B. Transitioning to warfarin

- If argatroban dose is >2 mcg/kg/min, switch to warfarin.
- Warfarin should be initiated when the INR is >2.5.
- Repeat procedure daily until INR is >2.5.
- If INR is <2, restart argatroban.
- Repeat procedure daily until INR is >2.5.

C. Duration of anticoagulation

- For patients with HIT without thrombosis (i.e., isolated HIT), anticoagulation for a defined course (typically 3-6 months) is recommended.
- For patients with HIT-associated thrombosis (i.e., HITT), anticoagulation should continue for at least 30 days after the diagnosis of HIT.
- Postoperative anticoagulation is recommended in all patients with HIT, whether or not there is a history of thrombosis.
- Bilateral lower extremity compression ultrasonography should be performed in all patients with HIT, whether or not there is a history of thrombosis.

D. Platelet transfusion

- Due to the theoretical risk that platelet transfusion may precipitate thrombosis in HIT, prophylactic platelet transfusions should not be given to patients with confirmed or strongly suspected HIT (Grade 1B).
- Platelet transfusion may be appropriate in situations of diagnostic uncertainty, high bleeding risk, or clinically significant bleeding.

V. Heparin Re-Exposure in Patients with a History of HIT

A. Cardiac and vascular surgery

- HIT laboratory testing should be used to determine the safety of exposing a patient with a history of HIT to intravenous heparin.
- UFH should be used. 2American College of Chest Physicians Grading System: 1=strong recommendation; 2=weak recommendation; A=based on high quality evidence; B=based on moderate quality evidence; C=based on low quality evidence.

B. Cardiac catheterization/percutaneous coronary intervention

- HIT laboratory testing should be used to determine the safety of exposing a patient with a history of HIT to intravenous heparin.

This document summarizes selected recommendations from the American College of Chest Physicians Evidence-Based Clinical Practice Guideline on Antithrombotic and Thrombolytic Therapy (8th Edition).

Guidelines provide the practitioner with clear principles and strategies for quality patient care and do not establish a fixed set of rules that preempt physician judgment.

For further information, please see the complete guidelines on the Chest Web site at www.chestjournal.org/content/133/6_suppl/340S.long or refer to the Practice Guidelines section of the ASH Web site at www.hematology.org/doc/ resources/guidelines. You may also contact the ASH Policy & Practice Department at 202-776-0544.

American Society of Hematology. © 2009. All Rights Reserved.
I. History and Physical Examination: Evaluating the Clinical Probability of HIT

A. Features of the history and physical examination that support a diagnosis of HIT

<table>
<thead>
<tr>
<th>Feature</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nadir platelet count</td>
<td>20-10 x 10^9/L</td>
</tr>
<tr>
<td>Fall in platelet count</td>
<td>≥50% or platelet nadir &lt;20 x 10^9/L</td>
</tr>
<tr>
<td>Time</td>
<td>≥30-50% or platelet nadir 10-15 x 10^9/L</td>
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<tr>
<td>Time</td>
<td>Platelet count fall ≥30% or platelet nadir &lt;10 x 10^9/L</td>
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B. The 4Ts: A clinical probability scoring model

<table>
<thead>
<tr>
<th>4Ts</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>Fall in platelet count</td>
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<tr>
<td>Other causes</td>
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<tr>
<td>Clinical Events</td>
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C. Immunologic Detection

<table>
<thead>
<tr>
<th>Assay</th>
<th>Method</th>
<th>Examples</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tr>
<td>Directed antibody against PF4/</td>
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<tr>
<td>platelet-dependent</td>
<td>ELISA</td>
<td>PAPS</td>
<td>&gt;90%</td>
<td>90-95%</td>
<td>OQ of result correlates with clinical probability of HIT</td>
</tr>
<tr>
<td>Directed antibody against PF4/</td>
<td></td>
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<td>platelet-dependent</td>
<td>ELISA</td>
<td>UTPS</td>
<td>&gt;90%</td>
<td>90-95%</td>
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<td>Directed antibody against PF4/</td>
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</tr>
<tr>
<td>platelet-dependent</td>
<td>ELISA</td>
<td>PEA</td>
<td>&gt;90%</td>
<td>90-95%</td>
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<td>Directed antibody against PF4/</td>
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<td>ELISA</td>
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<td>90-95%</td>
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D. Treatment

