GUIDELINE: VENOUS THROMBOEMBOLISM (VTE) PROPHYLAXIS IN CHILDREN AND ADOLESCENTS, INPATIENT

July 30, 2024

Clinical algorithm:

Thrombosis Risk Factors

Acute
Family history of thrombosis
Recent Orthopedic surgeries
Spinal Cord Injury
Cancer*
Recent trauma
Presence of CVC
Bacteremia
Medications (Asparaginase)
Severe dehydration
Iron Deficiency
Long bone or complex fractures
Cardiac Care Unit
Critical Illness
Inflammatory states (ie MIS-C)

Chronic:
Obesity
Estrogen Containing Compounds
Nephrotic Syndrome
Inflammatory Bowel Disease / Protein Losing Enteropathies
Acquired/Inherited Thrombophilia

Historical Information:
Family history of VTE
Personal History of VTE

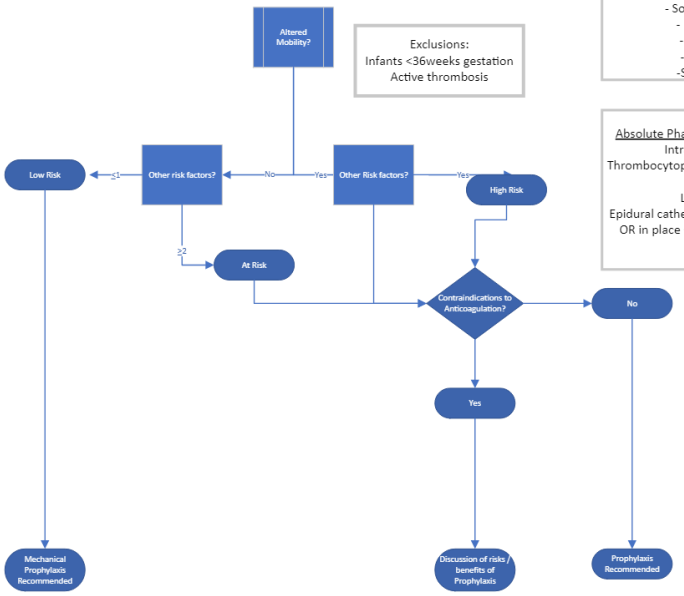
+Patients ≥10 y/o increased risk than their younger cohorts

* For patients with underlying cancer diagnosis please see oncology supplemental algorythm

Should reassess every 48-72 hours AND at time of discharge

Any patient discharging home with anticoagulation should been seen in PHO clinic within one week of discharge.

Thromboprophylaxis in Hospitalized Pediatric Patients



Exclusions:
Infants <36weeks gestation
Active thrombosis

Mechanical Contraindications
Recent surgery (Surgery input needed)
Acute DVT (within 72 hours)

Relative Pharmacologic Contraindications
Recent surgery (Surgery input needed)
Bleeding disorder (not all the same)
- Some coagulopathies
- Intracranial Mass
- HIT/Pork allergy
- Pelvic Fractures
-Spinal Cord Injury

Absolute Pharmacologic Contraindications
Intracranial hemorrhage
Thrombocytopenia <50k (unable to maintain)
Active Bleeding
LP within 18 hours
Epidural catheter placement within 24 hours OR in place OR planned removal within 2 hours

Testing for Thrombophilia

- When:
  - Significant family history
  - Unprovoked x2
  - Shared decision-making with patient/family
- What to include:
  - APC resistance/ Factor V Leiden
  - Prothrombin Gene Mutation (Prothrombin G20210A)
  - Protein C Activity
  - Protein S Activity
  - Antithrombin III
  - Antiphospholipid Antibody (aPL AND B2 glycoprotein)

Dosing:

Lovenox starting dose (>2 months of age)
Prophylaxis: 0.5 mg/kg Q12H

Xarelto dosing
Prophylaxis: weight based as below
2.6-2.9kg - 0.8 mg/dose q8h
3-3.9kg - 0.9 mg/dose q8h
4-4.9kg - 1.4 mg/dose q8h
5-6.9kg - 1.6 mg/dose q8h
7-7.9kg - 1.8 mg/dose q8h
8-8.9kg - 2.4 mg/dose q8h
9-9.9kg - 2.8 mg/dose q8h
10-11.9kg - 3 mg/dose q8hr
12-19.9kg - 2 mg/dose q12h
20-29.9kg - 2.5 mg/dose q12h
30-49.9kg - 7.5 mg/dose q24h
>50kg - 10 mg/dose q24h

This dosing EXCLUDES patients with Fontan's.

