Table 1: Reversal for ANTICOAGULANT therapy

ANTITHROMBOTIC	REVERSAL AGENT	COMMENTS
DIRECT THROMBIN INHIBITORS (DTIs) **IV:** – Argatroban – Bivalirudin (Angiomax®) Half-life 10-90 minutes **PO:** – Dabigatran (Pradaxa®) Half-life 12-17 hours in normal renal function **The aPTT is currently the only readily available lab test to QUALITATIVELY measure dabigatran. Do not use PT/INR**	Short half-life and discontinuation of DTI are primary means of attenuating bleed – support with crystalloid and blood products to facilitate rapid renal clearance of drug **4 Factor PCC** Dose*: 50 units/kg **(dose cap at 100 kg to mitigate thrombotic risk)** Administration: Place in empty IV bag and give slow IV push over 10 minutes – Use within 4 hours of reconstitution Onset: <30 minutes Caution: thrombotic risk **rFVIIa** Dose*: 100 mcg/kg **(dose cap at 100 kg to mitigate thrombotic risk)** – May repeat in 2 hours if continued bleeding Administration: IV bolus over 3-5 minutes – Use within 3 hours of reconstitution Onset: <30 minutes Caution: thrombotic risk	*Off-label use of rFVIIa/PCC:* – **REQUIRES ATTENDING APPROVAL** – Document attending name in the order comments Additional options: – If dabigatran ingested within 1 hour, consider activated charcoal. – Mechanical methods, such as dialysis, may be considered as a last resort Recommend not giving rFVIIa and PCC together due to high risk of thrombosis unless clinical situation warrants
FACTOR XA INHIBITORS – Fondaparinux (Arixtra®) Half-life 17-21 hours in normal renal function – Rivaroxaban (Xarelto®) Half-life 5-9 hours (up to 13 hours in elderly) – Apixaban (Eliquis®) Half-life 8-15 hours – Edoxaban (Savaysa ®) Half-life 10-14 hours) **The PT and the UFH/LMWH anti-Factor XA assay are currently the only readily available labs test to QUALITATIVELY measure rivaroxaban, apixaban or edoxaban. Do not use INR.**	**4 Factor PCC** Dose*: 50 units/kg **(dose cap at 100 kg to mitigate thrombotic risk)** Administration: Place in empty IV bag and give slow IV push over 10 minutes – Use within 4 hours of reconstitution Onset: <30 minutes Caution: thrombotic risk **rFVIIa** Dose*: 100 mcg/kg **(dose cap at 100 kg to mitigate thrombotic risk)** – May repeat in 2 hours if continued bleeding Administration: IV bolus over 3-5 minutes – Use within 3 hours of reconstitution Onset: <30 minutes Caution: thrombotic risk	*Off-label use of rFVIIa/PCC:* – **REQUIRES ATTENDING APPROVAL** – Document attending name in the order comments Additional option: If rivaroxaban, apixaban or edoxaban ingested within 1 hour, consider activated charcoal Recommend not giving rFVIIa and PCC together due to high risk of thrombosis unless clinical situation warrants

<table>
<tr>
<td>HEPARIN
Half-life: 1-2 hours</td>
<td colspan="2">Protamine
Dose: 1 mg reverses 100 units of UFH
<table>
<tr><th>Time since UFH</th><th>Dose per 100units UFH over last 3h</th></tr>
<tr><td><30 min</td><td>1 mg</td></tr>
<tr><td>30-120 min</td><td>0.5 mg</td></tr>
<tr><td>>120 min</td><td>0.25 mg</td></tr>
</table>
– Do not exceed 50mg in a single dose; high doses can have an undesirable ANTIcoagulant effect
– In clinical practice, give 50 mg IV x1 over 10 minutes. May redose if bleeding continues.
Administration: Slow IV push not to exceed 5mg/minute
Onset: 5-15 minutes
Caution: Rapid administration can cause severe hypotension and anaphylaxis</td>
<td>Prophylactic SQ doses of UFH do not lead to increased risk of hemorrhage. Look for other causes of hemorrhage</td>
</tr>
<tr>
<td>LMWHs
(enoxaparin)
Half-life: 2-8 hours</td>
<td colspan="2">Protamine (Does not reverse LMWH as effectively as it does UFH)
Dose: 1 mg for each 1 mg of enoxaparin in last 8 hours
– If >12 hrs have elapsed since LMWH administration, protamine may not be needed
– Do not exceed 50mg in a single dose; high doses can have an undesirable ANTIcoagulant effect
– In clinical practice, give 50 mg IV x1 over 10 minutes. May redose if bleeding continues.
Administration: Slow IV push not to exceed 5mg/minute
Onset: 5-15 minutes
Caution: Rapid administration can cause severe hypotension and anaphylaxis</td>
<td>If aPTT remains prolonged, may give 2nd dose of 0.5mg protamine per 1 mg LMWH