**A. Non-heparin anticoagulants: selection, dosing, and monitoring**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose recommendation</th>
<th>Initial dosing</th>
<th>Monitoring</th>
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<tr>
<td>Adapted from Warkentin TE et al., Chest 2008.</td>
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<td>Aratoglan 1C</td>
<td>None</td>
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<td>Argatroban 1C</td>
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<td>Bivalirudin 1C</td>
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</tbody>
</table>
I. History and Physical Examination: Evaluating the Clinical Probability of HIT

A. Features of the history and physical examination that support a diagnosis of HIT

I. History and Physical Examination:

- Fall in platelet count begins 5-14 days after heparin exposure
- Absence of alternative causes of thrombocytopenia
- Absence of petechiae and other signs of thrombocytopenia
- Anaphylactoid reaction within 30 minutes after intravenous heparin

II. Laboratory Diagnosis

B. The 4Ts: A clinical probability scoring model

<table>
<thead>
<tr>
<th>Feature</th>
<th>2 Points</th>
<th>1 Point</th>
<th>0 Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 day</td>
<td>Loss of platelet count</td>
<td>50-60%</td>
<td>platelet nadir ≥20 x 10^9/L</td>
</tr>
<tr>
<td>≥1 day</td>
<td>Clear onset</td>
<td>(prior to day 14)</td>
<td>(prior to day 14)</td>
</tr>
<tr>
<td>≥1 day</td>
<td>Consistent with days</td>
<td>5-14 fall, but not clear (e.g. missing platelet counts)</td>
<td>Pluripotent count fall ≤30% or platelet nadir &lt; 10 x 10^9/L</td>
</tr>
</tbody>
</table>

III. Diagnostic and Initial Treatment Algorithm

<table>
<thead>
<tr>
<th>HIT susceptibility</th>
<th>Intermediate/high clinical probability</th>
<th>Low clinical probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinue heparin; start alternative anticoagulant</td>
<td>Obtain immunologic assay</td>
<td></td>
</tr>
</tbody>
</table>


IV. Treatment

A. Non-heparin anticoagulants: selection, dosing, and monitoring

- Danaparoid: 1B
- Argatroban: 1C
- Fondaparinux: 2C
- LMWH: 3C

<table>
<thead>
<tr>
<th>Agent</th>
<th>Direct recommendation/Indications</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argatroban</td>
<td>No monitor</td>
<td>Adjust dose by APTT 1.5-2.0 times patient baseline. Monitor APTT every 4 hours during dose titration.</td>
</tr>
<tr>
<td>Danaparoid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fondaparinux</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LMWH</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Warkentin TE et al., Chest 2008.

- APTT: activated partial thromboplastin time
- APTT: activated partial thromboplastin time
- HIT: heparin-induced thrombocytopenia
- HIT: heparin-induced thrombocytopenia
- HIT: heparin-induced thrombocytopenia

Cover Image: (in skin microscopy showing monocytes (in red), platelets (in green), and areas of overlap (in yellow) being incorporated into a growing thrombus in a mouse model of HIT. Courtesy of L. Reau and M. Ponzi. Children’s Hospital of Philadelphia.)
I. History and Physical Examination: Evaluating the Clinical Probability of HIT

A. Features of the history and physical examination that support a diagnosis of HIT

I. History and Physical Examination:

- **Blood count:** Platelet count fall ≥ 20 × 10⁹/L. May be < 20 × 10⁹/L in cases associated with nadir platelet count ≥ 5-14 days after heparin exposure. Fall in platelet count begins 5-14 or platelet counts) or clear (e.g. missing thrombosis and DIC.
- **Thrombosis or Other sequelae:** New thrombosis (confirmed); thrombocytopenia (erythematous) skin necrosis; thrombosis (not confirmed).
- **Skin necrosis:** At subcutaneous heparin injection sites; skin necrosis.
- **Absence of alternative causes of thrombocytopenia:** Such as infection, other medications known to cause thrombocytopenia, cardiopulmonary bypass within previous 48 hours, etc.
- **Absence of petechiae and other signs of significant bleeding:**

