**Scottish Paediatric Cardiac Services**

# Anticoagulation and antiplatelet therapy in paediatric cardiac patients

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Glasgow

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| Anti-coagulation therapy in the post-operative cardiac patient guideline | Version: 3.9 | Page 1 of 29 |
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## 1. Rationale, Purpose, Objective

To allow standardised anticoagulation practice in paediatric cardiac patients and provide guidance for staff administering or prescribing anticoagulation therapy. This guideline does not replace the clinical experience and judgement of the practitioners looking after the patient. When a tailored patient-specific approach to anticoagulation is required, the rationale and collegiate discussion must be clearly documented in the patient medical record

## 2. Scope

This guideline applies to any cardiac patient being prescribed or administered anticoagulation therapy.

## 3. Roles and responsibilities

All healthcare professionals prescribing, supplying or administering anticoagulation therapy should be aware of this guideline.

## 4. Evidence for guidelines

These guidelines have been written in consultation with the medical literature using the current gold standard for anticoagulation practice which reviews the best levels of evidence available. There are few randomised controlled trials (RCT) available in this area and the majority of evidence is level 3. The guidelines incorporate extensive consultation with intensive care, cardiology, cardiac surgery, haematology and pharmacy taking into consideration local practice, as well as current practice guidelines from other paediatric cardiac surgical centres.

## 5. Monitoring

These guidelines will be reviewed with reference to clinical governance including review of clinical incidents and audit and will be reviewed every 3 years, or sooner if indicated.

## Antithrombotic therapy for all patients except valves surgery

| Condition or procedure | Antithrombotic therapy required? | Immediate post-operative period | Long term antithrombotic therapy |
|---|---|---|---|
| Arterial shunts (BTT Shunt / Central Shunt/Norwood 1* *antithrombotic therapy should be instituted as soon as safely possible | Yes | Prophylactic heparin @ 20 units/kg/hr if no bleeding concern<br>➢ Do not need to target specific aPTT range unless specific concern<br>➢ Check aPTT 4 hours after starting heparin and then once daily to ensure not over-anticoagulated | Aspirin when tolerating feeds<br>Stop Heparin after 2nd dose<br>Adding Clopidogrel may be considered in high thrombotic risk (e.g.wrapped shunt, 3 mm shunt) in absence of complications e.g. GI bleed |
| ASD/VSD | No | | |
| AVSD | No | | |
| Coronary aneurysm | Yes | Warfarin or LMWH if giant aneurysms, Aspirin or Clopidogrel if smaller aneurysms or ectasia, or combination | |
| Glenn / BCPC | Yes | Prophylactic heparin @ 20 units/kg/hr if no bleeding concern | Aspirin when tolerating feeds from 2nd post-op day & Heparin may be stopped after 2nd dose of Aspirin<br>If thrombotic complications, consider Warfarin |
| Fontan / TCPC **<br><br>** High thrombotic risk: high Fontan pressure, ventricular dysfunction, heart failure, arrhythmias, previous thrombosis. | Yes | Therapeutic heparin regime if no bleeding concern<br>➢ Target aPTT 60 – 90 using dose adjustment suggestions in "**therapeutic heparin regime**" noted below<br>➢ If established on Aspirin then once second dose is given Heparin may be ceased<br>➢ Continue heparin until INR above 2.0 for 2 consecutive days in high thrombosis risk patients started on Warfarin | Aspirin lifelong or Warfarin for 3-12 months then change to Aspirin for low thrombotic risk TCPC patients**<br>For patients at higher risks of thrombosis**, consider Warfarin (target INR range 2-3)<br>**In the UK, DOACs use in children post-TCPC remains off-label** |
| Hybrid Procedure (stented PDA) | Yes | Prophylactic heparin @ 20 units/kg/hr if no bleeding concern | Aspirin when tolerating feeds & Heparin may be stopped after 2nd dose of Aspirin<br>Clopidogrel may be added in higher risk patients |
| Poor systemic ventricular function | Yes | If intracardiac thrombus present, consider Heparin/LMWH | Aspirin or Warfarin depending on condition and function |
| Pulmonary artery stents, aortic stents, percutaneous pulmonary valve implant (PPVI), RVOT stents | Yes | Consider heparin @ 20 units/kg/hr if ventilated/not feeding (Interventional Cardiologist decision) | Aspirin +/-<br>Clopidogrel (Interventional Cardiologist decision) |
| TGA | No (if difficult coronary transfer, consider Aspirin) | | |
| T of Fallot | No | | |
| TAPVD | No | | |

## Antithrombotic therapy after valve repair/replacement surgery

**DOACs use in prosthetic valves in children is off label and must be discussed with Cardiologist and Pharmacist**
**Apixaban is not licenced in children for any indication at the time of this guideline being finalised, paediatric dosage not available**

| Condition | Antithrombotic therapy required? | Immediate postoperative period | Long term antithrombotic therapy |
|---|---|---|---|
| **Homograft Valves (aortic or pulmonary), Autograft in Ross Procedure and low thrombotic risk** | No* | It is reasonable to forego anticoagulation<br><br>**Prophylactic heparin @ 20 units/kg/hr if no bleeding can be considered in discussion with duty Cardiologist, Cardiac Surgeon and Intensivist* | Aspirin for 3-6 months (*consider long-term Aspirin after discussion of risk/benefit with family)*<br>In patients with high thromboembolic risk, consider Warfarin (see last section of this table) |
| **Bioprosthetic valve (Contegra, Hancock, Perimount) with or without conduit and low thrombotic risk** | Yes | Prophylactic heparin @ 20 units/kg/hr if no bleeding concern<br><br>In patients with high thromboembolic risk, ***increase to therapeutic IV heparin on post-op Day 1 & continue until INR >2.0 for 2 consecutive days*** | Once feeding, start Aspirin for 3 months post-op (*consider long-term Aspirin)*<br>Alternative anticoagulation such as therapeutic LMWH or Warfarin (target INR 2 to 3) for 3 months can be considered |
| **Total aortic valve reconstruction (Ozaki) and low thrombotic risk** | Yes | Prophylactic heparin @ 20 units/kg/hr if no bleeding concerns | Aspirin, or<br>Warfarin (target INR 2-3) for 3 months |
| **Ozaki, homograft or biological valve replacement and high thrombotic risk*:**<br>**peripheral venous or arterial thrombosis, history of hypercoagulability or thromboembolism , poor ventricular function (LVEF <35%, spontaneous echo contrast), multiple valve replacements, hypercoagulability, history of thromboembolism; poorly controlled arrhythmias* | Yes | Prophylactic Heparin @ 20 units/kg/hr if no bleeding concern on the day of surgery and then titrate to therapeutic IV heparin on post-op Day 1 | Start Warfarin on post-op day 1 or when practical (please refer to section on pacing wires and intracardiac lines removal)<br>Target INR 2-3<br><br>Once Warfarin started, continue Heparin until INR >2.0 for 2 consecutive days |
| Valve-sparing aortic surgery, e.g. David Procedure | No* | It is reasonable to forego anticoagulation<br><br>**Prophylactic heparin @ 20 units/kg/hr can be considered* | Once feeding start Aspirin for 3-6 months |