Consider FFP and other blood product support.</td>
</tr>
<tr>
<td>WARFARIN
Half-life 36 hours
(5 days for INR normalization)</td>
<td>SUPRATHERAPEUTIC INR
▪ INR 5-9: Omit 1-2 warfarin doses ± 1-2.5mg PO Vit K
▪ INR > 9 (NO BLEED): omit 1-2 warfarin doses ± 2.5-5mg PO Vit K

ACTIVE BLEEDING AT ANY INR:
▪ Hold warfarin & give Vit K 5-10mg IV (may repeat q12h) PLUS either PCC or FFP (PCC is PREFERRED)

▪ 4 Factor PCC 25 units/kg if INR >1.7 -<4*
4 Factor PCC 35 units/kg if INR 4-6*
4 Factor PCC 50 units/kg if INR > 6*
(dose cap at 100 kg to mitigate thrombotic risk)
OR
▪ FFP 10-30 mL/kg

SURGERY REVERSAL
▪ INR > 1.5-2.5
Surgery <24 hours: 0.5-1mg IV Vit K x1 +/- 5-8mL/kg FFP
Surgery 24-96 hours: 0.5-1mg PO Vit K x1 monitor INR q12-24h
▪ INR >2.5-5
Surgery <24 hours: 1-2.5mg IV Vit K x1 +/- 5-8mL/kg FFP
Surgery 24-96 hours: 1-2.5mg PO Vit K x1 monitor INR q12-24h</td>
<td>Phytonadione (Vitamin K)
Dose: See box on left
Administration: IV- dilute in 50 ml NS and give over 30 minutes
Onset: PO=24 hours; IV=12 hours
Caution: IV - may be associated with very small risk of anaphylaxis

FFP
Dose: See box on left
Administration: At least 10 ml/min
Onset: 2-6 hours
Caution: Carries risk of infection, must be thawed and a large volume is required (often > 1 liter)

PCC
Dose: See box on left
Administration: Place in empty IV bag and give slow IV push over 10 minutes
– Use within 4 hours of reconstitution
Onset: <30 minutes
Caution: thrombotic risk</td>
<td>Off-label use of rFVIIa/PCC:
– REQUIRES ATTENDING APPROVAL
– Document attending name in the order comments

ROUND DOSE TO NEAREST WHOLE VIAL

REPEAT INR 30 MINUTES AFTER END OF PCC INFUSION.

Although rarely needed, may consider repeat PCC dose if INR target not achieved</td>
</tr>
</table>

UFH=unfractionated heparin, PCC = prothrombin complex concentrates (Bebulin), FFP = fresh frozen plasma, rVIIa = recombinant active factor VIIa (NovoSeven), DDAVP = desmopressin, SIVP = slow intravenous push, LMWH=low molecular weight heparin

*Denotes that doses are NOT based on high quality evidence

Consider the following agents, along with ROTEM testing, if patient refractory to standard therapies:

DDAVP

Mechanism: increases release of vWF and enhances platelet adhesion and aggregation

Dose: 0.3 mcg/kg in 50 ml NS IV over 15 minutes

Caution: Serial doses associated with tachyphylaxis, hyponatremia, and seizures

Aminocaproic acid:

Mechanism: antifibrinolytic

Dose: 4-5 gm loading dose in 250 ml NS over 15 minutes followed by infusion of 1gm/hr infusion until bleeding subsides (max 30 gm/day)

Caution: May require renal adjustment

Tranexamic acid:

Mechanism: antifibrinolytic

Dose: 1 gm loading dose in 50 ml NS IV over 10 minutes followed by 1 gm in 250 ml NS infused over the next 8 hours