B. The 4Ts: A clinical probability scoring model

- **Thrombocytopenia:**
  - Clinical features: Clear onset after day 14 (prior to heparin exposure) or clear (e.g. missing thrombosis and DIC).
  - Laboratory features: None apparent; Possible; Definite.
  - High probability: 8-10 points; intermediate probability: 4-5 points; low probability: <3 points.

C. Laboratory Diagnosis

- **Assay:** Anti-β²GPI antibody.
- **Method:** ELISA.
- **Examples:** Normal organ function: 5 mg/kg/min.
- **Sensitivity:** 50-80%.
- **Specificity:** 50-90%.

D. Diagnostic and Initial Treatment Algorithm

- **HIT suspected:**
  - Intermediate/high clinical probability:
    - Discontinue heparin; start non-heparin anticoagulant.
  - Low clinical probability:
    - Obtain immunologic assay.

E. Treatment

- **A. Non-heparin anticoagulants:** selection, dosing, and monitoring
  - **Agent:** Bivalirudin
  - **Dose recommendation:** Initial dosing.
  - **Monitoring:**
    - **Dosage:**
      - **Bolus:**
        - Weight 500 kg: 150 U/hr
        - Weight 60-70 kg: 200 U/hr
        - Weight 75-90 kg: 250 U/hr
        - Weight 90-100 kg: 300 U/hr
        - Weight >100 kg: 375 U/hr
        - **Continuous infusion:**
          - 150 U/hr:
            - Normal renal function
          - 200 U/hr:
            - Maintenance infusion:
              - Liver dysfunction (total serum bilirubin >1.5 mg/dl; heart failure; portal vein surgery; atria
tis >0.5-1.2 mg/dl).

- **B. Non-heparin anticoagulants:** selection, dosing, and monitoring
  - **Agent:** Danaparoid
  - **Dose recommendation:** Initial dosing.
  - **Monitoring:**
    - **Dosage:**
      - **Bolus:**
        - 0.15 mg/kg/hr.
      - **Continuous infusion:**
        - 10-15 mg/kg/hr.

- **C. Non-heparin anticoagulants:** selection, dosing, and monitoring
  - **Agent:** Argatroban
  - **Dose recommendation:** Initial dosing.
  - **Monitoring:**
    - **Dosage:**
      - **Bolus:**
        - 2 mcg/kg/min.
      - **Continuous infusion:**
        - 4-5 mcg/kg/min.

- **D. Non-heparin anticoagulants:** selection, dosing, and monitoring
  - **Agent:** Fondaparinux
  - **Dose recommendation:** Initial dosing.
  - **Monitoring:**
    - **Dosage:**
      - **Bolus:**
        - 0.5 mcg/kg.
      - **Continuous infusion:**
        - 1-2 mg/kg/hr.

- **E. Non-heparin anticoagulants:** selection, dosing, and monitoring
  - **Agent:** Lepirudin
  - **Dose recommendation:** Initial dosing.
  - **Monitoring:**
    - **Dosage:**
      - **Bolus:**
        - 0.15 mg/kg/hr.
      - **Continuous infusion:**
        - 1-3 mg/kg/hr.

- **F. Non-heparin anticoagulants:** selection, dosing, and monitoring
  - **Agent:** Bivalirudin
  - **Dose recommendation:** Initial dosing.
  - **Monitoring:**
    - **Dosage:**
      - **Bolus:**
        - 1-2 mg/kg/hr.
      - **Continuous infusion:**
        - 2-4 mg/kg/hr.

