Summarizes selected recommendations from the: American College of Chest Physicians Evidence-Based Clinical Practice Guideline on Antithrombotic and Thrombolytic Therapy (8th Edition).
http://chestjournal.chestpubs.org/content/133/6_suppl/110S.abstract

HASHTI
1. Hold further doses of anticoagulant
2. Consider Antidote
3. Supportive treatment: volume resuscitation, inotropes as needed
4. Local or surgical Hemostatic measures: topical agents (aminocaproic acid, tranexamic acid)
5. Transfusion (red cells, platelets, FFP as indicated)
6. Investigate for bleeding source

Definitions Used for Reversal Situations
Non-urgent: Reversal is elective (procedures >7 days away)
Urgent (without bleeding): Reversal needed within hours
Urgent (with bleeding): Emergency reversal

1. Reversal of Warfarin (Coumadin®, Jantoven®)

<table>
<thead>
<tr>
<th>Non-Urgent</th>
<th>Urgent (Not Bleeding)</th>
<th>Urgent (Bleeding)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stop 5 days prior to procedure</td>
<td>• If procedure can be delayed 6-24 hours, vitamin K 5-10 mg PO/IV; otherwise</td>
<td>• HASHTI</td>
</tr>
<tr>
<td>• Check INR 1-2 days prior</td>
<td>• FFP or PCC prior to procedure. Repeat in 6-12 hours if INR high and</td>
<td>• Vitamin K 5-10 mg IV; repeat every 12 hours as needed</td>
</tr>
<tr>
<td>◦ If INR &gt;1.5 administer vitamin K 1-2 mg PO</td>
<td>• Vitamin K 5-10 mg PO/IV if sustained reversal is desired</td>
<td>• PCC or FFP; repeat every 6 hours as needed</td>
</tr>
</tbody>
</table>


1) Vitamin K therapy (10 mg) should be administered immediately by slow intravenous infusion over 30 minutes, and a repeat dose should be considered at 12 hours.
2) FFP 15 mL/kg - 30 mL/kg unless the patient is unable to tolerate the volume (4-8 U in an adult patient) should be infused. Use diuretic therapy when needed.
3) No proven superiority of 3-factor, 4-factor PCCs, or rVIIa over FFP. Clinical benefits are not established for these agents, and risk of thrombotic adverse events must be considered. Doses used in the literature have included 25 IU/kg (therapeutic INR) or 30-50 IU/kg (supratherapeutic INR) for PCCs, fixed dose of 2 mg for rVIIa.

Up to Date: 3-factor PCC plus 2U FFP, substitute rVIIa 20 mcg/kg for 2 U FFP if volume overloaded
2. **Reversal of Low-Molecular-Weight Heparins (Enoxaparin/ Lovenox®, Dalteparin/Fragmin®, Tinzaparin/Innohep®) and Fondaparinux¹ (Arixtra®)**

<table>
<thead>
<tr>
<th>Non-Urgent</th>
<th>Urgent (Not Bleeding)</th>
<th>Urgent (Bleeding)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hold day of procedure</td>
<td>• Wait 12-24 hours if possible</td>
<td>• HASHTI</td>
</tr>
<tr>
<td>• Once-daily regimens</td>
<td>• Consider protamine sulfate if delay not possible for high bleeding risk procedure</td>
<td>• Protamine sulfate</td>
</tr>
<tr>
<td>○ ½ dose day prior</td>
<td></td>
<td>• Consider rVIIa</td>
</tr>
<tr>
<td>• Twice-daily regimens</td>
<td></td>
<td></td>
</tr>
<tr>
<td>○ Hold evening dose day prior</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹Fondaparinux has no specific antidote

3. **Protamine Dose for Reversal of Heparin and LMWH**

<table>
<thead>
<tr>
<th>Agent*</th>
<th>Half-Life</th>
<th>Protamine Sulfate Dosing for Reversal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin</td>
<td>1-2 hours</td>
<td>Maximum dose is 50 mg</td>
</tr>
<tr>
<td>All</td>
<td>1-2 hours</td>
<td>• 1 mg per 90-100 units heparin given in previous 2-3 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• e.g., 25-35 mg if 1000-1250 units/hour heparin infusion</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>4.5 hours</td>
<td>• 1 mg per 1 mg Enoxaparin in previous 8 hours</td>
</tr>
<tr>
<td>Dalteparin</td>
<td>2.2 hours</td>
<td>• 1 mg per 100 units Dalteparin in previous 8 hours</td>
</tr>
<tr>
<td>Tinzaparin</td>
<td>3.9 hours</td>
<td>• 1 mg per 100 units Tinzaparin in previous 8 hours</td>
</tr>
</tbody>
</table>

