Anticoagulation in Pediatric Cardiology

Loren Brown, BSN, RN, CCRN, Boston Children’s Hospital
Jenna Murray, MSN, RN, CPNP-AC, Lucile Packard Children’s Hospital Stanford,
Kaye Remo, RN, University of California San Francisco Benioff Children’s Hospital
Mary Rummell MN, RN, CNS, CPNP, FAHA, Oregon Health and Science University

Introduction:

The use of antithrombotic therapy in neonates, infants, and children is increasing. This increase is multifactorial involving the prevalence of patients hospitalized with congenital heart disease (CHD); the increase in survival from both surgical and catheter interventions used to address complex CHD; and recognized improvement in outcomes with antithrombotic prophylaxis. Recognition of the potentially left-threatening complication of thrombosis is evident in patients with CHD and acquired heart disease. These high-risk groups include patients with shunt-dependent single ventricles, post-operative central lines, Fontan circulation, arrhythmias, Kawasaki disease with coronary aneurysms, and cardiomyopathy/myocarditis. (Diab 2013; Giglia 2013; Monagle, 2012 Supp) Anticoagulation for pediatric patients with mechanical valves, although historically more prevalent, continues to present management challenges for the caregiver and professional.

Critical Thinking Points: (Biss 2013; Giglia 2013; Rummell 2013)

- Normal developmental changes in the hemostatic system
- Different physiological, pharmacological, and genetic response to medication management
- Difficulty administering anticoagulant therapy related to lack of suitable preparations
- Difficulty monitoring due to physiologically abnormal baseline tests and problems obtaining appropriate samples of blood
- Increased risk for bleeding complications related to cardiac pathophysiology and interventions
- Lack of randomized, controlled trials to guide therapy

Breakdown of Critical Thinking Points: (Giglia 2013)

Developmental changes

- Neonatal antithrombin levels are <50% of adult levels – do not reach adult levels until approximately 6 months of age.
- Neonatal – altered platelet function – hyporeactive to platelet-activating agents: thrombin, adenosine, phosphate/epinephrine, and thromboxane A2. However, the
bleeding time in neonates, a reflection of platelet function, is normal because of increased RBC size, Hematocrit and vWF multimers.

- Different levels of constituent proteins and inhibitors of coagulation (Decreased FII, FVII, FIX, FXI, FXII, protein C, protein S) and fibrinolysis – varies with age.
  - Greater difference in patients < 3 months.
  - Reach adult levels at approximately 5 years.
  - Greater impact with cyanotic defects.
- Physiologically decreased plasma levels of vitamin K-dependent factors.

** Syndromes that have an effect on coagulation **

- 22q11.2 microdeletion syndrome
- Jacobsen
- Noonan – thrombocytopenia, platelet dysfunction
- Multiple coagulation factor deficiencies – FXI
- Congenital or acquired decrease in hemostatic protein(s)

** Cardiac conditions and associated issues **

- CHD – especially cyanotic conditions, abnormal blood flow, decreased vessel diameter
- Invasive cardiovascular (CV) procedures
- Indwelling vascular devices – catheters, stents, transvenous pacemaker, septal occluders, and valves -- alter the blood flow shear stress, disrupt the endothelium, and activate the coagulation system.
- Inflammatory response to ECMO and bypass circuits, deep hypothermic circulatory arrest
- Increased usage of blood product transfusion
- Surgically created conduits and shunts
- Excessive fibrinolysis, hypothermia, acidosis, decreased platelet count
- Liver congestion – results in decreased vitamin K-dependent proteins, including proteins C & S, decreased metabolism of anticoagulants
- Decreased renal function – decreased clearance of anticoagulants
- Heparin resistance
  - Secondary to antithrombin consumption and to competitive heparin binding to inflammation-related circulating proteins.
- Longer storage of blood products – esp. RBCs results in disruption of coagulation factors

