Management of heparin induced thrombocytopenia

**Diagnosis:**
1. Thrombocytopenia- A 50% or greater reduction in platelet count during heparin or LMWH exposure
2. Timing- Classic presentation- Platelet count decline begins 5-10 days after heparin initiation
   - Rapid onset- within first 24 hours
   - Delay onset- rare- Thrombocytopenia develops 1-3 weeks after heparin discontinued
   - Cardiac Surgery- After recovery from initial post-bypass thrombocytopenia, platelet count drops again post-op day 4-10
3. Look for other causes of thrombocytopenia
4. Testing- Send blood for HIT antibody ELISA

**Treatment:**
1. Discontinue all heparin exposure
2. Order warning signs for patient’s door and above their bed
3. Stop warfarin and reverse (if INR elevated) with vitamin K
4. Start a direct thrombin inhibitor
5. Screen for asymptomatic thrombosis with duplex
6. Warfarin may be started at 2.5-5 mg once platelet count recovers to baseline (150,000 or more)

**Direct thrombin inhibitor dosing:**

**Argatroban dosing** (Half life 45 minutes- Hepatic metabolism) **NEED HEMATOLOGY APPROVAL**

- Standard dose- (normal liver function) – 2 micrograms/kg/min
- Reduced dose- (for ICU patients or reduced liver function) - 0.25 µg/kg/min
- For severe liver dysfunction use lepirudin or very low dose argatroban (0.1 µg/kg/min)
- Dose adjustments (Argatroban)
  - Subtherapeutic- increase by 20-25% and recheck the aPTT in 4 hours
  - Supratherapeutic- decrease by 25-50% and recheck the aPTT in 4 hours
    - aPTT ratio is > 3.0 hold the infusion 30 minutes
    - aPTT ratio > 4.0, hold 1 hour before restarting at the lower rate

**Lepirudin dosing** (Half life 80 minutes- Renal metabolism) **NEED HEMATOLOGY APPROVAL**

- Normal renal function (> 60 ml/min) 0.1 mg/kg/hr
- For patients with creatinine clearance < 45 ml/min Argatroban preferred
- Dose adjustments (Lepirudin)
  - Subtherapeutic, increase the infusion rate by 20-25% and recheck the aPTT in 6 hours
  - Supratherapeutic, decrease the infusion rate by 25-50% and recheck the aPTT in 6 hours
  - If aPTT ratio is > 3.0 hold the infusion 1 hour then restart at the lower rate
  - If aPTT ratio is > 4.0, hold 2 hours then restarting at the lower rate

**Bivalirudin dosing** (Half life 25 minutes-plasma hydrolysis/renal) **NEED APPROVAL OF DR PETTY**

- Normal renal function-0.15 mg/kg/hr
- Renal failure- 0.05 mg/kg/hr
- Combined hepatic/renal failure- 0.03 mg/kg/hr
- Dose adjustments (Lepirudin)
  - Subtherapeutic, increase the infusion rate by 20-25% and recheck the aPTT in 4 hours
  - Supratherapeutic, decrease the infusion rate by 25-50% and recheck the aPTT in 4 hours
  - If aPTT ratio is > 4.0 hold the infusion 30 minutes hour then restart at the lower rate

**Warfarin dosing:**
1. Begin warfarin once platelet count has returned to normal on therapeutic doses of a DTI
2. Start warfarin at 2.5-5 mg
3. Argatroban (at a dose of 2 mcg/kg/min) will double the INR. Therefore, when the INR is double the intended target range (INR 4-6 for intended range 2-3), the argatroban infusion may be discontinued with close follow up of the aPTT and INR (q 4 hours to make sure the patient is therapeutic on warfarin (INR 2.0 or more) when all traces of argatroban effect are gone (e.g., aPTT ratio is normal).

**Four T Score**

<table>
<thead>
<tr>
<th>Suspications of HIT based upon the ‘4 Ts’*</th>
<th>Score 2</th>
<th>Score 1</th>
<th>Score 0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>nadir 20-100, or &gt;50% platelet fall</td>
<td>nadir 10-19, or 30-50% platelet fall</td>
<td>nadir &lt;10, or &lt;30% platelet fall</td>
</tr>
<tr>
<td>Timing of onset of platelet fall</td>
<td>day 5-10, or day 1 with recent heparin*</td>
<td>day 10 or timing unclear (but fits with HIT)</td>
<td>day 1 (no recent heparin)</td>
</tr>
<tr>
<td>Thrombosis or other sequelae</td>
<td>proven thrombosis, skin necrosis, or ASR†</td>
<td>progressive, recurrent, or silent thrombosis, erythematosus skin lesions</td>
<td>none</td>
</tr>
<tr>
<td>Other cause of platelet fall</td>
<td>none evident</td>
<td>possible</td>
<td>definite</td>
</tr>
</tbody>
</table>

**Total Pre-test Probability Score**

<table>
<thead>
<tr>
<th>High</th>
<th>Moderate</th>
<th>Low</th>
</tr>
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<tbody>
<tr>
<td>8</td>
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<td>6</td>
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<tr>
<td>5</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

**Stop heparin‡, give alternative**
non-heparin anticoagulant
argatroban† or lepirudin or danaparoid**
(bivalirudin†† or fondaparinux††)

**Physician judgment**

**Continue (LMW) heparin**

**Positive test for HIT antibodies**

**Continuous non-heparin anticoagulant until platelet count recovery**

**Thrombosis***

If HIT, continue non-heparin anticoagulant until platelet count recovery, then cautious coumarin overlap "

**Negate test for HIT antibodies**

**Imaging studies for lower-limb DVT †††**

No Thrombosis

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