P

atients receive blood thinners (anti-coagulants) 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.1

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><strong>Agents that cause HIT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<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><strong>Agents used in treatment of HIT</strong></td>
<td></td>
<td></td>
<td></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>

IV indicates intravenous infusion; FDA, Food and Drug Administration; and PCI, percutaneous coronary intervention.

Heparin-induced thrombocytopenia (HIT) is a complication that can develop after administration of heparin or other anticoagulant medications. HIT typically occurs when the immune system recognizes a foreign substance (in this case, a heparin fragment) as a threat and produces antibodies against it. These antibodies can then bind to platelets, leading to their destruction and decreased platelet count. HIT is characterized by the development of thrombocytopenia (low platelet count) and the presence of antibodies against the platelet factor 4 (PF4) complex, which is a combination of PF4 and heparin.

HIT can be classified into two categories: HIT type 1 and HIT type 2. HIT type 1 is typically associated with heparin administration and does not involve antibodies, while HIT type 2 is associated with antibodies against PF4/heparin complexes.

HIT can lead to serious complications such as blood clots, strokes, and heart attacks. It is important to monitor patients for signs of HIT and to manage the condition appropriately to prevent these complications.

**What if I Need Anticoagulants in the Future?**

Although HIT is caused by a reaction to heparin that is similar to other allergic reactions, it is not a true allergy. In contrast to many allergies to other medications or foods, the allergy to heparin is not long-lasting. The PF4 antibody that causes HIT will usually disappear after approximately 3 months. Thereafter, heparin may be considered for use if a new clot did not develop from HIT and if the PF4 antibody test is negative.

If you have been told that you have HIT or an allergy to heparin, inform your doctor before taking any form of heparin. It is extremely helpful to write down when you were exposed to heparin and when HIT occurred. Helpful information for your healthcare provider is shown in the figure.

Early identification of HIT and avoidance of inappropriate heparin therapy can help promote a safe and effective anticoagulation strategy.

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**Disclosures**

None.

**References**

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