** Laboratory tests **

- Samples drawn from central lines and arterial lines may be contaminated with heparin and falsely elevated the levels, should confirm with peripheral stick sampling
• D-dimers (indicative of active coagulation and fibrin production in adults) – not formally evaluated in children

• Heparin Levels
  o ACT, TOTEM, and TEG – no well-designed studies to evaluate safety and efficacy of use of ACT to monitor anticoagulation in children – used for ECMO and CP bypass
  o Anti-Factor Xa Levels
    ▪ Used to measure the effect of UFH and LMWH on coagulation – levels extrapolated from adult studies. NO pediatric studies establishing the safety and efficacy of any laboratory test to measure the effects of heparin. Poor correlation between heparin levels and PTT.
    ▪ LMWH is a short-chain heparin that does not influence the PTT. Therefore, the anti-Factor Xa level is the ONLY measure of the effect of LMWH therap

• International Normalized Ratio (INR)
  o Ultimately this means that no matter how or where the lab is drawn it can be compared to another INR
  o All people, regardless of anticoagulation status, have a baseline INR around 1
  o Many centers draw a baseline INR and CBC before initial dose of anticoagulant
  o If the baseline INR is >1.3 (which is common at times in the Fontan and post-pump population) LFTs should be checked as well.
    ▪ INRs post bypass can be falsely elevated due to heightening of the coagulation cascade at this time

**Indications for Anticoagulation:** (Monagle 2004, 2008; Giglia 2013)

<table>
<thead>
<tr>
<th>Goal INR Range Levels based on indication</th>
<th>Indication Goal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial Fibrillation</td>
<td>2.0–3.0</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>2.0–3.0</td>
</tr>
<tr>
<td>DVT/PE</td>
<td>2.0–3.0</td>
</tr>
<tr>
<td>DVT prophylaxis</td>
<td>1.5–2.0</td>
</tr>
<tr>
<td>Fontan</td>
<td>2.0–2.5</td>
</tr>
<tr>
<td>Kawasaki Disease</td>
<td>2.0–3.0</td>
</tr>
<tr>
<td>Prosthetic Aortic Valves</td>
<td>2.0–3.0</td>
</tr>
<tr>
<td>Prosthetic Mitral Valves</td>
<td>2.5–3.5</td>
</tr>
<tr>
<td>Pulmonary Hypertension</td>
<td>1.5–2.5</td>
</tr>
</tbody>
</table>
**Anticoagulation in the immediate post-operative period:** (Giglia 2013; Diab 2013; Biss 2013; Monagle 2011, Personal communication, Karamlou, T)

**Neonates: Systemic – pulmonary Shunts**

- **Placement criteria**
  - Palliation in two ventricle repair (Tetralogy of Fallot, severe pulmonary stenosis or right ventricular outflow obstruction.)
  - Include in initial stage I palliation for single ventricle (Hypoplastic right or left ventricle)
- Preferred material - polytetrafluoroethylene (Gortex®)
- Post procedure complications:
  - Significant risk
  - Thrombosis
    - Most significant cause and/or contributor to shunt failure.
    - Associated with hypovolemia related to:
      - Bleeding
      - Pleural drainage
      - Infection
    - Complicated with coagulopathies
  - Assessment includes:
    - Both partial thrombosis/full thrombosis
    - Decreasing and uncorrectable oxygen saturations
    - Marked hypoxemia and decreased cardiac output
  - Management of acute shunt thrombosis
    - Requires immediate intervention:
      - Systemic anticoagulation
        - Bolus of IV heparin (50-100 U/Kg)
        - Consider continuous heparin infusion
        - Monitor UFH levels according to institutional guidelines
      - Increasing systemic blood pressure in effort to improve flow through shunt

*Goal INRs for commonly used ventricular assist devices used in pediatrics include:

- Berlin Heart 2.7-3.5
- Heartware 2.5-3.5

**If a patient has more than one indication for anticoagulation or has had a thromboembolic event in the setting of therapeutic anticoagulation, consider using the higher of the two ranges or increasing the range by 0.5 on either end.
• Intubation, mechanical ventilation and neuromuscular blockade to maximize oxygen delivery and minimize oxygen consumption
• Interventional catheterization, manual shunt manipulation, surgical shunt revision
  o ECMO should be anticipated
  o Post-operative anticoagulation management
    ▪ Greatest period of management variability
    ▪ Common to use low dose aspirin until next scheduled staged procedure
      • With polytetrafluoroethylene (PTFE) shunt
      • Patient with low risk of bleeding
    ▪ Timing and pharmacologic management controversial
      • Timing and choice of medical management depend on risk factors for coagulation and personal experience of surgeon
      • Increased risk-factors include:
        o Age (neonatal developmental coagulation factors)
        o Elevated pulmonary vascular resistance (PVR)
        o Shunt < 3.5 mm
        o History of clots or hypercoagulable state
        o Stented shunt or native ductus arteriosus
    ▪ Initiation in the operating room
      • Continuous unfractionated heparin (UFH) infusion
        o Some studies show intraoperative and post-operative UFH for 48 hours decrease risk of thrombosis
        o May increase risk of post-operative bleeding
        o Therapeutic approach varies:
          ▪ Low-dose (10 - 20 units/kg/hr with no bolus)
          ▪ Full systemic heparinization (Bolus dose of 50-100 units/kg followed by 10-20units/kg/HR to achieve a therapeutic PTT (Per hospital guidelines)).
        o Patients with increased risk-factor for thrombosis,
          ▪ Systemic heparinization is recommended for early postoperative period
      • Initiation of low dose aspirin varies between centers:
        o Initial dose given rectally in operating room
        o Rectal dose: 20 – 40 mg for neonates or 5 mg/kg for all patients
    ▪ Initiation after leaving the operating room
      • After concerns for bleeding have been resolved.
        o Normalization of tests of hemostasis
        o Tests include: Hematocrit, platelet count, PT-INR, aPTT, Fibrinogen level
      • May use UFH or low dose aspirin
        o Some wait to initiate aspirin after chest tubes and pacing wires are out
        o Others start Low dose aspirin PR with decrease in bleeding risk
      • Patients with sustained high risk for thrombosis,
Combined LMWH plus oral low dose aspirin, monitor with Antifactor Xa levels per institutional guidelines
Clopidogrel may be considered
Monitoring varies between centers: (More specific guidelines suggested later in this document)
- Anticoagulation continuous until next stage or more definitive establishment of pulmonary blood flow.
- Includes PTT, anti-F Xa, AT III levels, heparin levels
- Continuous depending on agent and coagulation risk

Additional considerations:
- No anticoagulation is recommended for neonates with single ventricle palliation and a Sano shunt.
- Evaluate coagulation status if chronic effusions
- Cerebral venous infarct
  - Alter anticoagulation
  - Consult neurology

Infants: Venous to Pulmonary Artery Shunts (Bi-directional Glenn Shunt)

- Antiplatelet therapy for ongoing thromboprophylaxis
  - Low dose aspirin – most common
  - Initial timing varies:
    - Rectal dose administered in OR (5 mg/kg)
    - Gastric dose (oral or nasogastric tube) started with resumption of bowel sounds
- Systemic heparinization if increased risk of clot (infection, stented shunt, hypercoagulable state, line thrombus)
- Chronic effusions, evaluate for anticoagulation needs
- Cerebral venous infarct
  - Alter anticoagulation
  - Consult neurology
- LMWH with ASA/clopidogrel if sustained high risk for clot (stented shunt, hypercoagulable state or existing clot)
- Decrease use of upper extremity deep venous lines.
- Maintenance until Fontan

Children: Single Ventricle Repair (Fontan) (Monagle, 2011)