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Clinical guideline summary

1.1. **CLINICAL GUIDELINE NAME:** Venous Thromboembolism (VTE) Prophylaxis in Children and Adolescents, Inpatient

1.2. **PATIENT POPULATION AND DIAGNOSIS:** VTE risk screening is strongly encouraged for all pediatric patients, regardless of age. As children increase in age and reach puberty, their VTE risk profile becomes like that of adult patients. Initial screening should be completed within 24 hours of admission. Reassessment of risk should be done when the patient changes level of care, has a surgical/ invasive procedure, or a catheter placed during the inpatient stay. Prophylaxis should be considered based on the risk score algorithm. Mechanical and pharmacologic dosing recommendations are found in this guideline. *Consultation with Pediatric Hematology is not necessary unless a VTE is identified, unless there is a plan to discharge a patient on prophylaxis.*

1.3. Included:

1.3.1. All patients admitted to the children's hospital.

1.4. Excluded:

1.4.1. Patients with current venous thromboembolism

1.4.2. Premature infants (less than 36 weeks' gestation)

1.5. **APPLICABLE TO:** Corwell Health West, Helen DeVos Children's Hospital

1.6. **BRIEF DESCRIPTION:** The rate of venous thromboembolism (VTE) among hospitalized children and adolescents is low compared to adults, but substantially increasing over time. Recent statistics report nearly 60 events of VTE per 10,000 admissions. At Helen DeVos Children's Hospital, VTE is the second most common hospital acquired condition behind Central Line Associated Blood Stream Infection. VTE occurrence is bimodal, peaking in children less than 1 year old (mostly associated with central venous lines) and those over 10. In addition, many children's hospitals care for individuals in the 18-25-year age range who should also follow VTE prophylaxis guidelines. Although there are no validated scoring systems for VTE risk in children under 18 years of age, risk factors are clear and protocols have been established, evaluated, and published for a single center experience.

1.7. **OVERSIGHT TEAM LEADER(S):** Claudia Nadernejad MD, Albert Cornelius MD, Daniel Watkins MD, Heather Sowinski DO

1.8. **OWNING EXPERT IMPROVEMENT TEAM (EIT):** HDVCH VTE EIT

1.9. **MANAGING CLINICAL PRACTICE COUNCIL (CPC):** Children's Health CPC

1.10. **CPC APPROVAL DATE: October 2024**

1.11. **OTHER TEAM(S) IMPACTED:** Hospitalist, PICU, Nursing

1.12. **IMPLEMENTATION DATE:** March 2024

1.13. **LAST REVISED:** October 2024

1.14. **FOR MORE INFORMATION, CONTACT:** Liala Burmeister

GUIDELINE: VENOUS THROMBOEMBOLISM (VTE) PROPHYLAXIS IN CHILDREN AND ADOLESCENTS, INPATIENT

Clinical pathways clinical approach

TREATMENT AND MANAGEMENT

2. **Purpose**

2.1. **Background –** The rate of venous thromboembolism (VTE) among hospitalized children and adolescents is low compared to adults, but substantially increasing over time. Recent statistics report nearly 60 events of VTE per 10,000 admissions. At Helen DeVos Children's Hospital, VTE is the second most common hospital acquired condition behind Central Line Associated Blood Stream Infection. VTE occurrence is bimodal, peaking in children less than 1 year old (mostly associated with central venous lines) and those over 10. VTE risk screening is strongly encouraged for all pediatric patients, regardless of age. All children, except those <36 weeks gestation or with an active VTE must be screened for VTE risk. Initial screening should be completed within 24 hours of admission. Reassessment of risk should be done when the patient transfers to a different unit or care team, including discharge, has a surgical/ invasive procedure, or a catheter placed during the inpatient stay. Prophylaxis should be considered based on the risk score algorithm. Mechanical prophylaxis and pharmacologic prophylaxis with dosing recommendations are found in this guideline. *Consultation with Pediatric Hematology is not necessary unless a VTE is identified and planning to discharge/transfer to another facility*.

