Adult heparin infusion protocol

This protocol reflects current evidence-based clinical practice. It is not a substitute for appropriate clinical evaluation and does not supersede clinical judgment.

Heparin overview[1]

Heparin is a glycosaminoglycan which *inhibits* the mechanism that induces the clotting of blood and the formation of stable fibrin clots. It combines with antithrombin III (AT III) and blocks thrombosis by inactivating activated factor X and ultimately inhibiting prothrombin's (factor II) conversion to thrombin (activated factor II). It has various indications including but not limited to atrial fibrillation, venous thromboembolism (treatment and prophylaxis), and acute coronary syndromes. Its volume of distribution is 0.07 L/kg and has a half-life of about 1.5 hours.

1. Initial assessment and orders
   a. **No anticoagulation within 24 hours of tPA (alteplase, Activase) administration for ischemic stroke.**
   b. If patient currently has epidural in place, refer to VCMC Clinical Practice Guideline for Anticoagulation Management surrounding Epidural/Intrathecal/Lumbar Puncture for proper timing of initiation.
   c. Discontinue all intramuscular injections.
   d. Discontinue all prophylactic anticoagulation.
   e. Discontinue aspirin >162 mg.
   f. Order baseline PT/INR, aPTT, CBC, SCr if not done within previous 24 hours.
   g. Order anti-Xa level if known therapeutic enoxaparin administration prior to initiation of heparin drip.[2] Baseline anti-Xa is not needed for those who were not on enoxaparin previously.
2. Exclusion criteria
   a. Baseline platelets < 50,000, or INR >1.5 unless approved by attending physician.
   b. Suspected or proven disseminated intravascular coagulopathy (DIC), thrombocytopenic purpura (TTP), or heparin induced thrombocytopenia (HIT).
   c. If supratherapeutic anti-Xa level for enoxaparin prior to heparin drip, must wait until anti-Xa level is within therapeutic range to initiate heparin drip. Recommend not to order initial loading dose.
3. Dosing[3,4,5]
   a. **Do not** give loading dose for the following:
      1. Hypothermic patients – increase sensitivity to anticoagulation during hypothermia
      2. Post-Op and Trauma patients
      3. Use of HIGHEST BLEEDING RISK nomogram.
      4. Transition from therapeutic enoxaparin.
   b. Dosing is based on actual body weight.
   c. Do not hold heparin while awaiting baseline labs. Pharmacist may order baseline labs if provider has not already done so.
   d. Loading and re-bolus doses not rounded to the nearest 1,000 units will be changed by the pharmacist during verification.

Table 1. Loading Dose and Initial Infusion Rates			
INDICATION	**LOADING DOSE***	**INITIAL INFUSION RATE**	**Maximum doses**
• Deep venous thrombosis (DVT) • Pulmonary embolism (PE) • Arterial embolism	80 units/kg IV	18 units/kg/hr	Max loading dose = 10,000 units Max initial rate = 2,250 units/hr
• Acute coronary syndrome (ACS) • Atrial fibrillation • Arterial dissection	60 units/kg IV	12 units/kg/hr	Max loading dose = 5,000 units Max initial rate = 1,000 units/hr
AFTER thrombolytic • Acute coronary syndrome (ACS) • Atrial fibrillation	60 units/kg IV	12 units/kg/hr	Max loading dose = 4,000 units Max initial rate = 1,000 units/hr
• Cerebrovascular accident (CVA, TIA)	NONE	12 units/kg/hr	Max initial rate = 1,000 units/hr
* All loading doses will be rounded to the nearest 1000 units			