- Risk Factors of thrombosis: expert opinion/general review
  - Protein-losing enteropathy (PLE)
  - Prolonged pleural effusions
  - Prolonged immobilization
  - Ventricular dysfunction
  - Arrhythmia
  - Presence of thrombogenic foreign material
  - Atrial level fenestration
  - Kawashima connection
Abnormal thrombophilia profile

Thromboprophylaxis:
- Short term: warfarin or LMWH for 3-12 months after Fontan palliation
- Long-term warfarin thromboprophylaxis
- Use for patients with risk factors
  - Increase or initiation of warfarin magnitude in adolescence and adulthood
  - Stroke prevention warfarin for adults with fenestrations who also have a documented atrial thrombus, atrial arrhythmia, previous thromboembolism
  - Stroke prevention warfarin for adults with atrial level shunts (fenestration) without risk factors

Infants/children: Immediate Post-operative Prosthetic Valve Replacement:

- Thromboprophylaxis
  - Varies with type and anatomic location of valve
  - Medical management
  - Initial therapy with UFH as bridge to early management
  - Follow institutional guidelines for management of UFH infusions
  - Patients who cannot take warfarin, low dose aspirin is recommended

Aortic Valve
- Bi-leaflet mechanical or Medtronic Hall prostheses,
  - No risk factors: warfarin for first 3 months: INR 2.0-3.0
  - Risk factors: warfarin: INR of 2.5-3.5
- Starr - Edwards valves or mechanical disk valves
  - No risk factors: warfarin: INR goal of 2.5-3.5
- On-X valve mechanical valve
  - No risk factors:
    - First 6 months: warfarin: INR goal 2.0-3.0
    - After 6 months: aspirin and clopidogrel or warfarin: reduced INR goal of 1.5

- Bioprosthetic valve
  - No risk factors: aspirin
  - Risk factors: warfarin: INR goal of 2.0-3.0

Mitral valve
- Any mechanical valve
  - Warfarin: INR goal of 2.5-3.5
- Bioprosthetic valve
  - No risk factors: aspirin
  - Risk factors: warfarin: INR goal of 2.0-3.0
Adults: Post-operative Prosthetic Valve Replacement

- Both low dose aspirin and therapeutic warfarin
- Pulmonary valve
  - Bioprosthesis: may forgo anticoagulation
- Tricuspid valve
  - Bioprosthesis, normal ventricular function: low dose aspirin
  - Bioprosthesis, decreased right ventricular function or risk factors: warfarin: INR goal of 2.0-3.0
- Aortic and mitral valve follow same guidelines as children

Management Guidelines following immediate post-operative period:

Treatment: Warfarin

- Initial Response is usually with 24 hours after administration
- Peak anticoagulation response 72 to 96 hr.
- Duration of action of a single dose is 2-5 days
- Half-life: Following a single warfarin dose, the terminal half-life is about 1 week with a mean effective half-life of 40 hr. (range, 20 to 60 hr.)

(Prod Info COUMADIN(R) oral tablets, intravenous injection, 2010)

Induction

- Dosing is calculated over 7 days (i.e. total WEEKLY dose). Adjustments are made by increasing or decreasing the weekly dose between 5-20%.
- When a rapid effect is required, heparin or low molecular weight heparin should be given concurrently with warfarin for 4 days or until INR is therapeutic (see Procedural Bridging section of this document)
- Warfarin dosing may be separated into initial and maintenance phases
- INR response is monitored frequently until a stable dose-response relationship is obtained
- Once INR is stable, the frequency of INR testing is reduced
- Anticoagulant effect is observed within 2 to 7 days after beginning oral warfarin.