| | | | |
|---|---|---|---|
| **Aortic valve replacement (AVR)** with a mechanical valve (St Judes-Abbott, ATS-Medtronic, CarboMedics, "On-X" | Yes | Prophylactic Heparin @ 20 units/kg/hr if no bleeding concern on the day of surgery<br>and then titrate to therapeutic IV heparin on post-op Day 1 | Start Warfarin on post-op day 1 or when practical<br>Target INR 2-3<br>**Once Warfarin started, continue therapeutic IV Heparin until INR >2.0 for two consecutive days**<br>For "On-X" valve in patients with low thromboembolic risk, after 3 months post-surgery INR range 1.5-2.5 is acceptable<br>For "On-X" valve in patients with high thromboembolic risk*, add an anti-platelet agent to Warfarin and consider proton pump inhibitor (PPI) for GI protection |
| **Mitral valve replacement (MVR)** with a mechanical valve (St Judes-Abbott, ATS-Medtronic, CarboMedics, On-X)<br><br>**ATTENTION: HIGH RISK OF THROMBOSIS** | Yes | Prophylactic Heparin @ 20 units/kg/hr if no bleeding concern on the day of surgery<br>and then titrate to therapeutic IV heparin on post-op Day 1<br><br>**Once Warfarin started, continue Heparin until INR >2.5 for 2 consecutive days**<br>**ATTENTION: HIGH RISK OF THROMBOSIS, if subtherapeutic aPTT or INR, discuss with Cardiac Surgeon/ Cardiologist/Intensivist** | Start Warfarin 1800Hrs on post-op Day 1<br>Target INR range 2.5-4.0<br>Continue therapeutic IV heparin until INR >2.5<br><br>For "On-X" valve, after 3 months post-surgery INR range 2-3 may be acceptable for lower thrombotic risk patients |
| **Mitral valve replacement (MVR)** with a bioprosthetic valve | Yes | Prophylactic heparin @ 20 units/kg/hr if no bleeding concern<br><br>In patients with high thromboembolic risk, ***increase to therapeutic IV heparin on post-op Day 1 & continue until INR >2.0*** | Once feeding, long term Aspirin +/- Clopidogrel<br>May use therapeutic LMWH or Warfarin target INR 2 to 3 for 3 months, then Aspirin +/- Clopidogrel |

## Anticoagulation after catheter procedures

**Anticoagulation after PDA Stent, RVOT stent, PPVI, Aortic stent and some pulmonary artery stent insertion**

- Start prophylactic heparin 20units/kg/hr (do not target specific aPTT range, unless instructed by Interventional Cardiologist)
- Check aPTT 4 hours after starting heparin and then once daily to ensure not >90 (i.e. not over-anticoagulated)
- Start Aspirin when feeds reestablished (refer to BNFc or Paediatric Formulary for dosage)
- Consider adding Clopidogrel in high risk PDA, RVOT and PPVI stent (discuss with Interventional Cardiologist, refer to Paediatric Formulary for dosage)
- Stop heparin after 2nd dose of Aspirin

**Duration of antiplatelet therapy after discharge**

| | **Aspirin 5 mg/kg, max dose 75 mg, plus or minus Clopidogrel** |
|---|---|
| **Device closure of ASD or PFO** | 6 months |
| **Device closure of VSD** | 6 months |
| **Device closure of PDA** | Not required |
| **Pulmonary/Aortic Valvuloplasty** | Not required |
| **Balloon/Stenting of Pulmonary Artery/Conduit** | 6 months if stent insertion |
| **Balloon Atrial Septostomy** | Not required |
| **Balloon/Stenting of Aortic Arch** | 6 months if stent insertion |
| **Diagnostic catheter** | Not required |
| **MAPCA/Venous Collateral Occlusion** | Not required |
| **RFA** | 10 days if left sided pathway |
| **Percutaneous Pulmonary Valve Insertion (PPVI)** | Lifelong |
| **PDA stent insertion** | Whilst stent *in situ* |

## Prophylactic IV Heparin use

For most postoperative patients, heparin infusion rate is 20 iu/kg/hr (for specific procedures where prophylactic heparinisation is required, see tables above pp. 3-5). A loading dose of Heparin is not required.

- **Preparation and rate**:
  - Prepare infusion using 1000units/kg of heparin sodium, diluted to 50ml with 0.9% sodium chloride. Infusion rate of 1.0 ml/hr = 20 units/kg/hr
  - If patient weight >50 kg, maximum 50 000 units/50 ml
- **Monitoring:**
  - **Clotting profile** (aPTT, PT and fibrinogen) should be checked as follows:
    - On arrival back from theatre, **4 hours** after start of heparin infusion;
    - **One hour** after a syringe is changed (request aPTT only – upper limit of 80 is acceptable);
    - **Once daily** thereafter whilst on heparin infusion to check it is less than 90 (i.e. not over-anticoagulated)
  - **Platelets**
    - **Check FBC daily**. If platelets drop by >50% from baseline consider Heparin Induced Thrombocytopenia (HIT), this is more likely to occur after 5-10 days of treatment. However, there are many other reasons for thrombocytopenia (NEC /infection etc). Notify consultant. Consider sending HIT antibody screen.

## Therapeutic IV Heparin use

### Target aPTT range is 60s-90

**Preparation, loading, infusion rate, dosage management**

- Prepare infusion using 1000units/kg (for patients over 50 kg max is 50 000 units) of heparin sodium, diluted to 50ml with 0.9% sodium chloride.
  - **Only if aPTT is <50s** give initial loading dose of heparin at 50units/kg (2.5ml) over ten minutes and run at 20units/kg/hr
  - **Do not load if just returned from theatre**
  - **If aPTT 60-90,** start heparin infusion at 20 units/kg/hr (1ml/hr) without load and check aPTT in **4 hours**.
  - Manage heparin titration as follows aiming for an aPTT of 60-90, unless specific instructions

- **Monitoring:**
  - **Clotting profile** (aPTT, PT and fibrinogen) should be checked as follows:
    - On arrival back from theatre
    - **4 hours** after starting heparin infusion and after dose change
    - **Once daily** thereafter whilst on heparin infusion
  - **Platelets**
    - Check **FBC daily** whilst on heparin
    - If platelets drop by >50% from baseline, consider Heparin Induced Thrombocytopenia (HIT). HIT is more likely with 5- 10 days of treatment, however there are many other reasons for thrombocytopenia (NEC /infection etc) – discuss with duty Consultant Intensivist.
    -

| aPTT (s) | Bolus (iu/kg) | Stop infusion | Rate Change | Recheck aPTT (hr) |
|---|---|---|---|---|
| <50 | **50** | | **+10%** | In 4 hours |
| 50-59 | | | **+10%** | In 4 hours |
| 60-90 | | | | Next day |
| 90-99 | | | **-10%** | In 4 hours |
| 100-120 | | **For 30 mins** | **-10%** | In 4 hours |
| >120 | | **For 60 mins** | **-10%** | In 4 hours |

The need for more than 40 units/kg/hr of heparin to achieve target aPTT should be made known to the duty Consultant Intensivist if patient is on PICU or Cardiologist if on ward 1E. In this situation consider measuring anti-Xa level and anti-thrombin level (anti-thrombin levels are age-dependent). It is not unusual for a child under 1 year of age to require up to 40units/kg/hr to achieve therapeutic aPTT levels.

