Anticoagulation in Pediatric Venous Thromboembolism (v1.0)

Determining Need

- Anticoagulation is recommended for most cases of VTE, unless there is a strong contraindication.
- Asymptomatic, incidentally found VTE may not require anticoagulation.

For additional info about anticoagulation in VTE, visit www.anticoagulationtoolkit.org

Choice of Anticoagulant

- LMWH is the anticoagulant most frequently used for DVT or PE in children.
- Warfarin is less commonly used due to narrow therapeutic index, drug interactions, sensitivity to diet changes and difficulty with monitoring requirements (checking INRs in neonates, infants and small children difficult).
- DOACs (dabigatran, rivaroxaban, apixaban, and edoxaban) may be considered for some adolescent patients ≥ 50kg. Weight-based dosing recommendations for rivaroxaban have been published for children 2.6-49kg. Additional ongoing studies are underway to evaluate the safety, efficacy, and dosage in children.

LMWH Initiation and Dosing

- Prior to initiation of anticoagulation, baseline PT, PTT, CBCP, and serum creatinine are recommended. For renal insufficiency, dose and frequency will require adjustment from standard guidelines.
- Enoxaparin dosing and monitoring may vary, depending on institutional policy.

Enoxaparin Dosing by Age	
Treatment*	
Premature neonates	2mg/kg/dose SUBQ twice daily
Full term neonates (<1 month of age)	1.7mg/kg/dose SUBQ twice daily
1-3 months	1.5mg/kg/dose SUBQ twice daily
>3 months	1mg/kg SUBQ twice daily
Prophylaxis**	
<2 months	0.75mg/kg/dose SUBQ twice daily
>2 months	0.5mg/kg/dose SUBQ twice daily

- Anti-Xa level monitoring
  - Treatment: routine monitoring recommended with target of 0.5-1.0 IU/mL (peak level). Monitoring schedule can vary based on changes in pt status (bleeding/clotting events, weight, renal status).
  - Prophylaxis: target 0.1-0.3 IU/mL (peak level) (monitoring not routinely done unless renal dysfunction or extremes of body weight).
  - Draw levels 4 hours (3-6 hours acceptable) after the 3rd or 4th dose. May vary with institutional policies.

Depending on institutional policy, doses may be rounded up to the nearest whole MG.

***Obesity may require reduced dosing. Anti-Xa monitoring should be performed within 2 wks after initiation to assess for accumulation.**

****Prophylaxis (ie DVT prophylaxis in hospitalized patients) is not routinely recommended in non-adolescent pediatric patients.**

Warfarin Initiation and Dosing

- Baseline labs should be obtained prior to initiation and include PT/INR, PTT, CBCP, and comprehensive metabolic panel.
- Pregnancy testing should be performed before initiation in menstruating females.
- Goal INR 2-3 (or as determined based on underlying need – mechanical heart valves, APLAS, homozygous Protein C deficiency).
- Parenteral tx should be used for 5 days or until INR is within goal range.
- Inpatient initiation: Pts without liver dysfunction initiated on 0.2mg/kg (max 7.5mg) once daily. If known liver dysfunction, initiate on 0.1mg/kg (max 5mg) once daily. Further dose adjustments per institutional protocol. Tailor initial dose based on patient's risk of bleeding, potential sensitivity to warfarin, and presence of potential drug interactions. INR should be checked daily until therapeutic.
- Outpatient initiation: Follow institutional protocols.
- Adjustments are made to the total weekly dose of warfarin. Assess for missed doses, changes in meds, diet, bleeding or clotting symptoms or transient complications (ie acute illness) prior to making adjustments. Consider repeating INR if observed value markedly different. If enteral feeds, hold feeding for at least 1-2 hrs before/after warfarin (be consistent). No warfarin through J-tube.

Length of Treatment

Provoked VTE	Unprovoked VTE
≤3 months	**3 months and then evaluate risk/benefit ratio of extended treatment**

Patient Education

All Anti-coagulants	• Watch for s/sx of bleeding (esp. intracranial). • Use basic first aid for injuries. • Notify provider if any bleeding (seek immediate medical attention for serious bleeding). • Notify clinic before starting new meds (including OTC) or if having a procedure. • ASA/NSAIDs ↑ bleeding. Avoid NSAIDs. Only use ASA if clear indication. • When scheduling procedures, tell dentist/ surgeon about anticoagulant and contact anticoagulation provider for anticoagulation mgmt plan. • Avoid dangerous activities (use protective gear) and discuss sports participation with provider. • Don't stop without consulting provider.
Warfarin	• Maintain stable vitamin K intake. • Notify clinic if ill (N/V/D, fever) or change in medications/supplements or diet (can affect INR). • Alcohol can affect INR.

Long-term management

- Follow-up: assess for compliance, s/sx of bleeding or thrombosis, and interacting meds.
  - Warfarin: INRs 5-7 days (or per institutional policy) after re-starting or after any changes that can effect INR (ex. med, diet change, or illness) and approx. 7 days after any dose changes. Dose changes should be based on a standardized protocol.
- Bleeding: Minor bleeding (eg. epistaxis, bleeding gums): common and is not normally a reason to D/C. Teach pt how to prevent and manage. Major bleeds: Decision to resume anticoagulation should be based on risk for recurrence of VTE.
- Periprocedural (periprocedural management may vary based on institutional policy):
  - Interruption: Enoxaparin: hold for 12-24 hrs prior to procedure or surgery (depending on pt/procedure bleed risk) for patients on twice daily dosing, restart as soon as safe from a postoperative standpoint. Pts with renal insuff. may require longer hold periods. Warfarin: hold 3-5 days depending on latest INR and procedure bleed risk. DOACs: hold 1-2 days depending on procedure bleed risk. Longer holds may be required in pts with renal insufficiency.
  - Bridging: Should only be used for pts on warfarin with high thromboembolic risk. Stop warfarin 3-5 days prior to procedure. Bridge with LMWH or heparin infusion. Start LMWH within 36 hours of first held dose of warfarin. Discontinue LMWH 12 hours prior to procedure for patients on twice daily dosing. Discontinue UFH infusion at least four hours prior to procedure. Check INR stat on day of procedure, if INR>1.5 give Vitamin K 1.25mg orally, or follow institutional guidelines.

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Drug package inserts

- Apixaban: https://packageinserts.bms.com/pi/pi_eliquis.pdf
- Dabigatran: http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Pradaxa/Pradaxa.pdf
- Edoxaban: http://dsi.com/prescribing-information-portlet/getPIContent?productName=Savaysa&inline=true
- Rivaroxaban: https://www.xareltohcp.com/shared/product/xarelto/prescribing-information.pdf

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***This document may not reflect the exact management protocols utilized by reviewer institutions.**