4. Monitoring
   a. Obtain anti-Xa following dose changes as indicated per nomogram, CBC daily, and PT/INR once weekly.[2]
      1. aPTT will be affected by heparin but is also susceptible to change in other disease states such as DIC, shock liver, chronic liver disease, hemophilia, and dilutional coagulopathy. aPTT may be ordered if concern for these disease states but will not be used to manage heparin drip.
   b. Nursing to contact provider if:
      1. 2 consecutive anti-Xa are SUPRAtherapeutic or 3 consecutive anti-Xa are SUBtherapeutic at any point in therapy.
      2. Hemoglobin decrease >2 mg/dL from baseline; check for any potential bleeding.
      3. Platelet count falls by ≥30% from baseline (pharmacist to indicate value in order comments) or falls below 100,000 to rule out heparin induced thrombocytopenia.
      4. Rate >25 units/kg/hr, which may be due to heparin resistance.[2,6,7]
5. Dose Adjustments (Tables 2-4)[8]
   a. The rebolus dose in Table 1 will not exceed the initial bolus dose. Rebolus dose rounded to the nearest 1,000 units ordered and verified by provider and pharmacist will be located in PRN section of the MAR.
   b. In the event that the infusion has been turned off for > 60 minutes for a procedure:
      1. PROVIDER will discontinue the heparin powerplan, which include patient care, lab monitoring, drug order entry (infusion and re-bolus).
      2. The NURSE is to document the time when the drip was turned off by documenting zero rate.
      3. After the procedure, the PROVIDER will reorder the drip when it is safe to do so with new anti-Xa goals post review of the previous drip rates.
   c. Key points when restarting heparin drip after prolonged discontinuation:

Providers	• May reorder anti-Xa level to check for <u>supratherapeuti</u>c levels to determine if there is a need for possible delay in heparin drip re-initiation. • Consider giving a re-bolus only in select population, i.e. high risk for clotting. • Do not automatically restart at the initial starting rate per indication. • **<u>Review previous drip rates and restart at a rate that achieved goal anti-Xa levels.</u>** • Be sure to modify the "normalized rate" in Cerner during order entry.
Nursing	• If baseline anti-Xa was drawn post procedure and is out of goal range, do **NOT** make "rate adjustments" to the new starting rate written by the provider.

Table 2: Low Bleeding Risk (Goal anti-Xa: 0.3 – 0.7 unit/mL)			
Anti-Xa Level	**Rebolus or Hold**	**Rate Adjustment**	**Recheck anti-Xa**
<0.2	40 units/kg	↑ 2 units/kg/hr	6 hours
0.2 – 0.29	20 units/kg	↑ 1 units/kg/hr	6 hours
GOAL 0.3-0.7	**NONE**	**NONE**	**Continue q6hr until therapeutic x 2 then qAM**
0.71-0.8	NONE	↓ 1 unit/kg/hr	6 hours
>0.8	Hold 60 minutes	↓ 3 unit/kg/hr	6 hours

Table 3: Medium Bleeding Risk[8,9] (Goal anti-Xa: 0.3 – 0.55 unit/mL)			
Anti-Xa Level	**Rebolus or Hold**	**Rate Adjustment**	**Recheck anti-Xa**
<0.2	2000 units	↑ 2 units/kg/hr	6 hours
0.2-0.29	NONE	↑ 1 units/kg/hr	6 hours
GOAL 0.3-0.55	**NONE**	**NONE**	**Continue q6hr until therapeutic x 2 then qAM**
0.56-0.7	NONE	↓ 1 unit/kg/hr	6 hours
>0.7	HOLD 60 minutes	↓ 3 unit/kg/hr	6 hours

Table 4: Highest Bleeding Risk-Post Op/Trauma (Goal anti-Xa: 0.2 – 0.4 unit/mL)			
Anti-Xa Level	**Rebolus or Hold**	**Rate Adjustment**	**Recheck anti-Xa**
<0.2	NONE	↑ 1 units/kg/hr	6 hours
GOAL 0.2-0.4	**NONE**	**NONE**	**Continue q6hr until therapeutic x 2 then qAM**
0.41-0.5	NONE	↓ 0.5 unit/kg/hr	6 hours
0.51-0.6	NONE	↓ 1 unit/kg/hr	6 hours
0.61-0.7	HOLD 60 minutes	↓ 2 unit/kg/hr	6 hours
>0.71	HOLD 60 minutes	↓ 3 unit/kg/hr	6 hours