- **G. Non-heparin anticoagulants:** selection, dosing, and monitoring
  - **Agent:** Danaparoid
  - **Dose recommendation:** Initial dosing.
  - **Monitoring:**
    - **Dosage:**
      - **Bolus:**
        - 1-2 mg/kg/hr.
      - **Continuous infusion:**
        - 3-4 mg/kg/hr.

- **H. Non-heparin anticoagulants:** selection, dosing, and monitoring
  - **Agent:** Argatroban
  - **Dose recommendation:** Initial dosing.
  - **Monitoring:**
    - **Dosage:**
      - **Bolus:**
        - 1-2 mg/kg/hr.
      - **Continuous infusion:**
        - 3-4 mg/kg/hr.

- **I. Non-heparin anticoagulants:** selection, dosing, and monitoring
  - **Agent:** Fondaparinux
  - **Dose recommendation:** Initial dosing.
  - **Monitoring:**
    - **Dosage:**
      - **Bolus:**
        - 0.5 mcg/kg.
      - **Continuous infusion:**
        - 1-3 mg/kg/hr.

- **J. Non-heparin anticoagulants:** selection, dosing, and monitoring
  - **Agent:** Lepirudin
  - **Dose recommendation:** Initial dosing.
  - **Monitoring:**
    - **Dosage:**
      - **Bolus:**
        - 0.15 mg/kg/hr.
      - **Continuous infusion:**
        - 1-3 mg/kg/hr.

- **K. Non-heparin anticoagulants:** selection, dosing, and monitoring
  - **Agent:** Bivalirudin
  - **Dose recommendation:** Initial dosing.
  - **Monitoring:**
    - **Dosage:**
      - **Bolus:**
        - 1-2 mg/kg/hr.
      - **Continuous infusion:**
        - 3-4 mg/kg/hr.
I. History and Physical Examination: Evaluating the Clinical Probability of HIT

Feature | Comments
--- | ---
Absence of petechiae and other signs of platelet aggregation | 
Absence of alternative causes of thrombocytopenia | Skin necrosis at subcutaneous heparin injection sites
Anaphylactoid reaction | Within 30 minutes after intravenous heparin
Skin necrosis | At subcutaneous heparin injection sites
Non-necrotizing thrombosis | At heparin injection sites; Suspected (erythematous) skin lesions; Suspected thrombosis (not confirmed)

II. Laboratory Diagnosis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Absence of petechiae and other signs of platelet aggregation | Such as infection, other medications known to cause thrombocytopenia, cardiopulmonary bypass within previous 48 hours, etc.
| Absence of petechiae and other significant bleeding | 

High probability: 6-8 points; intermediate probability: 4-5 points; low probability: <3 points.

Adapted from Lo GK et al., J Thromb Haemost 2006.

III. Diagnostic and Initial Treatment Algorithm

A. Non-heparin anticoagulants: selection, dosing, and monitoring

**Agent** | **Dosage recommendation** | **Clinical monitoring** |
--- | --- | ---|
Bivalirudin | Bolus: Weight <50 kg: 0.5-1.2 mcg/kg/min | Adjust dose to anti-Xa levels of 0.5-1.5 U/ml. |
| Bolus: Weight 50-100 kg: 1-2 mcg/kg/min | (ES assay is available). |
| Continuous infusion: 0.05-0.1 mcg/kg/min | Continuous infusion: 0.05-0.1 mcg/kg/min |
| Argatroban | Bolus: 2.5 mcg/kg/min only if lifethreatening thrombosis is present | Adjust dose by APTT every 4 hours during dose titration. |
| | Continuous infusion: 0.8-4.5 mcg/kg/min | Adjust dose by APTT 1.5-2.0 times patient baseline. |
| | 0.01 mcg/kg/hr to 0.05 mcg/kg/hr | Monitor APTT every 4 hours during dose titration. |
| Enoxaparin | Bolus: 1 mg/kg | Adjust dose by APTT 1.5-2.0 times patient baseline. |
| | Continuous infusion: 1.6-4.0 mg/kg/day | Monitor APTT every 4 hours during dose titration. |
| | 0.10 mcg/kg/hr to 0.15 mcg/kg/hr | Adjust dose by APTT 1.5-2.0 times patient baseline. |
| | 0.01 mcg/kg/hr to 0.05 mcg/kg/hr | Monitor APTT every 4 hours during dose titration. |