Once the aPTT is achieved and the heparin infusion is stable – once daily clotting profile is acceptable.

## Procedures on IV Heparin, LMWH or Warfarin on PICU and Ward 1E

### Heparin

If patients are **prophylactically heparinised and/or aPTT is <60**

- **Chest drain removal or insertion** – there is no need to stop heparin prior to procedure

- **Intra-cardiac line & pacing wire removal** – stop heparin for 4 hours prior to procedure and check aPTT is <60 and platelet count is >100 within 2 hours period prior to removal of lines or wires.

If patients are **therapeutically heparinised (ie aPTT target 60-90)**

- **Chest drain removal or insertion** (unless clinical emergency) – there is no need to stop heparin prior to procedure unless specific surgical concern

- **Removal of intra-cardiac lines** - heparin should be stopped for 4 hours prior to procedure. Send a standard coagulation profile and FBC 2 hours after stopping heparin and check aPTT is <60 and Platelet count is >100. If any doubt discuss with Duty Intensivist.

- **Removal of *pacing wires*** - heparin should be stopped for 4 hours prior to removal. Send a standard coagulation profile and full blood count 2 hours after stopping heparin and check aPTT is <60 and Platelet count is >100. If any doubt discuss with Duty Intensivist if patient is on PICU or Cardiologist if on Ward 1E.

  ***NB no need for an active group & save or crossmatch for any of these procedures; O negative blood will be used if needed in the unlikely event of emergency.***

### LMWH e.g. Enoxaparin

- **Chest drain removal or insertion:** no need to stop Enoxaparin prior to insertion or removal of chest drains

- **Removal of pacing wires or intra-cardiac lines:** omit Enoxaparin dose at 2000Hrs evening before removal and at 0800 Hrs on morning of removal. Check FBC, coagulation screen and antiXa at 0800Hrs on day of removal to confirm that aXa assay <0.3, aPTT <60 and Platelets >100 prior to removal.

  ***NB no need for an active group & save or crossmatch for any of these procedures; O negative blood will be used if needed in the unlikely event of emergency.***

### Warfarin

- **Chest drains can be removed if INR<3.0 (if INR >3.0, discuss with duty Cardiac Surgeon)**
- **Pacing wires can be removed if INR <2.5**
- **Intra-cardiac lines** should be removed prior to initiation of warfarin

**Seek patient-specific advice from duty Cardiologist/Haematologist/Surgeon/Intensivist**

## Reversal of IV Heparin

If anticoagulation with heparin needs to be discontinued for clinical reasons, termination of the heparin infusion will usually suffice due to the rapid clearance of heparin, unless there is renal failure, and patient is not on any form of renal support. If an immediate effect is required, IV protamine sulphate will reverse heparin therapy.

The dose of protamine required is based on the amount of heparin received in the preceding 2 hours (see below & also BNF). **Maximum Protamine dose is 50 mg**

| Time since last heparin dose | Protamine dose |
|---|---|
| <30 mins | 1mg /100 units heparin received |
| 30-60 mins | 0.5mg-0.75mg/100 units heparin received |
| 60-120 mins | 0.375mg -0.5mg/100 units heparin received |
| >120 mins | 0.25mg-0.375mg/100 units heparin received |

Protamine infusion is usually given undiluted (10 mg/ml) at a rate not exceeding 5 mg/min. May be diluted in sodium chloride 0.9% if required. Hypersensitivity reactions to protamine sulphate may occur in patients with known hypersensitivity reactions to fish or those previously exposed to protamine therapy or protamine-containing insulin. Significant hypotension may occur in these cases.

## Aspirin Guidance

Must fulfill the following criteria to start aspirin:

- Chest closed
- Major intra-cardiac lines removed (pulmonary arterial/ left atrial lines)
- Absorbing feed

Aspirin is commenced at 3-5mg/kg (max 75mg) once daily.
Stop heparin after 2nd dose of aspirin.

Alternative antiplatelet agents can be used (Clopidogrel, Dipyridamole) on Consultant Cardiologist and Haematologist advice. Platelet function testing may need to be considered in discussion with Haematology during initiation of this treatment.

Please note that the nasal (live) influenza vaccine is contraindicated when on Aspirin (see SPCS Vaccine Advice & The Green Book at https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book#the-green-book.

## Warfarin Guidance

Since the half-life of the vitamin K dependent coagulation factors vary from 6 to 72 hour, and the half-life of Warfarin on average is between 20 and 60 hours, changes made in the dosage will not be fully reflected by the INR until day 3 or 4. Mainenance doses are highly dependent upon patient age, vitamin K intake, intercurrent illnesses and concurrent use of other drugs.

Prior to initiation of Warfarin therapy, please check coagulation screen, INR, FBC, UE and LFT.
If a thromboembolic event has occurred, discuss with Consultant Paediatric Haematologist before initiating any anticoagulant therapy (as a thrombophilia screen may be required).

**Warfarin should not be started without heparin cover due to its effect on proteins C and S; Warfarin induces a fall in these natural anticoagulant proteins which temporarily increases the thrombotic potential unless counteracted by heparin.**

**Starting warfarin on PICU**

In most patients Warfarin will be started after transfer to ward 1E. Criteria for commencing warfarin therapy in PICU:

- Warfarin indications and target INR range see *'Summary of anti-coagulation therapy for cardiac surgical procedures'* section of guideline (P 3-5)
- Therapeutic aPTT or antiXa level and patient is clinically stable
- Decision made by Duty Intensivist
- No Intracardiac lines *in situ*
- Child absorbing enteral feeds and not change in feed type (NB Monogen and other formulas have more Vitamin K than breast milk).

INR must be checked **prior** to starting Warfarin, to adjust loading dose if necessary (see dosage guidance in **Starting and managing warfarin on ward 1E** section). Sample for INR must be obtained from invasive lines or venepuncture and sent to the lab, not using Coaguchek (reserved for monitoring INR in stable inpatients and in outpatient setting). Manufacturer recommendation is that Coaguchek monitors should not be used to monitor children receiving concomitant Heparin/LMWH therapy and in children with Hct > 0.55.