Caution: May require renal adjustment

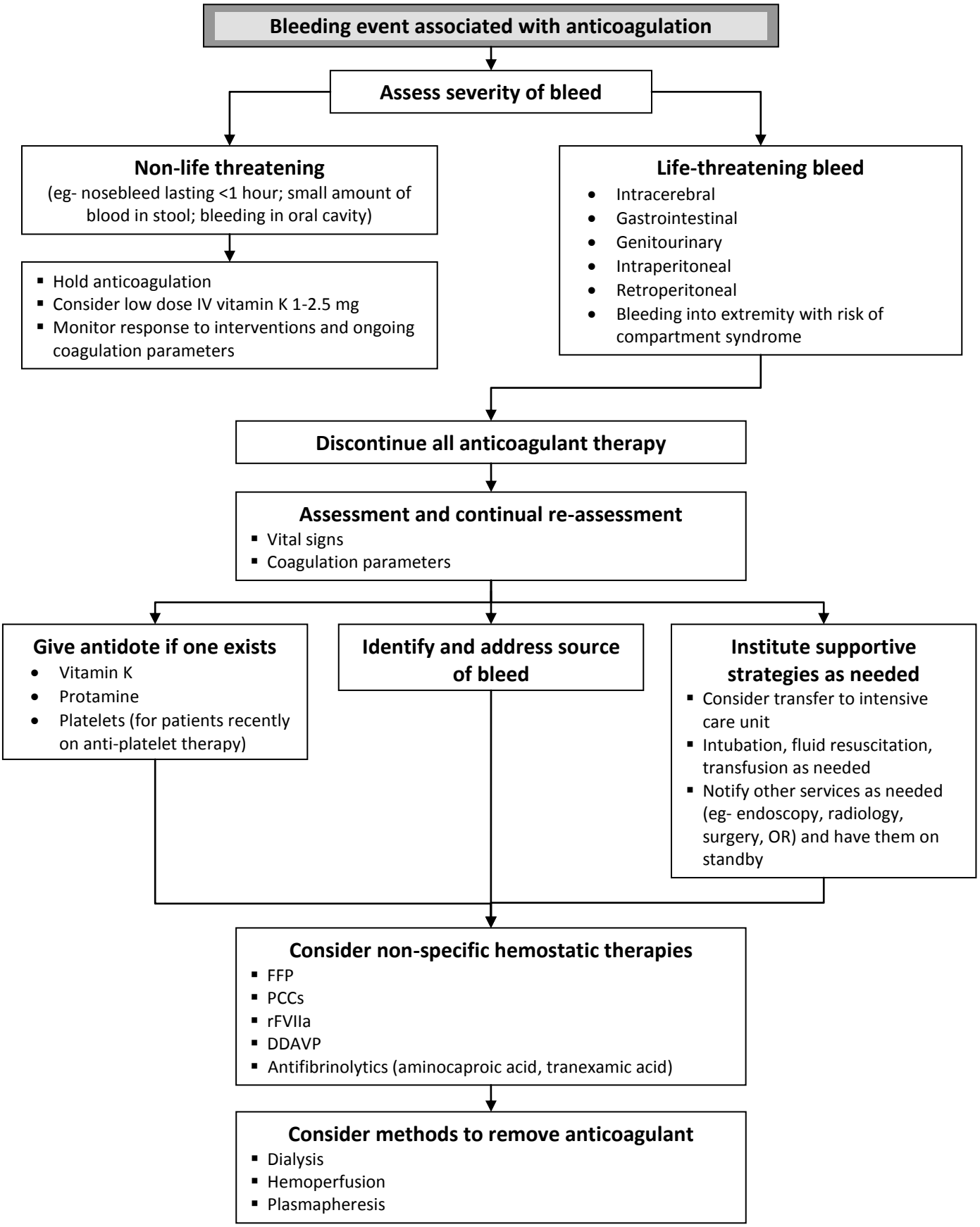
Table 2: Reversal for ANTIPLATELET therapy

	HALF-LIFE	REVERSAL AGENT	COMMENTS
ASPIRIN	15-30 minutes 5-10 days for platelet recovery	**DDVAP** Dose: 0.3 mcg/kg IV x 1 Administration: over 15 minutes Onset: Immediate Caution: Serial doses associated with tachyphylaxis, hyponatremia, and seizures	May need transfusion of functioning platelets to attenuate bleeding
CLOPIDOGREL (Plavix®)	8 hours ~ 5 days for platelet recovery		
PRASUGREL (Effient®)	7 hours ≤7 days for platelet recovery		
TICAGRELOR (Brilinta®)	~ 9 hours 3 days for platelet recovery		
Gp IIb-IIIa Eptifibatide (Integrilin®) Abciximab (Reopro®) Tirofiban (Aggrastat®)	30-120 minutes	**DDVAP** Dose: 0.3 mcg/kg IV x 1 Administration: over 15 minutes Onset: Immediate Caution: Serial doses associated with tachyphylaxis, hyponatremia, and seizures	- Short half-life and discontinuation of gpIIb-IIIa are primary means of attenuating bleed - May need transfusion of functioning platelets to attenuate bleeding - Mechanical methods, such as dialysis, may be considered as a last resort

UFH=unfractionated heparin, PCC = prothrombin complex concentrates (Bebulin), FFP = fresh frozen plasma, rVIIa = recombinant active factor VIIa (NovoSeven), DDAVP = desmopressin, SIVP = slow intravenous push, LMWH=low molecular weight heparin

***Denotes that doses are NOT based on high quality evidence**

OVERALL MANAGEMENT OF ANTICOAGULATED BLEEDING PATIENT



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