Guidelines when using a Loading dose (Children’s Hospital Boston Formulary, Boston, Massachusetts):

- **Loading Dose: Day 1**
  - Give 0.1 mg/kg (maximum 0.2 mg/kg) - maximum pediatric loading dose is 5mg
  - The 0.1mg/kg dose is a routine dose.
    - Consider assessing current medications and diet before deciding on a loading dose knowing that decreased PO intake and medications such
as antibiotics, steroids, and antiarrhythmics can INCREASE the INR quickly

- The higher end of loading dose (0.2mg/kg) may be considered when prompt elevation in INR desired and the patient’s INR can be monitored very closely (usually on a daily basis). Most often this loading dose is used in patients who have had cardiac surgery for implantation of mechanical heart valves
- A loading dose lower than 0.1mg/kg should be considered in patients with Fontan physiology, liver disease, decreased vitamin K intake and/or who are known slow metabolizers
- If patient was previously on warfarin, start with home dose (or 10%-20% above home dose if INR less than 1.5)
  - Consider dose DECREASING if patients are not eating post-surgery, have chest tubes still in place and/or are on post-op antibiotics

  - **Loading Dose: Days 2-7**
    - Check INR in the morning; use each result to plan that evening’s warfarin dose:
    - In the patient with baseline normal INR/PT, normal liver functions and who is not on medication interacting with warfarin, may check INR on days 3, 4, 5 and 7 or at clinician’s discretion
    - A reasonable method of adjusting warfarin disease according to INR is as follows:
      - If INR is 1.1-1.3, repeat the initial loading dose*
      - If INR is 1.4-1.9, reduce the initial loading dose by 50%
      - If INR is 2-3, reduce the initial loading dose by 50%
      - If INR is 3-4, reduce the initial loading dose by 25%
      - If INR is 4-4.4, hold dose, check INR following day then resume warfarin at 50% of previous dose
      - If INR >4.5, hold until INR <4.5 then resume warfarin at 50% of previous dose
      - If INR >5.5, hold and check INR daily, when INR <5, restart at 25% less than previous dose or at discretion of primary clinician.
    - Experienced clinicians sometimes increase the designated initial loading dose 25-50% if the response to the chosen loading dose is very slow (e.g., little or no response after two doses). This maneuver shortens the time to therapeutic anticoagulation but increases the risk of overshooting target.
    - In the patient whose baseline physiology and metabolism are stable, the dose on Day 8 of therapy can be calculated by dividing the total dose over the first week by 7, and one can proceed to recommendations for Long-Term Monitoring.
Long Term Monitoring:

*Treatment: Warfarin*

Routine monitoring of INR

- Once every 1-4 weeks depending on patient’s age, compliance, and risk for thrombosis
- Clinical indications for more frequent monitoring include
  - Antibiotic courses (SBE prophylaxis usually does not affect INRs)
  - Started on new medication known to interact with warfarin or a dose adjustment in a medication known to interact with warfarin
  - GI or other illness that decreased or altered the normal dietary intake
  - Symptoms of bleeding

Guidelines for Managing INR

*Maintaining INRs between 2.0 and 3.0*

If INR is 1.1-1.4, Check for compliance, if compliant, increase maintenance dose by 20%
If INR is 1.5-1.9, increase maintenance dose by 10%
If INR is 2-3, no change
If INR is 3.1-4, decrease dose by 10%
If INR is 4.1-4.5, decrease dose by 20%
If INR >4.5, hold one dose, then restart 20% lower the previous dose*
If INR >5, hold and check INR daily, when INR <4.5, restart at 25% less than the previous dose or at discretion of the primary clinician. *

*Depending on the reason for anticoagulation and the perceived greater risk (risk of bleed versus risk of thrombus) dose reduction may be the preferred method of management over holding a dose to avoid a possible sub therapeutic level/ thrombus.

*Other dose adjustment considerations:*

- When the INR is above the therapeutic range but <5, and the patient is asymptomatic (no clinically significant bleeding) and reversal is not required for surgical
intervention, the dose of warfarin can be reduced or the next dose omitted and resumed (at a lower dose) when the INR approaches the desired range.