1.1.1. Included:

1.1.1.1. All patients admitted to the children's hospital

1.1.2. Excluded:

1.1.2.1. Patients with current venous thromboembolism

1.1.2.2. Premature infants (less than 36 weeks gestation)

3. **Definitions**

3.1. Altered mobility: a permanent or temporary state in which the child has a limitation in independent, purposeful physical movement of the body or of one or more extremities

1.1.2.3. Immobility: permanent state of altered mobility (e.g., paralysis)

1.1.2.4. Impaired physical mobility: temporary state of immobility (e.g., cast, post-op)

3.2. Bleeding, defined by The International Society of Hemostasis and Thrombosis:

1.1.3. Major Bleeding: fatal bleeding, overt bleeding with a hemoglobin decreases of greater than or equal to 2 g/dL in 24 hours, bleeding into a critical organ (brain, lung, retroperitoneal), or bleeding requiring surgical intervention

1.1.4. Minor Bleeding: overt or macroscopic bleeding that does not meet criteria for major bleeding.

3.3. Mechanical prophylaxis: any method to assist the flow of blood in the deep veins of the leg (e.g., sequential compression devices).

1.1.5. Sequential Compression Device (SCD): a device designed to intermittently squeeze blood from underlying deep veins in the leg upon compression of an inflatable sleeve, and to allow the blood to flow again when it decompresses; also known as intermittent compression device (ICD) or intermittent pneumatic compression (IPC)

3.4. Superior Vena Cava (SVC) Syndrome: thrombus that obstructs the superior vena cava causing swelling of the face and neck

3.5. Thrombophilia: an inherent or acquired condition that may result in the increased formation of blood clots / thrombus (blood clotting disorder)

3.6. Venous Thromboembolism (VTE): a blood clot (thrombus) in a vein or one that has broken free and is carried in the bloodstream (embolus)

3.7. Critical Illness: Admitted to PCCU **and** has any of the following-sepsis or systemic inflammatory response syndrome (SIRS), acute mechanical ventilation (not home vent dependent on usual settings), requires a vasoactive infusion, cyanotic heart disease or poor myocardial contractility (SF < 15%)

4. **Guideline Recommendations**

A. VTE prophylaxis with a sequential compression device (SCD) is indicated for the following-
   i. During surgery, patients expected to undergo a procedure lasting over 60 minutes. SCDs should be applied to the lower extremities from time of induction of general anesthesia; Refer to **Table 1** for contraindications to mechanical prophylaxis.
   ii. For patients falling into the moderate risk category for VTE (and a few in the low moderate risk category). Evidence to support mechanical prophylaxis in younger children is sparse, but active or passive range of motion (ROM) should be encouraged in younger children with altered mobility. SCDs should be considered in younger children at risk for VTE if appropriately sized sleeves are available, especially in higher risk children for whom pharmacologic prophylaxis would be contraindicated: Refer to **Table 1** for contraindications to mechanical prophylaxis.

Table 1: Contraindications to Mechanical Prophylaxis
• Lower extremity Deep Vein Thrombosis (DVT), present or suspected • Extremity with an acute fracture • Extremity with peripheral IV (PIV) access in place • Skin conditions involving the extremity (e.g., dermatitis, burn) • Unable to achieve correct fit due to patient size

B. Patients should be assessed for VTE risk factors (see **Table 2**) and assigned to the risk category (see **Table 3**) respective to their assessment:
   i. At the time of inpatient admission, and
   ii. VTE Risk should be reassessed every 48-72 hours of hospitalization, and
   iii. With procedural intervention, any change in level of care, or catheter placement
   iv. At time of transfer either to another facility or unit and and/or discharge

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Table 2: VTE Risk Factors*	
Acute • Family history of thrombosis • Recent Orthopedic surgeries • Spinal Cord Injury • Cancer* • Recent trauma • Presence of CVC • Bacteremia • Medications (Asparaginase) • Severe dehydration • Iron Deficiency • Long bone or complex fractures • Cardiac Care Unit • Critical Illness • Inflammatory states (ie MIS-C)	Chronic • Obesity • Estrogen Containing Compounds • Nephrotic Syndrome • Inflammatory Bowel Disease / Protein Losing Enteropathies • Acquired/Inherited Thrombophilia Historical Information: • Family history of VTE • Personal History of VTE +Patients <1 year and ≥10 y/o increased risk than their younger cohorts

*to be used in conjunction with risk category scoring Table 3 (see below)

Table 3: Determining VTE Risk Category		
Expected **altered mobility** >48hrs	**+** Number of **VTE risk factors**	**=** **Risk category**
NO	None	Very Low
NO	1 or more	Low Moderate
YES	0 or 1	Moderate
YES	2 or more	High

C. VTE risk assessment will be completed by an ordering provider (i.e. attending physician, resident, Physician Assistant, Nurse Practitioner) and documented accordingly in the medical record.
D. When indicated, it is recommended that VTE prophylaxis (see **Table 4**) begin no later than 24 hours after admission, unless contraindicated (see **Table 1** and **Table 5**).
    i. **NOTE:** Example strategies for risk factor mitigation include removing venous catheters as soon as possible, treating infections, encouraging mobility, and avoiding estrogen therapy