Heparin or LMWH must be continued **until the INR is within target range for 2 consecutive days.**

**Warfarin on Ward 1E**

**If warfarin has been started on PICU:**

1. Daily INR until stable
2. Prescribe warfarin on HEPMA "as charted" for 1800 hrs, referring to tables below for doses
3. Utilise INR Monitoring & Warfarin Prescribing Chart
4. Consult Duty Cardiologist or Haematologist prior to withholding doses to avoid an 'up and down' cycle of INR results

5. If prolonged period of intravenous heparin anticipated, convert to LMWH
6. Stop Heparin/LMWH when INR within target range for 2 consecutive days (as per P 3-5)
7. Decide on frequency of INR monitoring considering stability of INR

**Starting warfarin on Ward 1E:**

- Although Warfarin can be started with pacing wires and drain still *in situ*, consider if these can be removed before starting warfarin
- Follow steps 1-7 above
- Cardiology ANP team to counsel child and family on warfarin home monitoring, including instruction on use of Coaguchek machine. Ideally this conselling process will have been started in the planning stage prior to surgery by cardiology and cardiac surgery consultant team
- The anticoagulant effect of warfarin is delayed by 48-72 hours after the dose. Avoid withholding warfarin if possible by giving a small dose instead, to avoid an up and down INR cycle; if in doubt, seek advice of on call Cardiologist or Haematologist
- Coaguchek monitors do not accurately define high INR values. If INR > 6, a repeat venous sample is required. Coaguchek monitors should not be used to monitor children receiving concomitant Heparin/LMWH therapy and if patients has Hct >0.55

**Warfarin Dosing**

The tables below are intended as a guidance only and do not replace the clinical experience and judgement of the practitioner involved in the dosing and prescribing of warfarin.

For target INR ranges, see Summary of antithrombotic therapy for all cardiac patients and valve surgery

**Loading with Warfarin**

**Initial dosing on Day 1 for all target ranges** (**check FBC, U&E, LFT, Bone profile, INR before starting).**

**0.2mg/kg** (maximal dose 5 mg for patient Wt <50 kg and 10mg for Wt >50 kg) orally at 1800hrs, if none of the below is present
**0.1 mg/kg** (max 5 mg for any Wt) if:

- Patient is receiving drugs interacting with warfarin (see Appendix, BNFc or consult a Pharmacist for all interactions)
- Baseline INR >1.3
- TCPC and reduced RV function
- Significant hepatic impairment

**Days 2 - 4**

| **Target INR 2.0-3.0** | **Warfarin dose** |
|---|---|

| | |
|---|---|
| 1.1-1.3 | Repeat day 1 loading dose |
| 1.4-3.0 | 50% of day 1 loading dose |
| 3.1-3.5 | 25% of day 1 loading dose |
| 3.6-5.0 | Discuss with Cardiologist or Haematologist to decide whether to reduce next dose by 50% of previous dose or omit next dose |
| >5.0 | Omit next dose. Discuss with Cardiologist or Haematologist |

If INR is less than 1.5 on day 4, increase warfarin dose to 0.3 mg/kg (maximum 10 mg) and recheck INR daily. Contact Consultant Haematologist for further advice as necessary.

**Maintainance regime (Day 5 onwards)**, based on target INR and individual response

| **Target INR 2.0-3.0** | **Warfarin dose** |
|---|---|
| 1.1 – 1.5 | Increase dose by 20% and start LMWH if required |
| 1.6 – 1.9 | Increase dose by 10% |
| 2.0 – 3.2 | No dose change |
| 3.3 – 5.0 | Dicscuss with Cardiologist/Haematologist and decrease dose by 10-20% or withhold |
| 5.1 – 6.0 | Discuss with Cardiologist/Haematologist and decrease dose by 20-33% or withhold |
| 6.1 – 7.9 | Stop Warfarin. Check venous INR daily. Discuss with Cardiologist/Haematologist. If no active bleeding, restart warfarin at a lower dose when INR < 5. If active bleeding, consider reversal of anticoagulation (see below). |
| >8 | Stop Warfarin. Check venous INR daily. Discuss with Cardiologist and Haematologist and follow reversal of anticoagulation guidance. Restart Warfarin when INR <5 at 50% of last dose |

**Days 2 - 4**

| **Target INR 2.5-3.5** | **Warfarin dose** |
|---|---|
| 1.1-1.3 | Repeat day 1 loading dose |
| 1.4-3.0 | 50% of day 1 loading dose |
| 3.1-4.0 | 25% of day 1 loading dose |
| 4.0-4.9 | 50% of previous dose |
| >5.0 | Discuss with Cardiologist or Haematologist. If no major bleeding, withhold or reduce dose by 50% of previous dose when INR < 5 |

If INR is less than 1.5 on day 4, increase warfarin dose to 0.3 mg/kg (maximum 10 mg) and recheck INR daily. Contact Consultant Haematologist for further advice as necessary.

**Maintenance regime (Day 5 onwards)**, based on target INR and individual response

| **Target INR 2.5-3.5** | Warfarin dose |
|---|---|
| ≤2.0 | Increase dose by 20%. Start Enoxaparin twice daily (therapeutic), |

| | |
|---|---|
| | monitor antiXa. Stop Enoxaparin when INR within target range |
| 2.1 – 2.4 | Increase dose by 10%. Start Enoxaparin twice daily (therapeutic). Monitor antiXa. Stop Enoxaparin when INR within target range |
| 2.5– 4.0 | No dose change |
| 4.1 - 5.0 | Discuss with Cardiologist/Haematologist lower dose by 10% |
| 5.1 – 6.0 | Discuss with Cardiologist/Haematologist and lower dose by 20% or withhold next dose and restart warfarin at a lower dose when INR < 5. |
| 6.1 – 7.9 | Stop Warfarin. Check venous INR daily. If no active bleeding, in consultation with Cardiologist/Haematologist restart at a lower dose when INR <5. If active bleeding, call Haematology for advice on reversal of anticoagulation |
| >8 | Stop Warfarin. Check venous INR daily. Call Haematology for advice on reversal of anticoagulation. Resume warfarin at a lower dose when INR < 5. |

## Reversal of warfarin

**If INR >8, with or without haemorrhage, obtain Consultant Haematologist and Cardiologist advice urgently and refer to RHC Antithrombotic protocol at** http://www.clinicalguidelines.scot.nhs.uk/ggc-paediatric-guidelines/ggc-guidelines/haematologyoncology/anti-thrombotic-protocol/

**Do not give vitamin K without discussion with Haematologist and Cardiologist**

## Significant drug interactions with warfarin

The following drugs frequently used in paediatrics interact with warfarin (for complete list, check BNFC):

| Increase the effect of warfarin | Reduce the effect of warfarin | Variable effect |
|---|---|---|
| Amiodarone | Carbamazepine | Phenytoin |
| Chloral Hydrate | Rifampicin | |
| Ciprofloxacin | Vitamin K | |
| Erythromycin | Barbiturates | |
| Fluconazole | | |
| Itraconazole | | |
| Thyroxine | | |
| Aspirin | | |
| Long term Paracetamol use | | |
| Cotrimoxazole | | |
| Ibuprofen | | |
| Glucagon | | |
| Steroids | | |
| Cranberry juice | | |

## Low Molecular Weight Heparin (LMWH) Enoxaparin guidance

**Therapeutic Enoxaparin dose regime**

- **< 2 months old**
  - 1.5mg/kg twice daily subcutaneously
  - Ideally prescribe for 0600Hrs & 1800Hrs (but do not delay commencing treatment unless converting from Unfractionated heparin)
  - Administer dose via SC injection (insuflon should not be used)
- **>2 months old**
  - 1mg/kg twice daily subcutaneously
  - Ideally prescribe for 0600Hrs & 1800Hrs
  - Administer dose via SC injection (insuflon should not be used)