- If the INR is between 5 and 9 and the patient is not bleeding and has no risk factors that predispose to bleeding, the next 1 or 2 doses of warfarin can be omitted and warfarin reinstated at a lower dose when the INR falls into the therapeutic range. Alternatively, the next dose of warfarin may be omitted and vitamin K1 (0.5-2 mg) given orally. This approach should be used if the patient is at increased risk of bleeding.

- When more rapid reversal is required to allow urgent surgery or dental extraction, vitamin K1 can be given IV or subcutaneously in a dose of 0.5-2 mg, anticipating reduction of the INR within 12-24 hours.

- If the INR is 9 but clinically significant bleeding has not occurred, vitamin K should be given PO at a dose of 0.5-2 mg, anticipating that the INR will fall within 12-24 hours. The INR should be monitored closely and vitamin K repeated as necessary.

- When rapid reversal of anticoagulation is required because of serious bleeding or major warfarin overdose (e.g., INR 20), vitamin K1 should be given by slow intravenous infusion or subcutaneously in a dose of 2-5 mg, supplemented with transfusion of fresh plasma or prothrombin complex concentrate, according to the urgency of the situation. It may be necessary to give additional doses of vitamin K1 every 12 hours.

- In cases of life-threatening bleeding or serious warfarin overdose, prothrombin complex concentrate replacement therapy is indicated supplemented with 5 mg of vitamin K1 by slow intravenous infusion; this can be repeated, according to the INR. If warfarin is to be resumed after administration of high doses of vitamin K, then heparin can be given until the effects of vitamin K have been reversed and the patient again becomes responsive to warfarin.
**Treatment: Enoxaparin**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Goal Anti Xa/LMWH level: Standard Risk of bleeding 0.5-1unit/ml; High Risk of bleeding 0.4-0.6units/ml.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Initial Dosing</td>
</tr>
<tr>
<td>&lt;2 months</td>
<td>1.5 mg/kg/dose SC every 12 hours</td>
</tr>
<tr>
<td>≥2 months and &lt;18 y</td>
<td>1 mg/kg/dose SC every 12 hours</td>
</tr>
<tr>
<td>≥18 y</td>
<td>1 mg/kg/dose SC every 12 hours</td>
</tr>
</tbody>
</table>

- Binds to antithrombin to inhibit Factor Xa
- Before initiating: assess **Serum Creatinine and Platelets**.
- Consult Lexi-comp for renal dosing recommendations in patients with elevated CrC
- Levels need to be drawn for **4-6hrs after 2ND dose is given to be accurate in titration.**
- See below for starting doses for prophylactic and treatment level enoxaparin. Consult Lexicomp and hospital specific guideline for dose adjustment for sub therapeutic levels
- Should **not** use INSUFLON CATHETERS for doses <5mg or in patients <5kgs or in medically fragile patients

**Chronic Anticoagulation Patient Considerations:**

- **Sub therapeutic INRs:** Inquire about
  - Missed doses or recent dose changes of existing medications
  - Diet or exercise changes (increased exercise, or “healthy” dietary habits can lower an INR)
  - New medications
  - Weight gain/ growth spurt
- **Supratherapeutic INRs:** Inquire about
• Missed doses that have been caught up (i.e. two doses in <24 hour period)
• New medications or recent dose changes of existing medications
• Illness that affects appetite (i.e. sore throat, nausea/vomiting/diarrhea)
• Alcohol consumption

