical or obstetric patients treated with therapeutic or prophylactic UFH

Low (<0.1%)  
- Medical or Obstetric Patients treated with LMWH

## Estimating Pretest Probability of HIT (4Ts)

General:  
0-3 points - low probability (<5% have HIT antibodies)  
4-5 points - intermediate  
6-8 points - high (>80% have HIT antibodies)

1. Thrombocytopenia  
2 points - >50% platelet decrease to nadir >20  
1 point - 30-50% decrease or nadir 10-19 or >50% decrease post surgery  
0 points - <30% platelet decrease or nadir <10

2. Timing of onset of platelet decrease or other HIT sequelae  
2 points - days 5-10 or <1 day with heparin in past 30 days  
1 point - >10 days or timing unclear or <1 day with heparin in past 31-100 days  
0 points - <day 4 with no recent heparin  
NB: 1st day considered day 0

3. Thrombosis or other sequelae  
2 points - proven new thrombosis, skin necrosis or acute systemic reaction after iv UFH  
1 point - progressive or recurrent thrombosis, erythematous skin lesions, suspected thrombosis  
0 points - none

4. Other causes of platelet decrease  
2 points - none evident  
1 point - possible  
0 points - definite

## Principles of Treatment (6As)

1. Avoid & discontinue all heparin (including LMWH)
2. Administer nonheparin alternative anticoagulant
3. Anti-PF4/heparin antibody test for confirmation
4. Avoid platelet transfusion
5. Await platelet recovery before initiation of warfarin
6. Assess for lower extremity DVT

## Specific treatments

1. danaparoid  
- a heparinoid with predominant anti-factor Xa activity  
- exhibits cross reactivity to HIT antibodies in 10-20% of patients but this does not result in adverse clinical effect
2. lepirudin  
- a direct thrombin inhibitor  
- renally eliminated and requires significant dose reduction in renal impairment  
- clinical data demonstrate a relative risk reduction of death, amputation and new thrombotic complications in HITTS when lepirudin is used (compared with controls)
3. Warfarin therapy  
- reduction in protein C synthesis by warfarin may lead to significant thrombosis and worsening of clinical condition in HITTS  
- Warfarin should be delayed until danaparoid or lepirudin is therapeutic and platelet count has significantly recovered  
- There should be an overlap of 5 days and danaparoid or lepirudin should not be ceased until INR has been over 2 for 2 consecutive days

## Complications of HIT

1. Venous thrombosis  
- DVT (50%)  
- Warfarin-Induced venous limb gangrene  
- PE (25%)  
- cerebral venous thrombosis  
- adrenal infarction
2. Arterial Thrombosis  
- lower limb arterial thrombosis (20% require amputation)  
- CVA  
- myocardial infarction (3-5%)  
- other arterial thrombosis (including mesenteric, brachial and spinal)
3. Skin Lesions (at heparin injection sites)  
- skin necrosis  
- erythematous plaques
4. other complications  
- acute systemic reaction after intravenous heparin bolus (may include fevers, chills, tachycardia, hypertension, flushing, chest pain, dyspnoea, nausea, diarrhoea and even cardiac or respiratory arrest)  
- hypofibrinogenaemia secondary to decompensated DIC  
- death (10-30% risk)

## Laboratory testing for HIT

1. Functional Assays (eg serotonin release assay, visual assessment of platelet aggregation)  
- detect antibodies based on their ability to activate platelets in the presence of heparin
2. Antigen assays (PF4/polyanion EIA)  
- detect antibodies reactive against the PF4/Heparin complex using ELISA  
- commercial PF4/polyanion EIA assay is widely available; it has high sensitivity (90-98%) and high negative predictive value; it has low specificity