* Half-life is longer with subcutaneous administration for all agents so may require monitoring with PTT (heparin) or anti-Xa level (LMWH) every 3 hours with repeat protamine (0.5 mg per indicated amount of LMWH or heparin) if bleeding continues
4. Reversal of Dabigatran

**Non-urgent:** Hold further doses of dabigatran
- CrCl > 50 ml/min: Hold 1-2 days
- CrCl < 50 ml/min: Hold 3-5 days
Consider longer times for major surgery, placement of spinal or epidural catheter or port

**Urgent:**

Hold dabigatran and check aPTT

- **Normal aPTT**
  - Unlikely dabigatran is contributing to bleeding

- **Prolonged aPTT**
  - Dabigatran present and may be contributing to bleeding

- **No antidote available**
  - For bleeding consider:
    - PCC†
    - activated PCC (FEIBA)†
    - rFVIIa†
    - hemodialysis

Reassess patient
Repeat abnormal coagulation tests*

**Abbreviations:** PCC = prothrombin complex concentrates; rFVIIa = recombinant factor VIIa
* Dabigatran primarily excreted in the urine, therefore maintain adequate diuresis
† Experimental evidence supports these agents but no clinical trial data available; PCC may not lower PTT
III. Antiplatelet Agent Reversal

Aspirin, Dipyramide/Persantine®, Aggrenox®, Clopidogrel/Plavix®, Ticlopidine/Ticlid®, Prasugrel/Effient®, Ticagrelor/Brilinta®

General Considerations

1. Half-lives
   a. Clopidogrel, ticlopidine, dipyramide, prasugrel, ticagrelor: 7-10 hours
   b. Low-dose aspirin (150 mg daily): 2-4.5 hours
   c. Overdose aspirin (>4000 mg): 15-30 hours
2. Reversibility of anti-platelet effect
   a. Aspirin, clopidogrel, ticlopidine, and prasugrel inhibit platelet function for lifetime of platelet. Inhibition takes 7-10 days to resolve as new platelets are generated.
   b. Ticagrelor is a reversible inhibitor, so platelet function normalizes after drug clearance.
3. Circulating drug or active metabolites can inhibit transfused platelets.
4. Must consider indication for use in decision to reverse
   a. Risk of coronary stent occlusion (which can be fatal) within 3 months of bare metal stent implantation; period of risk is likely longer for drug-eluting stents.
   b. Consult cardiologist if uncertain.

Reversal of Antiplatelet Agents

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</tr>
</thead>
<tbody>
<tr>
<td>• Discontinue agent 5-10 days prior to procedure</td>
<td>• Consider platelet transfusion prior to high risk bleeding procedures</td>
<td>• HASHTI • Platelet transfusion</td>
</tr>
</tbody>
</table>

Bracey AW et al. How do we manage patients treated with antithrombotic therapy in the perioperative interval. *Transfusion* 2011;51:2066-2077

Consider desmopressin (ddAVP) as an adjunct for aspirin reversal in patients without a history that contraindicates its use (e.g., previous cerebrovascular accident, hyponatremia).

Maintain aspirin treatment in patients who undergo CABG.
### C. Converting Anticoagulants to and from Dabigatran

<table>
<thead>
<tr>
<th>Current Anticoagulant</th>
<th>Anticoagulant to be Converted to</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin (INR 2-3)</td>
<td>Dabigatran</td>
<td>Discontinue warfarin and start dabigatran when INR &lt;2.0</td>
</tr>
</tbody>
</table>
| Dabigatran            | Warfarin (INR 2-3)              | • CrCl >50 ml/min: start warfarin 3 days before stopping dabigatran  
                        |                                  | • CrCl 31-50 ml/min: start warfarin 2 days before stopping dabigatran  
                        |                                  | • CrCl 15-30 ml/min: start warfarin 1 day before stopping dabigatran  
                        |                                  | • CrCl <15 ml/min: no recommendation |
| LMWH, heparin         | Dabigatran                      | Start dabigatran 0-2 hours before administration of last heparin/LMWH dose, or at same time as discontinuation of infusional heparin |
| Dabigatran            | LMWH, heparin                   | • CrCl ≥ 30 ml/min: start 12 hours after last dose of dabigatran  
                        |                                  | • CrCl < 30 ml/min: start 24 hours after last dose of dabigatran |

Abbreviations: CrCl = creatinine clearance; INR = international normalized ratio; LMWH = low-molecular-weight heparin

Pradaxa ® product monograph, 2010