  o INR values are affected with many different drugs; antibiotics are the largest group of medications that will raise an INR in children. Managing practitioners should have INR checked 2-3 days after beginning a course of therapy to evaluate for elevation and potential dose adjustment and a repeat INR towards the end of the course for patients with an INR increase.
  o Patients who have a low intake of vitamin K have been found to have more fluctuation in their INR. A consistent moderate intake or daily supplementation has been shown to decrease fluctuations in INR levels.
  o **Dietary considerations**
    • Warfarin use in children can present several unique challenges. Chronically hospitalized children often have oral taste and textural aversions which create a limited diet. As their dietary intake choices expand, the child who previously ate little or no dietary vitamin K may suddenly find a food that they like. Although that food may be considered to have comparatively low amount of vitamin K, this new intake of vitamin K in a previously restricted diet presents a proportionally large increase in vitamin K compared to their previous diet, and may drive down the INR significantly.
    • A child that consistently gets vitamin K in their diet will have less fluctuation in their INR when that vitamin K intake increases or decreases
    • Children who avoid fruits and vegetables will have a dramatic change (drop) in their INR when a new food is introduced that does contain vitamin K— even if it is on the “moderate” or “low” list. (Example— blueberries)
    • The child/young adult may eat differently during the school year than he or she does during the summer. There may be a brief adjustment in warfarin dosing at the start of the school year and again during the summer.
    • Vacation diets and meals at the holiday may also vary the amount of dietary vitamin K from the norm.
    • Patients who are having many highs and lows in their INR and do not eat vegetables, may not be getting enough vitamin K in their diet. In these cases the practitioner may consider adding a multi-vitamin that has vitamin K to the daily routine. A dose between 10-40 micrograms of vitamin K daily (more for the older child). The RDA recommended adult dose is 80 micrograms.
    • Patients receiving formula feedings or supplements should notify their practitioner if the formula changes, the amount of volume per feeding, or number of feedings per day changes. Most formulas have vitamin K and changes in rate or volume with alter the amount of vitamin K receive
Home INR Monitoring

- Home INR monitors are available for long term anticoagulation management. Machines may not be feasible for all patients depending on the indication, anticipated length of time on warfarin and insurance coverage.
- Diagnosis of prosthetic aortic or mitral valve, atrial fibrillation or flutter, stroke or deep vein thrombosis may be covered by insurance (Pulmonary hypertension, Kawasaki’s disease and Fontan physiology may not be covered diagnoses)
- The machine is typically not covered for the first 90 days the patient is on warfarin
- Requires the anticipated duration of anticoagulation be one year
- Requires testing every other week
- Machines may be available for purchase by the patient/family with a cost of approximately $2500 for the machine and testing strips $80 for 6 strips depending on the model and company.
- Studies have shown an increased time in the therapeutic range for patients, improvement of quality of life, and decreased thromboembolic events.

The below algorithms are been developed and reviewed jointly by the Boston Children’s Hospital Cardiology Anticoagulation Service and Hematology Anticoagulation Service.

Authors: Jenna Murray CPNP-AC, Kathy Harney PNP, Juliann Duzan RN, Christopher Almond MD, MPH, Alan Michelson MD and Cameron Trenor MD
Is the procedure HIGH Risk for bleeding?

YES: (For Example)
Cardiac Surgery
Vascular Surgery
Orthopedic Surgery
Neuro-Surgery
Urogenital Surgery
Endoscopy (w/biopsy)

NO: (For Example)
Dental Surgery
Endoscopy (no biopsy)
Cardiac Catheterization
Pacemaker Change
Laparoscopic Procedure
Gtube Changes

EXCLUSION CRITERIA:
- Vascular Malformations
- Concurrent Bleeding Diagnoses
- Patients that are actively bleeding
- Non-adherent patients
- Patients that refuse to give themselves the injection
- Patients that have not had LMWH injection teaching

RISK FOR CLOTTING DIAGNOSIS STRATIFICATION

HIGH RISK
- Prosthetic Mitral Valve
- PE/DVT/CSVT (Within the last 3 months)
- Kawasaki’s w/Giant Coronary Aneurysms
- Left Ventricular Thrombus/Intra-Cardiac Thrombus (Within the last 3 months)
- Atrial Arrhythmias + another risk factor (stroke, thrombus, AVR, etc.)