**Monitoring when on therapeutic Enoxaparin regime**

- Check anticoagulation effect of Enoxaparin 4 hours after 1st dose. Order "Control of Heparin – Child" on TrakCare stating Enoxaparin therapy and dose regime and time of last dose.
- Target Anti-Xa assay 0.5 – 1.0 U/ml
- Dose adjust as per chart below
- Repeat "Control of Heparin – Child" 4 hrs after 3rd dose and dose adjust as per chart. Check Full Blood Count at the same time to ensure there is no evidence of Heparin Induced Thrombocytopaenia (HIT)
- Once target Anti-Xa levels are achieved, re- check anti-Xa and FBC every Monday & Thursday
- Remember Enoxaparin effect results will be affected by:
  - Use of Unfractionated Heparin & diuretic use
  - Delayed excretion of LMWH e.g. in renal failure
  - Hepatic failure
  - Coexisting coagulopathy e.g. in sepsis
- Increase frequency of "Control of Heparin – Child" testing if:
  - Bleeding concern (consider HIT)
  - Planned surgery

Enoxaparin should be continued for between 6 weeks and 3 months post-diagnosis of a venous thrombo-embolism (VTE), unless converted to DOAC.

- Ensure referral to Haematology team @ RHC.
- Remove CVL associated with VTE as soon as possible. Ensure follow-up ultrasound to screen for extension or resolution of VTE.

**Occasionally a patient will be discharged from RHC-G on LMWH/Enoxaparin:**

- To ensure Haematology follow up, please copy the discharge summary to the Haematology Consultant involved with the patient and email a copy to ggc.rhcnonmalignantnurses@ggc.scot.nhs.uk ).

| Anti-Xa level | Dose adjustment | Next Anti-Xa level |
|---|---|---|
| **<0.35** | **Increase dose by 25%** | **4 hrs post dose** |
| **0.35 – 0.49** | **Increase dose by 10%** | **Next day** |
| **0.5 – 1.0** | **No change** | **Next Monday or Thursday** |
| **1.01 – 1.5** | **Decrease dose by 10%** | **Next day** |
| **1.51 - 2.0** | **Delay dose by 12hrs & decrease by 25%** | **Check Anti-Xa every 12 hrs till <1.0** |
| **>2** | **Delay dose till Anti-Xa is <1.0**<br>**Decrease dose by 40%** | **Check Anti-Xa every 12 hrs till <1.0**<br>**Check Anti-Xa 4 hrs after dose** |

**Prophylactic Enoxaparin therapy**

Venous thromboembolism (VTE) prophylaxis with Enoxaparin should be used in combination with measures including early mobilisation, removal of CVL's and TED stockings (see appendix *VTE Risk assessment*).

- **< 2 months old**
  - 0.75mg/kg twice daily subcutaneously
  - Prescribe for 0600Hrs & 1800Hrs
  - Administer dose via SC injection (insuflon should not be used)
- **>2 months old**
  - 0.5mg/kg twice daily subcutaneously (maximal dose 20 mg)
  - Prescribe for 0600Hrs & 1800Hrs
  - Administer dose via SC injection (insuflon should not be used)

➢ **Prophylactic Enoxaparin monitoring regime**

- Check anticoagulation effect of Enoxaparin 4 hrs after 3rd dose
  - Order "Control of Heparin – Child" on Trakcare stating Enoxaparin therapy and dose regime and time of last dose.
- Target Anti-Xa assay 0.3 – 0.5 U/ml
- Dose adjust as per chart below
- Once target Anti-Xa assays are achieved, re- check every Monday along with a Full Blood Count
- Remember Enoxaparin effect results will be affected by:
  - Use of Unfractionated Heparin
  - Delayed excretion of LMWH e.g. in renal failure
  - Hepatic failure
  - Coexisting coagulopathy e.g. in sepsis
- Increase frequency of "Control of Heparin – Child" testing if:
  - Bleeding concern (consider HIT)
  - Planned surgery

| Anti-Xa level | Dose adjustment | Next Anti-Xa level |
|---|---|---|
| **<0.3** | **Increase dose by 25%** | **4 hrs post dose** |
| **0.3 – 0.5** | **-** | **4 hrs post dose on next Monday** |
| **0.5 – 1.0** | **Decrease dose by 25%** | **Next day** |
| **>1.0** | **Delay dose till Anti-Xa is <0.5**<br>**Decrease dose by 40%** | **Check Anti-Xa every 12 hrs till <1.0**<br>**Check Anti-Xa 4 hrs after dose** |

## Central Venous Line (CVL)-related Venous Thrombosis

Venous thrombosis is a recognized morbidity in post-operative cardiac patients. There is no evidence that prophylactic heparin prevents clot formation.

Unless there are other bleeding concerns the following steps should be taken:

1. If possible the CVL associated with the clot should be removed as soon as possible
2. Therapeutic anticoagulation with heparin should be commenced (**See therapeutic heparin section, p.7)**.
3. Review evidence of clot radiologically (ultrasounds is ideal) between day 3-5
    a. If there is no clot evident or only a small clot visible with good blood flow, then heparin can be stopped, and no other investigations are required
    b. If the clot extends or remains present on radiological review, then
        i. Therapeutic anticoagulation with heparin should be continued. (**See therapeutic heparin section)**. Heparin can be converted to therapeutic LMWH (Enoxaparin) or DOAC. Length of treatment will be determined by radiological and clinical review with the haematology teams.
        ii. Initiate DOACs **after at least 5 days of initial parenteral anticoagulation treatment and at least 10 days of oral feeding (see DOACs use section).**

Following resolution of clot, if the CVL remains in-situ prophylactic LMWH should continue until the CVL can be removed. If in doubt, advice should be sought from Duty Haematology Consultant.

**When a patient is discharged from RHC-G on LMWH:**

- To ensure Haematology follow up, please copy the discharge summary to the Haematology Consultant involved with the patient and email a copy to ggc.rhcnonmalignantnurses@ggc.scot.nhs.uk ).

## Direct-acting Oral Anticoagulants (DOACs) use in postoperative period

Rivaroxaban is a reversible inhibitor of activated factor Xa, which prevents thrombin generation and thrombus development. It has the advantage over conventional anticoagulants, like warfarin, of being an oral medication with no food-drug interactions, limited drug-drug interactions and no requirement for venepunctures for monitoring, as well as possibly a more favourable safety profile.

Rivaroxaban suspension 1mg/ml is currently the only DOAC licensed for use in paediatrics in the UK.

**Indications**

- Per BNFc, only Rivaroxaban is currently licenced for treatment of venous thromboembolism (VTE) and prevention of VTE recurrence in term neonates, infants and toddlers, children and adolescents aged less than 18 years **after at least 5 days of initial parenteral anticoagulation treatment, i.e. unfractionated heparin or LMWH.** Neonates must weigh at least 2.6Kg and had at least 10 days of oral feeding.

