Heparin-Induced Thrombocytopenia
Steven A. Baroletti, PharmD; Samuel Z. Goldhaber, MD

Patients receive blood thinners (anticoagulants) to treat or prevent blood clots. The most commonly used intravenous anticoagulant is heparin. This Cardiology Patient Page focuses on heparin-induced thrombocytopenia (HIT), a complication of heparin therapy. This complication of heparin is often confusing because in HIT, heparin does the opposite of what it is supposed to do: It forms rather than prevents new blood clots.

What Is Heparin-Induced Thrombocytopenia?
Ordinarily, heparin prevents clotting and does not affect the platelets, components of the blood that help form blood clots. Triggered by the immune system in response to heparin, HIT causes a low platelet count (thrombocytopenia).

Two distinct types of HIT can occur: nonimmune and immune-mediated. Nonimmune HIT, which occurs most frequently, is characterized by a mild decrease in the platelet count and is not harmful. The second type, immune-mediated HIT, occurs much less frequently but is dangerous. Immune-mediated HIT causes much lower platelet counts. Paradoxically, despite a very low platelet count, patients who suffer from HIT are at risk for major clotting problems.

After heparin is administered to a patient, an immune complex can form between heparin and a specific blood factor (platelet factor 4, or “PF4”) that is released by platelets. The body views this “heparin-PF4” complex as a foreign substance. Therefore, an antibody is formed against the heparin-PF4 complex. The antibody binds to this complex and the platelets are destroyed.

This disruption of platelets can lead to the formation of new blood clots in patients with immune-mediated HIT. The result can be a deep vein thrombosis (in the veins of the thigh or pelvis), pulmonary embolism, or even a heart attack or stroke. However, this does not seem to occur with the mild decrease in platelets associated with nonimmune HIT.

When Does HIT Occur?
Immune-mediated HIT usually occurs between 5 to 14 days after first beginning heparin therapy. However, there are exceptions, with HIT developing infrequently either early (after a recent previous exposure to heparin) or late after heparin exposure.

How Is HIT Diagnosed?
HIT can often be diagnosed by measuring the platelet count and PF4 antibody level in the blood. Symptoms of new blood clot formation may suggest HIT.

Symptoms of deep vein thrombosis include pain or tenderness, sudden swelling, discoloration, visibly large veins, and skin that is warm to the touch. Dislodgement of clot from the deep leg veins and passage into the lungs (pulmonary embolism) may present as shortness of breath, a change in heart rate, sharp chest pain, dizziness, or feelings of anxiety and excessive sweating. Severe indicators of HIT are skin changes that present as bruising or blackening around the heparin injection site as well as the fingers, toes, and nipples that may progress to gangrene. The extremities are especially susceptible to the small clots that form because of HIT. If you have any of these signs or symptoms, call your doctor.

How Is HIT Treated?
The first step is to discontinue heparin on suspicion of HIT. The next step is to treat HIT using an alternative type of anticoagulant. Even though the platelet count is low, it is important to avoid platelet transfusions, which can “add fuel to the fire.”

Medications
Direct thrombin inhibitors (DTI) are a class of anticoagulant medications that do not cause HIT. These drugs are administered by continuous intrave-
Medications Associated With Heparin-Induced Thrombocytopenia

<table>
<thead>
<tr>
<th>Medication Name, Generic (Trade)</th>
<th>Therapeutic Class of Anticoagulant</th>
<th>Administration Method</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unfractionated heparin</td>
<td>Heparin</td>
<td>Continuous IV or injection</td>
<td>Most common cause of HIT</td>
</tr>
<tr>
<td>Enoxaparin (Lovenox)</td>
<td>Low-molecular-weight heparin</td>
<td>Injection (may be self-administered at home)</td>
<td>Least common cause of HIT</td>
</tr>
<tr>
<td>Dalteparin (Fragmin)</td>
<td>Low-molecular-weight heparin</td>
<td>Injection (may be self-administered at home)</td>
<td>Least common cause of HIT</td>
</tr>
<tr>
<td>Tinzaparin (Innohep)</td>
<td>Low-molecular-weight heparin</td>
<td>Injection (may be self-administered at home)</td>
<td>Least common cause of HIT</td>
</tr>
<tr>
<td>Lepirudin (Refludan)</td>
<td>Direct thrombin inhibitor</td>
<td>Continuous IV infusion or injection</td>
<td>FDA approved for treatment of HIT</td>
</tr>
<tr>
<td>Argatroban (Argatroban)</td>
<td>Direct thrombin inhibitor</td>
<td>Continuous IV infusion</td>
<td>FDA approved for treatment of HIT</td>
</tr>
<tr>
<td>Bivalirudin (Angiomax)</td>
<td>Direct thrombin inhibitor</td>
<td>Continuous IV infusion</td>
<td>FDA approved for treatment of HIT in PCI</td>
</tr>
<tr>
<td>Fondaparinux (Arixtra)</td>
<td>Factor Xa inhibitor</td>
<td>Injection (may be self-administered at home)</td>
<td>Has been used to treat HIT and suspected HIT (not currently FDA approved)</td>
</tr>
<tr>
<td>Warfarin (Coumadin)</td>
<td>Vitamin K antagonist</td>
<td>Orally as tablet</td>
<td>Avoid unopposed use for first 3 to 5 days until INR is at target value</td>
</tr>
</tbody>
</table>

**HIT information card.**

**Agents that cause HIT**

- Unfractionated heparin
- Enoxaparin (Lovenox)
- Dalteparin (Fragmin)
- Tinzaparin (Innohep)

**Agents used in treatment of HIT**

- Lepirudin (Refludan)
- Argatroban (Argatroban)
- Bivalirudin (Angiomax)
- Fondaparinux (Arixtra)
- Warfarin (Coumadin)

**Medications Associated With Heparin-Induced Thrombocytopenia**

**Heparin Induced Thrombocytopenia Alert**

- **Patient Name:**
- **Date of Birth:**
- **I was diagnosed with Heparin-Induced Thrombocytopenia (HIT) on (date):**
- **At ____________________________ Hospital/Office, while under the care of ____________________________ MD.**
- **I am currently taking Warfarin (Coumadin).**
- **I am currently on NO blood thinners (anticoagulation).**
- **My history of heparin-induced thrombocytopenia should be taken into consideration if I require anticoagulation. An alternative medication other than heparin and low molecular weight heparin may be required.**

**References**

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