MODERATE RISK
- Atrial Arrhythmias (only)
- Prosthetic Aortic Valve
- Long-term secondary anticoagulation for PE/DVT/CSVT

LOW RISK
- Fontan
- PH
- Cardiomyopathy (sinus rhythm)
- DVT Prophylaxis

Low-Moderate Risk for Clotting Diagnoses
Consider holding Warfarin 3-4 days pre-procedure.

High Risk for Clotting Diagnoses
Consider dose reducing Warfarin pre-procedure to bring the INR down to the low end of their therapeutic range.

*Base decision on the patient’s clinical assessment and when hemostasis is achieved post-procedure and in conjunction with the surgical/interventional teams
INCLUSION CRITERIA:
- 2-25 years of age on warfarin therapy
  (Or patients here at BCH post procedure and on warfarin therapy)
- High or moderate risk for clotting diagnosis
- S/p Phase 1

EXCLUSION CRITERIA:
- Vascular Malformations
- Concurrent Bleeding Diagnoses
- Patients that are actively bleeding
- Non-adherent patients
- Patients that refuse to give themselves the injection
- Patients that have not had LMWH injection teaching

RISK FOR CLOTTING DIAGNOSIS STRATIFICATION

**HIGH RISK**
- Prosthetic Mitral Valve
- PE/DVT/CSVT (Within the last 3 months)
- Kawasaki’s w/Giant Coronary Aneurysms
- Left Ventricular Thrombus/Intra-Cardiac Thrombus (Within the last 3 months)
- Atrial Arrhythmias + another risk factor (stroke, thrombus, AVR, etc.)

**MODERATE RISK**
- Atrial Arrhythmias (only)
- Prosthetic Aortic Valve
- Long-term secondary anticoagulation for PE/DVT/CSVT

*Base decision regarding re-initiation on the patient’s clinical assessment and when hemostasis is achieved post-procedure and in conjunction with the surgical/interventional teams.*

** Warfarin dosing can be temporarily increase by 10-15% during this time to help get the INR back to therapeutic range in a more timely manner.
Procedural and non-procedural anticoagulation bridging guidelines:

Phase 3: Subtherapeutic INR

*Patients at HIGH risk for clot

**HIGH RISK FOR CLOT DIAGNOSES**

- Prosthetic Mitral Valve
- Prosthetic Aortic Valve
- PE/DVT/CSVT
  (Within the last 3 months)
- Kawasaki’s w/ Giant Coronary Aneurysms
- Left Ventricular Thrombus/Intracardiac Thrombus
- Atrial Arrhythmias + another risk factor (stroke, thrombus, AVR, etc.)

**Common Causes of Subtherapeutic INRs included:**

- Missed doses/non adherence
- Excessive vitamin K intake
- Herbal Medications (Ginseng, St. John’s Wart)
- Antiepileptic Medications (Barbiturates, Phenytoin, Carbamazepine)
**Communication to Patient/Guardian**
- Ensure direct communication with patient or guardian. If leaving a VM, confirm information has been received.
- Review plan and have repeated back.
- Review bleeding

**EXCLUSION CRITERIA:**
- Non-adherent patients
- Patients that are actively bleeding

**Assess rationale for supratherapeutic INR**
*Common Causes of Supratherapeutic INRs included:*
- Change in vitamin K intake (diet)
- Addition of new medications
- Wrong dosage amount
- Addition of OTC/herbal medications
- GI or Influenza like illness
References:


Children’s Hospital Boston Formulary, Boston, Massachusetts


http://en.wikipedia.org/wiki/Warfarin

Micromedex™ available online by subscription


**Patient Resources:**

http://www.clotcare.com/clotcare/ptinr.aspx (about the INR test)


http://www.stoptheclot.org/natt_publications/KandWarfarin.pdf (vitamin K and warfarin patient information)

http://www.clotcare.com/vitaminkandwarfarin.aspx (vitamin K and warfarin patient information)