**B. The 4Ts: A clinical probability scoring model**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear onset after day 14</td>
<td>None apparent Possible Definite</td>
</tr>
<tr>
<td>Patients with previous heparin exposure</td>
<td></td>
</tr>
<tr>
<td>Fall in platelet count within 3 days</td>
<td>Clear (e.g. missing previous platelet counts)</td>
</tr>
<tr>
<td>Non-nadir platelet count &lt; 10 x 10^9/L</td>
<td>Not clear (e.g. missing previous platelet counts)</td>
</tr>
<tr>
<td>Duration of platelet count fall</td>
<td>30-50% or platelet nadir 10-14 x 10^9/L</td>
</tr>
<tr>
<td>Thrust above platelet nadir</td>
<td>Platelet count fall &lt; 30% or platelet nadir 10-14 x 10^9/L</td>
</tr>
</tbody>
</table>

**C. Laboratory testing**

<table>
<thead>
<tr>
<th><strong>Antigen</strong></th>
<th><strong>Mechanism</strong></th>
<th><strong>Examples</strong></th>
<th><strong>Sensitivity</strong></th>
<th><strong>Specificity</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunoassay</td>
<td>Detects antibodies against PF4/</td>
<td>Polyspecific ELISA</td>
<td>≥95%</td>
<td>50-60%</td>
</tr>
<tr>
<td></td>
<td>heparin complexes regardless of their capacity to activate platelets</td>
<td>IgG-specific ELISA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>PAGA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| | Functional assay | Detects antibodies that induce heparin-dependent platelet activation | 1. SRA | ≥90% | ≥90%
| | | 2. SRA | HPAI | Not available at many centers; may require referral to a reference laboratory |
| | | 3. PAT | HIT | |

Cover Image: In skin microscopy showing monocytes (in red), platelets (in green), and areas of overlap (in yellow) being incorporated into a growing thrombus in a mouse model of HIT. Courtesy of L. Rauova and M. Poncz, Children's Hospital of Philadelphia.

**B. Transitioning to warfarin**

- **If argatroban dose is >2 mcg/kg/min**
  1. Stop argatroban when INR on combined argatroban and warfarin is >4.
  2. Repeat INR in 4-6 hours.
  3. If INR is <4, restart argatroban.
  4. Repeat procedure daily until INR >2 is achieved.

- **If argatroban dose is <2 mcg/kg/min**
  1. Reduce argatroban dose to 2 mcg/kg/min.
  2. Repeat INR in 4-6 hours.
  3. Stop argatroban when INR on combined argatroban and warfarin is >4.
  4. Repeat INR in 4-6 hours.
  5. If INR is <2, restart argatroban.
  6. Repeat procedure daily until INR >2 is achieved.

**D. Platelet transfusion**

- **Due to theoretical risk that platelet transfusion may precipitate thrombosis in HIT, prophylactic platelet transfusions should not be given to patients with confirmed or strongly suspected HIT**.

- **Platelet transfusion may be appropriate in situations of diagnostic uncertainty, high bleeding risk, or clinically significant bleeding.**

**V. Heparin Re-Exposure in Patients with a History of HIT**

A. Cardiac and vascular surgery

- **HIT laboratory testing should be used to determine the safety of exposing a patient with a history of HIT to intravenous heparin.**

- **Initial warfarin dose should be ≥5 mg/day. Larger loading doses should be avoided (Grade 1B).**

- **If pre- or post-operative anticoagulation is indicated, a non-heparin anticoagulant should be used. Amended Chest of Physicians Grading System: 1=strong recommendation; 2=weak recommendation; 3=limited evidence; 4=based on low quality evidence; 5=based on moderate quality evidence; 6=based on high quality evidence.**

**C. Duration of anticoagulation**

- **Bilateral lower extremity compression ultrasonography should be performed in all patients with HIT, whether or not there is clinical evidence of lower-limb DVT (Grade 1C), because the finding of DVT may influence the recommended duration of anticoagulation.**