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Table 4: VTE Prophylaxis Stratified by Risk Category		
Very Low / Low Moderate risk	**Moderate risk**	**High risk**
• Encourage early ambulation • Mitigate risk factors (see **NOTE** under 3D) • Low/Moderate- also consider SCD while at rest for those patients with risk factors for lower extremity DVT	• Encourage early ambulation • Mitigate risk factors (see **NOTE** under 3D) • Administer mechanical prophylaxis (see **Table 1**) ○ SCD preferred ○ Make efforts to achieve 18 hours of daily use	• Encourage early ambulation • Mitigate risk factors (see **NOTE** under 3D) • Administer mechanical prophylaxis (see **Table 1**) ○ SCD preferred ○ Make efforts to achieve 18 hours of daily use • Recommend pharmacologic prophylaxis (see **Table 5**) ○ Consider Pediatric Hematology consult when weighing risk versus benefit in patients at risk of bleeding

Table 5: Contraindications to Pharmacologic Prophylaxis	
Absolute Contraindications	**Relative Contraindications**
Intracranial hemorrhage Thrombocytopenia <50k (unable to maintain) Active Bleeding LP within 18 hours Epidural catheter placement within 12 hours OR in place OR planned removal within 4 hours**	Recent surgery (Surgery input needed) Bleeding disorder (not all the same) Some coagulopathies Intracranial Mass HIT/Pork allergy Pelvic Fractures Spinal Cord Injury

**https://assets.contentstack.io/v3/assets/blt7b132cfc09cf5e18/blt14de51de4a169f39/Anticoagulation_Management_Pediatric_Inpatient.pdf

E. Recommendations to consider prior to prescribing pharmacologic prophylaxis:
   i. In surgical patients – seek input regarding bleeding risk prior to initiation
      a. Discuss timing of initiation or delay in therapy with surgical team (e.g., neurosurgery, orthopedic surgery).
   ii. Consider Pediatric Hematology consultation when considering alternative pharmacologic agents, when weighing risk versus benefit in patients at risk of bleeding, or if patient is thought to have a confirmed VTE

F. Review dosing and monitoring section for pharmacologic prophylaxis
   i. Evaluate renal function (i.e., serum creatinine) upon initiation & every 1-2 weeks while receiving anticoagulation prophylaxis; dose may need to be adjusted for patients with renal dysfunction.
   ii. Obtain a complete blood count (CBC) upon initiation & approximately every week while receiving anticoagulation prophylaxis.
      a. Maintain platelet count>50,000 mm^3; risk of bleeding may outweigh benefit of prophylaxis if the patient is unable to maintain the platelet parameter.
      b. Monitor for evidence of heparin-induced thrombocytopenia (HIT)
      c. A significant drop in hemoglobin should prompt immediate reassessment.

4. **Pharmacologic Prophylaxis Medication Recommendations**
   A. Pharmacologic agent dosing and administration
      i. Subcutaneous (SQ) administration of prophylactic unfractionated heparin (UFH) or LMWH (enoxaparin) is recommended.
      ii. **Always** discuss prophylaxis start and timing thereof with attending surgeon or anesthesia (when neuraxial procedure has been done or epidural catheter is in place or recently removed) prior to initiation
      iii. Initiate prophylactic therapy as described in **Tables 6**, **7**
         a. UFH: is preferred for patients who are recent post-op patients and those who are anticipated to go to surgery soon due to the ease of reversal with protamine and short half-life of the drug. It also may be considered instead of LMWH for patients with significant renal dysfunction or burn patients requiring VTE prophylaxis.
         b. LMWH (enoxaparin) is the preferred agent for thromboprophylaxis unless there is evidence of CNS bleeding, anticipated surgery, or epidural catheter in place.
      iv. The anti-factor Xa level is used as a measure of efficacy for low-molecular weight heparins (LMWH), when appropriate.
         a. **Note:** Epic identifies anti-factor Xa levels for LMWH (Lovenox) monitoring as "LMWH level"
         b. Monitor anti-factor Xa when indicated, as noted in **Table 6 but not required**
            1. Check the anti-factor Xa level 4 hours following third or 4^{th} dose administration (subcutaneous delivery).
         c. It is not necessary to monitor an anti-factor Xa level in patients receiving prophylactic LMWH therapy (hyperbilirubinemia or high plasma hemoglobin levels may interfere with assay and cause anti Xa levels to be falsely low). Consult lab for the most recent reference range for LMWH.
         d. Close monitoring is recommended for the following patient populations: young patients, obese patients, and patients with renal impairment or failure.
      v. Rivaroxaban (direct Xa inhibitor) may be used for VTE prophylaxis in some adolescent young adult patients with cancer. Discuss management with Pediatric Hematology and Oncology.
      vi. On rare occasions, agents other than LMWH, heparin, or rivaroxaban may be indicated for VTE prophylaxis. Consider Pediatric Hematology and pharmacy consultation.