Recent prospective multicentre open label RCT of Rivaroxaban use in children with single-ventricle physiology within 4 months of the Fontan-type procedure demonstrated similar safety profile and possibly fewer thrombotic events compared to Aspirin, suggesting a favourable risk/benefit profile for Rivaroxaban in TCPC patients; however currently Rivaroxaban use is not licenced for this indication

**Rivaroxaban must not be used for anticoagulation related to cardiac valves replacement**

**Dosage**

- Doses are weight dependent

| Bodyweight (kg) | Dose | Frequency | Total daily dose | Formulation |
|---|---|---|---|---|
| 2.6 to < 3 | 0.8 mg | TDS | 2.4 mg | Oral suspension |
| 3 to < 4 | 0.9 mg | | 2.7 mg | |
| 4 to < 5 | 1.4 mg | | 4.2 mg | |
| 5 to < 7 | 1.6 mg | | 4.8 mg | |
| 7 to < 8 | 1.8 mg | | 5.4 mg | |
| 8 to < 9 | 2.4 mg | | 7.2 mg | |
| 9 to < 10 | 2.8 mg | | 8.4 mg | |
| 10 to < 12 | 3 mg | | 9 mg | |
| 12 to < 30 | 5 mg | BD | 10 mg | 1st line: Oral suspension (Licensed)<br>2nd line: 2.5 mg tablets (Off-label) |
| 30 to < 50 | 15 mg | OD | 15 mg | 15 mg tablets |
| ≥ 50 | 20 mg | | 20 mg | 20 mg tablets |

**The weight of the child should be monitored, and the dose reviewed regularly to ensure a therapeutic dose is maintained.**

**Frequency of dosing**

- For a once daily regimen, doses should be approximately 24 hours apart
- For a twice daily regimen, doses should be approximately 12 hours apart
- For a three times daily regimen, doses should be approximately 8 hours apart
- Doses should be taken after food

**Monitoring**

- No routine anticoagulant monitoring is required with rivaroxaban (INR tests are unreliable to measure the anticoagulant activity of rivaroxaban and therefore should not be used)
- Biochemistry (U&E and LFT) should be re-checked about 2 weeks after starting rivaroxaban
- It is important to adjust the dose with increasing weight, so prior to discharge, clear arrangement should be put in place who is going to do it, e.g. Health Visitor weighs the child weekly and GP prescribes an adjusted dose (may require Cardiology Registrar to send electronic prescription request to GP via Clinical Portal electronic forms)
- Refer to Thrombosis clinic for outpatient follow up (Dr Fernando Pinto)
- Patients should be monitored for signs of bleeding or anaemia. Treatment should be stopped if severe bleeding occurs.

**Management of bleeding**

- Vitamin K and protamine sulphate do not affect the anticoagulant activity of rivaroxaban and should not be used if bleeding occurs.
- If bleeding cannot be controlled, obtain Haematology Consultant advice urgently and in consultation with Haematology consider administration of a specific procoagulant agent, such as Beriplex (4-factor Prothrombin Complex Concentrate – refer to RHC Antithrombotic guideline on management of surgical procedures in patients with bleeding disorders, Protocol for Reversal of Over-Anticoagulation section for dosage).

**Hepatic Impairment**

- **Rivaroxaban is contraindicated in patients with hepatic disease associated with coagulopathy and a clinically relevant bleeding risk**

**Renal Impairment**

- Rivaroxaban is not recommended in children over the age of 1 with moderate or severe renal impairment
- For children below 1 year of age with renal impairment, seek specialist advice
- Monitor renal function during treatment to ensure the dose remains appropriate

## Switching between different antithrombotic therapy modalities

Continuous Intravenous (IV) heparin to subcutaneous low molecular weight heparin (LMWH)

- Discontinue IV heparin,
- Administer subcutaneous LMWH simultaneously

Continuous IV heparin to direct oral anticoagulant (DOAC)

- Discontinue IV heparin
- Administer DOAC simultaneously

Continuous IV heparin to aspirin

- Administer 2 doses of Aspirin
- Discontinue IV heparin

Continuous IV heparin to warfarin

- Discontinue IV heparin when INR in range for 2 consecutive days

Subcutaneous LMWH to DOAC

- Discontinue LMWH
- Administer DOAC 12hrs after last dose of LMWH

Warfarin to Aspirin

- Discontinue Warfarin
- Administer Aspirin next day

Warfarin to DOAC

- Discontinue Warfarin
- Administer DOAC when INR $\leq$ 2.5

DOAC to IV heparin or subcutaneous LMWH

- Discontinue DOAC
- Administer IV heparin/subcutaneous LMWH when next dose of DOAC due

DOAC to warfarin

- Administer warfarin
- Continue DOAC for 48 hours, then stop when INR $\geq$ 2.0

DOAC to Aspirin

- Swap DOAC dose for Aspirin dose

## Adolescent risk of venous thromboembolism management

**See anti-thrombotic protocol at:** http://www.clinicalguidelines.scot.nhs.uk/ggc-paediatric-guidelines/ggc-guidelines/haematologyoncology/anti-thrombotic-protocol/

**Haematology and Oncology Unit**
**Royal Hospital for Children, Glasgow**

NHS Greater Glasgow and Clyde

**Appendix 2:** Adolescent Risk Assessment for VTE

| | |
|---|---|
| First Name: | |
| Surname: | |
| Hospital No: | |
| NHS No: | |
| DoB: | |
| Ward: | Hospital: |

**Royal Hospital for Sick Children, Glasgow.**

**ADOLESCENT RISK ASSESSMENT FOR VENOUS THROMBOEMBOLISM (VTE)**

| **Mobility - all patients** - (tick one box) | | | | | |
|---|---|---|---|---|---|
| Surgical patient and post pubertal or aged >13 years | | Non-surgical (Including PICU) patient expected to have ongoing reduced mobility relative to normal state and post pubertal or aged >13 years | | Non-Surgical patient aged >13 years not expected to have significant reduced mobility relative to normal state | |
| **Assess for thrombosis and bleeding risk below** | | | | **Risk assessment now complete** | |

| **THROMBOSIS RISK** | | | |
|---|---|---|---|
| **Patient related** | **Tick** | **Admission related** | **Tick** |
| Central venous line in situ | | Severe trauma | |
| Active cancer or cancer treatment | | Major orthopaedic surgery | |
| Dehydration | | Acute surgical admission with inflammatory or intra-abdominal condition | |
| Known thrombophilia | | Total anaesthetic + surgical time >90 minutes | |
| Obesity (BMI >30, take wt [in kg]/ height [m$^2$]) | | Intubated + ventilated | |
| One or more significant medical co-morbidities (e.g., nephrotic syndrome, sickle cell disease, inflammatory bowel disease, low output cardiac state) | | Acute severe sepsis | |
| Personal history of VTE | | Severe burns | |
| First degree relative with a history of VTE under the age of 40 years | | | |
| Use of oestrogen-containing contraceptive therapy | | | |
| Pregnancy or < 6 weeks post partum | | | |

| **BLEEDING RISK** | | | |
|---|---|---|---|
| **Patient related** | **Tick** | **Admission related** | **Tick** |
| Active bleeding | | Neurosurgery or eye surgery | |
| Acquired bleeding disorders (such as acute liver failure) | | Spinal surgery within previous 24 hours | |
| Concurrent use of anticoagulants known to increase the risk of bleeding | | Other procedure with high bleeding risk | |
| Acute stroke | | Lumbar puncture / epidural / spinal anaesthesia expected within the next 12 hours | |
| Thrombocytopenia (platelets < 75 x 10$^9$ / L) | | Lumbar puncture / epidural / spinal anaesthesia within the previous 4 hours | |
| Uncontrolled systolic hypertension | | Significant head injury | |
| Inherited bleeding disorder (such as haemophilia and von Willebrand's disease) | | | |

| | | |
|---|---|---|
| Anti-thrombotic Protocol | Version: 5 | Page 14 of 15 |
| Author: E Chalmers | Ratified: Sch Clin Gov Group | Issue Month: January 2021 |
| Review Month: January 2023 | Ref: RHC-HAEM-ONC-007 | **NB: Page 1 is a document control form and not printed** |