- **For patients with HIT-associated thrombosis (i.e., HITT), anticoagulate for a defined course (typically 3-6 months) as per the provided thrombosis.**

- **For patients with HIT without thrombosis (i.e. isolated HIT), anticoagulate for at least one 30 days after the diagnosis of HIT, anticoagulation for at least one month should be considered.**

- **For all patients, anticoagulation management should be based on an individualized risk/benefit assessment.**

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**Clinical scenario**

<table>
<thead>
<tr>
<th>Clinical scenario</th>
<th>Laboratory profile</th>
<th>Recommended intravenous anticoagulant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remote HIT</td>
<td>Negative</td>
<td>7.1 UFH (Grade 1B)</td>
</tr>
<tr>
<td>Subacute HIT</td>
<td>Positive</td>
<td>1. Delay surgery, if possible, until immunologic assay becomes negative (Grade 1B). 2. If surgery cannot be delayed, use UFH (Grade 2C)</td>
</tr>
<tr>
<td>Acute HIT</td>
<td>Positive</td>
<td>1. Delay surgery, if possible, until functional and immunologic assays become negative (Grade 1B). 2. If surgery cannot be delayed, use bivalirudin (Grade 1B)</td>
</tr>
</tbody>
</table>

If post- or pre-operative anticoagulation is indicated, a non-heparin anticoagulant should be used. Amended Chest of Physicians Grading System: 1=strong recommendation; 2=weak recommendation; 3=limited evidence; 4=based on low quality evidence; 5=based on moderate quality evidence; 6=based on high quality evidence.
B. Transitioning to warfarin

- **HIT patients are at risk of venous limb gangrene during initiation of warfarin.**
- Warfarin should not be initiated until platelet count is ≥ 150 x 10^9/L (Grade 1B).
- **Initial warfarin dose should be ≤ 5 mg/day.** Larger loading doses should be avoided (Grade 1C).
- **A parenteral non-heparin anticoagulant should be overlapped with warfarin for ≤ 5 days and until INR has reached intended target (Grade 1B).**
- **Because argatroban raises the INR, the following steps should be taken when transitioning a patient from argatroban to warfarin:**
  1. **If argatroban dose is >2 mcg/kg/min:**
     - Stop argatroban when INR on combined argatroban and warfarin is ≥1.
     - Repeat INR in 4-6 hours.
  2. **If argatroban dose is ≤2 mcg/kg/min:**
     - 1. **If INR is <2, restart argatroban:**
         - Repeat INR in 4-6 hours.
     - 2. **If INR is ≥2:**
         - If INR on combined argatroban and warfarin is ≥2:
             - Stop argatroban when INR on combined argatroban and warfarin is ≥2.
             - Repeat INR in 4-6 hours.
         - If INR on combined argatroban and warfarin is <2:
             - Stop argatroban when INR is ≥2.
             - Repeat INR in 4-6 hours.

C. Duration of anticoagulation

- **For all patients, anticoagulation management should be based on individual patient risk/benefit assessment.**
- **If** HIT **patients are at risk of venous limb gangrene during initiation of warfarin,** warfarin should not be initiated until platelet count is ≥ 150 x 10^9/L (Grade 1B).
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     - 1. **If INR is <2, restart argatroban:**
         - Repeat INR in 4-6 hours.
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         - If INR on combined argatroban and warfarin is ≥2:
             - Stop argatroban when INR on combined argatroban and warfarin is ≥2.
             - Repeat INR in 4-6 hours.
         - If INR on combined argatroban and warfarin is <2:
             - Stop argatroban when INR is ≥2.
             - Repeat INR in 4-6 hours.