Table 6: Prophylactic LMWH (enoxaparin) Dosing & Monitoring		
Patient type/age	**Enoxaparin dosing**	**Monitoring / Notes***
< 2 months	0.75 mg/kg/dose SQ Q12 hours	Monitoring of anti-factor Xa levels indicated/recommended

2 months or < 60 kg (up to 18 years)	0.5 mg/kg/dose SQ Q12 hours (max starting dose of 30 mg/dose)	Monitoring of anti-factor Xa levels *may be* indicated if enoxaparin continued ≥ 3 days
> 18 years or ≥ 60 kg (up to 125 kg)	40 mg SQ once daily OR 30 mg SQ every 12 hours	Monitoring of anti-factor Xa levels *may be* indicated if enoxaparin continued ≥ 7 days
> 125 kg	40 mg SQ every 12 hours	Monitoring of anti-factor Xa levels indicated/recommended
Renal dysfunction	Consider decreasing dose, switching to UFH, and/or consult pharmacy)	Monitoring of anti-factor Xa levels indicated/recommended

* Anti-Xa levels can be drawn 4 hours after the 3rd or 4th SQ dose and should be 0.1-0.3 units/mL for prophylaxis for those with renal dysfunction or <2months of age but would otherwise ***not*** recommend obtaining. Consult lab for the most recent reference range for LMWH. Consult with pharmacy for dose change recommendations.

Table 7: Prophylactic Unfractionated Heparin (UFH) Dosing & Monitoring		
Patient type/age	**UF Heparin dosing**	**Monitoring / Notes**
≤ 60 kg	75 units/kg/dose SQ Q12 hours	Consider CBC monitoring
> 60 kg	5000 units SQ every 12 hours	
> 18 yrs or > 125 kg	5000 units SQ every 8 hours	
Continuous infusion	≤ 10units/kg/hr	
Renal dysfunction	No adjustment required	

B. Adhere to the following precautions when administering LMWH:

i. **Always discuss prophylaxis timing with attending surgeon prior to initiation / re-initiation**
ii. Avoid intramuscular injections and arterial punctures while receiving LMWH prophylaxis; consider appropriate precautions if arterial punctures are warranted.
iii. Avoid aspirin or other antiplatelet drugs while receiving LMWH prophylaxis; acetaminophen is the preferred drug if analgesia or an antipyretic is required.
iv. Hold the 2 doses of LMWH prior to a scheduled lumbar puncture (at least 12 hours from last injection).
    a. Note: Paraspinal hematomas and paralysis have been reported in patients undergoing a lumbar puncture while receiving LMWH.
v. Do NOT use twice daily dosing of LMWH in patients receiving continuous epidural anesthesia. **Any** VTE prophylaxis with an epidural catheter in place should be discussed with anesthesia.
vi. Discontinue LMWH 24 to 36 hours prior to scheduled surgical procedures (e.g., administer the last dose of LMWH in the morning the day before).

C. American Society of Regional Anesthesia and Pain Medicine Guidelines - Corewell Health Anesthesia follows these guidelines for **ADULT** VTE prophylaxis and neuraxial blockage.

i. Refer also to Neuraxial Anesthesia and Anticoagulation Guidelines

ii. Discuss anticoagulation with anesthesiology, primary care team, and pharmacy about how long to hold prophylaxis anticoagulation prior to epidural catheter placement or manipulation whether prophylaxis anticoagulation can be restarted while a catheter remains in place, and when to restart prophylaxis anticoagulation after a catheter is removed.

iii. https://assets.contentstack.io/v3/assets/blt7b132cfc09cf5e18/blt14de51de4a169f39/Anticoagulation_Management_Pediatric_Inpatient.pdf

D. Medication management

i. The primary care team is responsible for communicating with involved surgical teams regarding recommendations on holding anticoagulation prior to and following procedures / surgeries

ii. The primary care team is responsible for entering appropriate orders into the Electronic Medical Record and communicating the plan.

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