Adult Heparin Infusion Protocol

PURPOSE:

To provide guidelines for the safe administration and monitoring of adult weight-based heparin continuous infusion. This protocol reflects current evidence-based clinical practice. It is not a substitute for appropriate clinical evaluation and does not supersede clinical judgement.

BACKGROUND:

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.

PROTOCOL:

Initial Assessment and Orders

1) The Licensed Independent Practitioner (LIP) shall initiate the heparin protocol by entering an order for the PowerPlan PHA Heparin in the electronic health record (EHR). The order must specify the indication, intended dosing regimen, and if an initial loading dose is indicated.
2) Exclusion criteria
    a. **No anticoagulation within 24 hours of tPA (alteplase, Activase) administration for ischemic stroke.**
    b. Baseline platelets < 50, 000 or INR >1.5 unless approved by attending physician
    c. Suspected or proven disseminated intravascular coagulopathy (DIC), thrombocytopenic purpura (TTP), or heparin induced thrombocytopenia (HIT).
    d. If the anti-Xa level (Low Molecular Weight enoxaparin) is supratherapeutic, do not initiate the heparin infusion until the anti-Xa level (Low Molecular Weight enoxaparin) is within therapeutic range. Recommend not to order the initial loading dose.
3) A heparin loading dose may be ordered and administered prior to the start of the infusion. Loading and re-bolus doses must be rounded to the nearest 1,000 units.
4) Do not order a loading dose for the following:
    a. Hypothermic patients – increased sensitivity to anticoagulation during hypothermia
    b. Postop and trauma patients
    c. Use of the highest bleeding risk nomogram
    d. Transition from therapeutic enoxaparin to heparin infusion.
5) The LIP must assess for labs and order as indicated.
    a. Baseline PT/INR, CBC, Serum Creatinine (Scr) if not done within previous 24 hours
    b. Anti-Xa (Low Molecular Weight Enoxaparin) level if known therapeutic enoxaparin administration is not needed for those who were not on enoxaparin previously.
    c. Pharmacists may order baseline labs if LIP has not already done so.
6) If the patient currently has an epidural in place, refer to CPG.46 Anticoagulation Management Surrounding Epidural-Intrathecal-Lumbar Puncture for proper timing of initiation.
7) From the LIP's PHA Heparin PowerPlan orders, nurses shall complete the following patient care orders:
    a. Discontinue all intramuscular injections
    b. Discontinue all prophylactic anticoagulation
    c. Discontinue aspirin >162 mg

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. Use heparin 1000 units/mL vials for all loading doses. Do not give loading dose of heparin if patient on Highest Bleeding Risk Algorithm.			

8) Nursing shall review the heparin infusion order taking note of the ordered dosing regimen, whether an initial loading dose has been ordered, and the desired anti-Xa therapeutic goal range.
9) Dosing is based on actual body weight.
10) Do not hold heparin while awaiting baseline labs.
11) Heparin is a high alert medication. Nursing must complete an independent double check (IDC) prior to administering boluses, the initial infusion rate and rate changes, and when a new bag of heparin is hung. See policy PH.70 High Alert Medications.

Monitoring

1) Nursing to obtain anti-Xa level (Unfractionated heparin) following dose changes as indicated per nomogram in addition to CBC daily, and PT/INR once weekly.[2]
    a. 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.
2) Nursing to contact LIP if:
    a. There are 2 consecutive anti-Xa Level (Unfractionated heparin) are SUPRAtherapeutic or 3 consecutive anti-Xa Level (Unfractionated heparin) are SUBtherapeutic at any point in therapy. This is the LIP's opportunity to assess if an off-protocol adjustment is indicated to achieve goal more safely and quickly.
    b. Hemoglobin decrease > 2 mg/dL from baseline; check for any potential bleeding.
    c. 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.
    d. Rate > 25 units/kg/hr, which may be due to heparin resistance.[2,6,7]

Dose Adjustments

3) Nursing Driven Dose Adjustments (Tables 2-4)[8]
    a. The re-bolus dose in Table 1 will not exceed the initial bolus dose. Re-bolus dose rounded to the nearest 1,000 units ordered and verified by LIP and pharmacist will be in the as needed (PRN) section of the Medical Administration Record (MAR).
    b. Nursing is to document the following on the MAR: boluses, rate changes including when the drip is held (rate = 0), infusion rates at change of shift and when a new bags is hung, and IDCs.

4) Table 2: Low Bleeding Risk (Goal anti-Xa level [unfractionated heparin]: 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

Use heparin 1000 units/mL vials for all re-bolus doses.

Table 3: Medium Bleeding Risk[8,9] (Goal anti-Xa level [unfractionated heparin]: 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

Use heparin 1000 units/mL vials for all re-bolus doses.

Table 4: Highest Bleeding Risk-No initial or repeat boluses (Goal anti-Xa level [unfractionated heparin]: 0.3 – 0.45 unit/mL)			
Anti-Xa Level	**Rebolus or Hold**	**Rate Adjustment**	**Recheck anti-Xa**
< 0.2	NONE	↑ 2 units/kg/hr	6 hours
0.2-0.29	NONE	↑ 1 units/kg/hr	6 hours
GOAL 0.3-0.45	**NONE**	**NONE**	**Continue q6hr until therapeutic x 2 then qAM**
0.46-0.6	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

Use heparin 1000 units/mL vials for all re-bolus doses.

5) In the event that the heparin infusion has been turned off for > 60 minutes for a procedure:
   a. The LIP shall discontinue the heparin powerplan, which include patient care, lab monitoring, drug order entry (infusion and re-bolus).
   b. The NURSE is to document the time when the drip was turned off by documenting zero rate.
   c. After the procedure, the LIP shall reorder the drip when it is safe to do so with new anti-Xa level (Unfractionated Heparin) goals post review of the previous drip rates.
   d. Key points when restarting heparin drip after prolonged discontinuation:

LIP	• May reorder anti-Xa level (Unfractionated heparin) level to check for supratherapeutic levels to determine ifthere 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. • **Review previous drip rates and restart at a rate that achieved goal anti-Xa levels.** • Be sure to modify the "normalized rate" in Cerner during order entry.
Nursing	• If baseline anti-Xa level (Unfractionated heparin) was drawn post procedure and is out of goal range, do **NOT** make "rate adjustments" to the new starting rate written by the provider.

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. Initiate argatroban within 2 hours after discontinuation of heparin infusion. 2. Refer to VCMC Adult Argatroban Drip Protocol.
	Enoxaparin	Wait 2 hours after discontinuation of heparin infusion to start enoxaparin.
	DOAC	See CPG.41 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)

1) If reversal of heparin anticoagulation is indicated the LIP may order the following
    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.
2) For the perioperative management of heparin, the LIP may
    a. Discontinue heparin infusion 4 – 6 hours prior to surgery or sooner per discretion by surgeon or anti-Xa level (Unfractionated heparin) 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.