**Haematology and Oncology Unit**
**Royal Hospital for Children, Glasgow**

NHS

## BASIC RISK ASSESSMENT FOR VENOUS THROMBOEMBOLISM (VTE)

**A risk assessment should be conducted for ALL ADOLESCENT OR POSTPUBERTAL PATIENTS on admission to hospital or in preadmission. It is recommended that all patients should be periodically re-assessed during their inpatient stay as risk may change. Re-assessment after at least 48 to 72 hours is recommended.**

### STEP ONE

- Use a patient specific addressograph to identify the patient you are assessing
- **Assess all patients admitted to hospital for level of mobility *(tick one box)***
- **Review the patient-related factors shown on the assessment sheet for thrombosis risk, ticking each box that applies *(more than one box can be ticked)* and admission-related risk**
- The risk factors identified are not exhaustive. Clinicians may consider additional risks in individual patients and offer thromboprophylaxis as appropriate.

### STEP TWO

- **Review the patient-related and admission-related factors shown against bleeding risk and tick each box that applies *(more than one box can be ticked)*.**

### STEP THREE

**IN AT-RISK PATIENTS, ALWAYS:-**

**Consider general measures to reduce the risk of VTE:**

- *Maintain adequate hydration*
- *Mobilise early*
- *Remove central venous lines as soon as possible*

**Consider specific measures to reduce the risk of VTE:**

- *Mechanical prophylaxis, e.g. Graduated compression stockings/TEDs, IPC devices*
- *Thromboprophylaxis with low molecular weight heparin (LMWH)*

**The team looking after the patient must bear in mind the following:**

- *Although the risk of VTE increases during adolescence compared to younger children, the absolute risk remains low compared to older adults*
- *There is little evidence to support the use of specific measures, including LMWH, to reduce the risk of VTE in this age group*
- *Physical methods to reduce the risk of VTE will only be suitable in older and larger adolescents and should be used according to local protocols and experience*
- ***If an increased risk of bleeding is documented on the risk assessment- thromboprophylaxis with LMWH is relatively contraindicated***
- *The use of LMWH outside of locally agreed specialty group protocols should always be discussed with a haematologist*

| OUTCOME | No thromboprophylaxis | Mechanical thromboprophylaxis | LMWH |
|---|---|---|---|
| *(please tick any that apply)* | | | |

**Completed by:** ..... **Date:** .....

**Prescribe the appropriate intervention if required, and complete all the prescription chart documentation. *File this assessment in the patient's medical notes.***

| | | |
|---|---|---|
| Anti-thrombotic Protocol | Version: 5 | Page 15 of 15 |
| Author: E Chalmers | Ratified: Sch Clin Gov Group | Issue Month: January 2021 |
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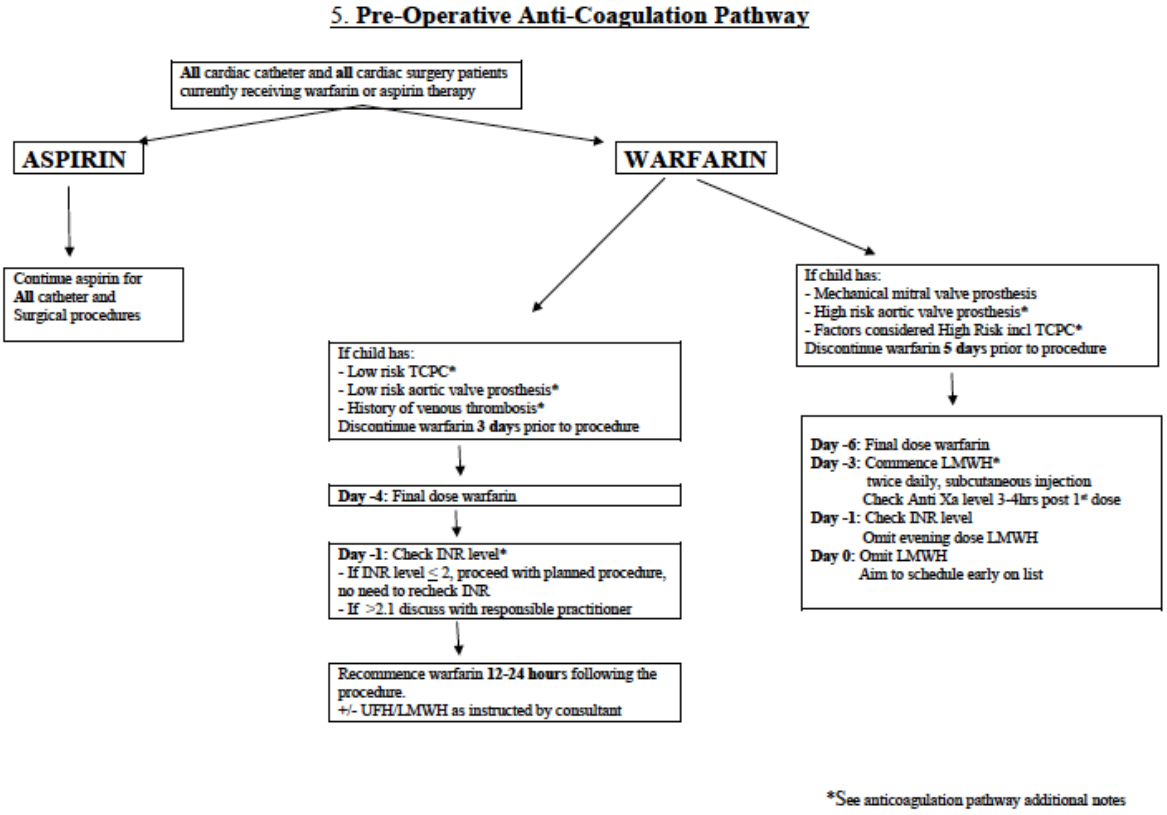
## Management of established antithrombotic therapy for patients with congenital heart disease requiring cardiac catheterisation, surgical or dental procedures

### Preoperative anticoagulation pathway

Children requiring invasive dental procedures or elective surgery with a high risk of bleeding, will require interruption of their usual anticoagulant preoperatively, **putting them at higher risk of thromboembolic complications related to their underlying condition**.