D. Platelet transfusion

- **Due to theoretical risk that platelet transfusion may precipitate thrombosis in HIT, prophylactic platelet transfusions should not be given to patients with confirmed or strongly suspected HIT (Grade 2C).**
- **Platelet transfusion may be appropriate in situations of diagnostic uncertainty, high bleeding risk, or clinically significant bleeding.**

V. Heparin Re-Exposure in Patients with a History of HIT

A. Cardiac and vascular surgery

- **HIT laboratory testing should be used to determine the safety of exposing a patient with a history of HIT to intravenous heparin:**
  - **Clinical evidence of lower-limb DVT (Grade 1C), because the finding of DVT may influence the recommended duration of anticoagulation.**
  - Bilateral lower extremity compression ultrasonography should be performed in all patients with HIT, whether or not there is clinical evidence of lower-limb DVT (Grade 1C), because the finding of DVT may influence the recommended duration of anticoagulation.
  - For patients with HIT-associated thrombosis (i.e. HITT), anticoagulate for a defined course (typically 3-6 months) as per other provoked thrombosis.
  - **Remote HIT Negative Negative 1. Use a non-heparin anticoagulant (Grade 1B)**
  - **Immunologic assay Functional assay**
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  1. Stop argatroban when INR on combined argatroban and warfarin is ≥4.
  2. Repeat INR in 4-6 hours.
  3. If INR is <2, restart argatroban.
  4. Repeat procedure daily until INR ≥2 is achieved.

If argatroban dose is ≥2 mcg/kg/min:

1. Reduce argatroban dose to 2 mcg/kg/min.
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V. Heparin Re-Exposure in Patients with a History of HIT

A. Cardiac and vascular surgery

- HIT laboratory testing should be used to determine the safety of exposing a patient with a history of HIT to intravenous heparin.

**Clinical Situation** | **Laboratory profile** | **Recommended intraprocedural anticoagulation**
--- | --- | ---
Remote HIT | Negative | 1. UFH (Grade 1B)
Subacute HIT | Positive | 1. Delay surgery, if possible, until immunologic assay becomes negative (Grade 1B)
2. If surgery cannot be delayed, use UFH (Grade 2C)
Acute HIT | Positive | 1. Delay surgery, if possible, until functional and immunologic assays become negative (Grade 1B)
2. If surgery cannot be delayed, use lepirudin (Grade 1B)

If pre- or post-operative anticoagulation is indicated, a non-heparin anticoagulant should be used. American College of Chest Physicians Grading System: 1=strong recommendation; 2=weak recommendation; 3=based on high quality evidence; 4=based on moderate quality evidence; 5=based on low quality evidence; UFH, unfractionated heparin.

B. Cardiac catheterization/percutaneous coronary intervention

**Clinical situation** | **Laboratory profile** | **Recommended intraprocedural anticoagulation**
--- | --- | ---
Remote HIT | Negative | 1. Use a non-heparin anticoagulant (Grade 1B), argatroban (Grade 1C), lepirudin (Grade 1C), or bivalirudin (Grade 1C), or discontinu (Grade 1C)
2. If a non-heparin anticoagulant is not available, use UFH
Subacute HIT | Positive | 1. Use a non-heparin anticoagulant (Grade 1B), argatroban (Grade 1C), lepirudin (Grade 1C), or bivalirudin (Grade 1C)
Acute HIT | Positive | 1. Use a non-heparin anticoagulant (Grade 1B), argatroban (Grade 1C), lepirudin (Grade 1C), or bivalirudin (Grade 1C)

American College of Chest Physicians Grading System: 1=strong recommendation; 2=weak recommendation; 3=based on high quality evidence; 4=based on moderate quality evidence; 5=based on low quality evidence.

This document summarizes selected recommendations from the American College of Chest Physicians Evidence-Based Clinical Practice Guideline on Antithrombotic and Thrombolytic Therapy (8th Edition).

Guidelines provide the practitioner with clear principles and strategies for quality patient care and do not establish a fixed set of rules that preempt physician judgment.

For further information, please see the complete guidelines on the Chest Web site at www.chestjournal.org/content/135/6_suppl/340S.long or refer to the Practice Guidelines section of the ASH Web site at www.hematology.org/education/resources/guidelines. You may also contact the ASH Policy & Practice Department at 202-776-0544.

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