6. Bridge and Transitions[10]

Table 5. Heparin infusion conversion to other anticoagulant		
Heparin → following anticoagulants	Warfarin	1. For those with active clot or high risk for clotting, there must be a five day overlap of both drugs AND 2. Achieve single therapeutic INR ≥ 2 prior to stopping heparin infusion.
	Argatroban	1. Wait 3 hours after discontinuation of heparin infusion to start argatroban infusion. 2. Refer to VCMC Adult Argatroban Drip Protocol.
	Enoxaparin	Wait 2 hours after discontinuation of heparin infusion to start enoxaparin.
	DOAC	Refer to VCMC Clinical Practice Guideline: Guideline for the Prescribing of Direct Oral Anticoagulants (DOAC)

Table 6. Listed anticoagulant conversion to heparin infusion		
Warfarin	**To Heparin infusion**	1. If INR is subtherapeutic, start heparin infusion per protocol. 2. If INR is therapeutic or supratherapeutic, discuss with attending for optimal timing of heparin infusion initiation.
Argatroban*		If no hepatic insufficiency, start heparin infusion within 2 hours of stopping argatroban. Do not give loading dose. If there is hepatic insufficiency, start parenteral anticoagulant after 2-4 hours of stopping argatroban. Do not give loading dose. *The use of heparin assumes the patient does not have heparin allergy or heparin-induced thrombocytopenia.
Enoxaparin		From therapeutic enoxaparin doses: Initiate heparin infusion when next enoxaparin dose is expected to be given. No heparin loading dose.[6] From prophylactic enoxaparin doses: Initiate heparin infusion as clinically needed irrespective of time of enoxaparin dose.
DOAC		Refer to VCMC Clinical Practice Guideline: Guideline for the Prescribing of Direct Oral Anticoagulants (DOAC)

3. Reversal of heparin anticoagulation
    a. Discontinue heparin drip.
    b. Slow intravenous injection of Protamine 1% solution over 10 minutes.
    c. Dose: 1 mg Protamine for every 100 units of heparin administered over the last 3 hours; maximum 50 mg.
4. Perioperative management of heparin
    a. Discontinue heparin infusion 4 – 6 hours prior to surgery or sooner per discretion by surgeon or anti-Xa level < 0.2 unit/mL.
    b. Re-order heparin 12 – 24 hours after surgery when hemostasis is achieved and there is no evidence of bleeding in consultation with surgeon. May resume sooner if patient at high risk of clotting.

References:

1. Heparin, Package insert. [Online] 02 28, 2017
2. Rosenberg, A, et al. The Use of Anti-Xa Assay to Monitor Intravenous Unfractionated Heparin Therapy. Journal of Pharmacy Practice 2010; 23:210-216.
3. Garcia et al. *Parenteral Anticoagulants Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Eveidence-Based Clinical Practice Guidelines.* 2012; 141:e24s-343s.
4. Hohner et al. *Unfrationated heparin dosing for therapeutic anticoagulation in critically ill obese adults.* Journal of Critical Care 2015; 30:395-399.
5. Irwin et al. *Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.* Chest 2012;2_suppl
6. Gulseth et al. *Managing Anticoagulation Patients in the Hospital.* Bethesda : American Society of Health System Pharmacist, 2007.
7. Guervil, D. et al. *Activated Partial Thromboplastime Time versus Antifactor Xa Heparin Assay in Monitoring Unfractionated Heparin by Continuour Intravenous Infusion.* Ann Pharmacother 2011; 45:861-8
8. Vandiver, JW., et al. *Antifactor Xa Levels versus Activated Partial Thromboplastin Time for Monitoring Unfractionated Heparin.* Pharmacotherapy 2012; 32(6): 546-558
9. Hirsh et al. Heparin and low molecular weight heparin. Chest 2001;119:64s-94s
10. Hellerslia. Transition of Anticoagulants. Hospital Pharmacy 2014; p:1-2

11. Linkins et al. *Treatment and Prevention of Heparin-Induced Thrombocytopenia. Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physcians Evidence-Based Clinical Practice Guidelines*. Chest 2012; 141:e495s-e530s.