Below is only a suggested guidance; a multidisciplinary plan is required involving the cardiologist, haematologist and discipline performing the procedure to create an individualised anticoagulation plan.

There needs to be a clear communication with the discipline carrying out the intervention for the anticoagulated patient that the child is on warfarin and anticoagulation/thrombosis risk assessment and potential heparin/LMWH cover is required.




### Additional notes: Aortic Valve Prosthesis

**Low Risk**

A standard bi-leaflet aortic valve prosthesis with no additional risk factors

Absence of High Risk Factors (below).

***High Risk (including TCPC patients) that may require bridging to cardiac catheterisation/surgery with LWMH**

An increased risk of thrombosis may result from:

- Previous thromboembolism
- Left ventricular dysfunction
- Hypercoagulable conditions
- Atrial fibrillation

Therapeutic low molecular weight heparin (Enoxaparin) should be administered for these situations as per the pathway for mechanical mitral valve prosthesis.

**Low Molecular Weight Heparin (LMWH) for bridging to cardiac catheterisation/surgery**

**Dosing**

| | |
|---|---|
| Age <2 months | 1.5 mg/kg BD |
| Age >2 months | 1 mg/kg BD |

**"Control of Heparin" or Anti Xa levels**

Obtain blood sample 3-4 hours post dose. Order 'Control of Heparin – Child' on TrakCare. Target range 0.5-1 i.u/ml. Adjust dose per Low Molecular Weight Heparine chapter of this guidance. If level sub therapeutic (low) adjust dose, re prescribe enoxaparin for current time and 12 hourly thereafter (do not wait until next dose is due).

**Administration**

Do not administer Enoxaparin via insuflon. Doses of <0.1ml in volume to be diluted up to 0.1ml with 0.9% sodium chloride

**INR Level**

If INR is ≤ 2 when checked on day -1, procedure can go ahead, no need to re-check INR

If INR is >2.1 when checked on day -1, discuss with Consultant responsible for procedure and formulate a plan..

**Dental surgery in children receiving warfarin therapy**

Follow RHC Antithrombotic protocol.

## References


1. Monagle,P. *et al.* Antithrombotic therapy in neonates and children: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* **133**, 887S-968S (2008)

2. SPCS Cardiac Catheterisation Pathway

3. Lok,J.M., Spevak,P.J. & Nichols,D.G. Critical Heart Disease in Infants and Children. Nichols,D.G. *et al.* (eds.) (Mosby Inc, Philadelphia,2010)

4. Motz,R., Wessel,A., Ruschewski,W. & Bursch,J. Reduced frequency of occlusion of aorto-pulmonary shunts in infants receiving aspirin. *Cardiol. Young.* **9**, 474-477 (1999).

5. Tweddell,J.S. Aspirin: a treatment for the headache of shunt-dependent pulmonary blood flow and parallel circulation? *Circulation* **116**, 236-237 (2007).

6. Mullen,J.C., Lemermeyer,G. & Bentley,M.J. Modified Blalock-Taussig shunts: to heparinize or not to heparinize? *Can. J. Cardiol.* **12**, 645-647 (1996).

7. Andrew,M. Anticoagulation and thrombolysis in children. *Tex. Heart Inst. J.* **19**, 168-177 (1992).

8. BNF for Children https://bnfc.nice.org.uk

9. Schroeder A, Axelrol D, Silverman N et al. A continuous heparin infusion does not prevent catheter-related thrombosis in infants after cardiac surgery. *Pediatric Crit Care Med* **11**,489-495 (2010).

10. McCrindle BW[1], Manlhiot C, Cochrane A, Roberts R, Hughes M, Szechtman B, Weintraub R, Andrew M, Monagle P; Fontan Anticoagulation Study Group. Factors associated with thrombotic complications after the Fontan procedure: a secondary analysis of a multicenter, randomized trial of primary thromboprophylaxis for 2 years after the Fontan procedure. *J Am Coll Cardiol.* **22** 61, 346-53 (2013)

11. Potter BJ[1], Leong-Sit P, Fernandes SM, Feifer A, Mayer JE Jr, Triedman JK, Walsh EP, Landzberg MJ, Khairy P. Effect of aspirin and warfarin therapy on thromboembolic events in patients with univentricular hearts and Fontan palliation. *Int J Cardiol*. **168,**3940-3 (2013)

12. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Muñoz DR, Rosenhek R, Sjögren J, Tornos Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL; 2017 **ESC**/EACTS Guidelines for the management of **valvular heart disease**. **ESC** Scientific Document Group. Eur **Heart** J. 2017 Sep 21;38(36):2739-2791

13. Paediatric Formulary https://app.clinibee.com/signin?returnUrl=%2F

14. McCrindle BW, Michelson AD, Van Bergen AH, et al. Thromboprophylaxis for Children Post-Fontan Procedure: Insights From the UNIVERSE Study [published correction appears in J Am Heart Assoc. 2021 Dec 21;10(24):e020766]. *J Am Heart Assoc*. 2021;10(22):e021765.

15. GOS Guidelines for the management of anticoagulation and antiplatelet therapy in children 2012 and 2020

16. Warfarin (starship.org.nz)

17. BCH angicoagulation policy https://kids.bwc.nhs.uk/wp-content/uploads/2021/06/Anticoagulation-protocol-March-2020.pdf

18. University Hospital Bristol Warfarin Management for Paediatric Cardiac patients https://uhbw.mystaffapp.org/diliboards/83/diliboard_contents/456/document_view.pdf

19. Palaniswamy, C. & Selvaraj, D. R. (2011). Periprocedural Bridging Anticoagulation: Current Perspectives. *American Journal of Therapeutics, 18* (4), e89-e94. doi: 10.1097/MJT.0b013e3181d41ed6.

20. Keeling D, Baglin T, Tait C, et al. Guidelines on oral anticoagulation with warfarin - fourth edition. *Br J Haematol*. 2011;154(3):311-324

21. Chalmers E. Anti-Thrombotic Protocol, RHC v.5 2021

22. Baglin TP, Keeling DM, Watson HG; British Committee for Standards in Haematology. Guidelines on oral anticoagulation (warfarin): third edition--2005 update. *Br J Haematol*. 2006;132(3):277-285.

23. Palaniswamy, Chandrasekar MD*; Selvaraj, Dhana R MD. Periprocedural Bridging Anticoagulation: Current Perspectives. American Journal of Therapeutics 18(4):p e89-e94, July 2011.

24. Douketis, J. D. (2011). Perioperative management of patients who are receiving warfarin therapy: an evidence-based and practical approach. *Blood, The Journal of the American Society of Hematology*, *117*(19), 5044-5049.

25. Hirsh, J., Guyatt, G., Albers, G. W., Harrington, R., & Schünemann, H. J. (2008). Executive summary: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*, *133*(6), 71S-109S.

26. Antithrombotic therapy in paediatric cardiology patients. Clinical guidance. Evelina Children's Hospital, Guy's and St Thomas NHS Foundation Trust, 31st January 2024