Paediatric Thrombosis and Anticoagulation Guidelines

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Paediatric Thrombosis and Anticoagulation Guidelines

Introduction

Compared with adult patients the incidence of thromboembolic disease in children is much lower. As with fluid management, treatment of infection, glycaemic control etc. all doctors caring for in-patients (whatever their age) should have a working knowledge of the safe and correct use of anticoagulation. Unfortunately unless some care is taken it is possible to get the process wrong with potentially devastating consequences. The clinician must walk the knife edge between the dangers of thrombi and the perils of over anticoagulation.

The guideline will be divided into 2 sections:

A) Management of Thrombosis

There are several common scenarios in paediatric thrombosis and they most easily split into

1) The neonate/PICU
2) The cardiac patient
3) The cancer patient/General paediatrics

B) Safe Use of Medicines

The anticoagulants themselves are potentially dangerous agents and require careful prescribing within a Quality Managed System. This document is part of that system.

All anticoagulants commonly used in children require dose monitoring

Generally LMWH is preferred. Check renal function, FBC and clotting screen before use.
Use UFH if there are concerns about possible bleeding. Check renal function, FBC and clotting screen before use
Use Warfarin/asparin for specific cardiology indications

Over & under dosing with Low Molecular Weight Heparin (LMWH) is a common error given the dose size of the commercial vials/syringes.

UHW Hospital pharmacy will prepare suitable syringe doses for neonatal patients. See page 16

Warfarin and Unfractionated Heparin (UFH) are notoriously difficult to “get in range”

These guidelines are a much shorter, locally adapted version of the 2012 9th edition of the American College of Chest Physicians guidance:

A) Management of Thrombosis

The Neonate/PICU

Neonatal thrombosis is rare and occurs in 2.4/1000 admissions to the neonatal unit. The evidence base for the management of neonatal thrombosis is minimal and is largely based on case series and extrapolated data from adult literature.

Thrombotic events on PICU are frequently associated with intravascular catheters and can be managed in a similar way.

Predisposing factors: Include indwelling intravascular catheters, congenital heart disease, polycythaemia, poor deformability of neonatal red cells, shock, sepsis and dehydration.

Congenital prothrombotic disorders account for 5-20% of all thrombotic episodes and they should be considered in any neonate with a clinically significant thrombosis, spontaneous thrombotic events, unanticipated or extensive venous thrombosis, ischaemic skin lesions, purpura fulminans or family history of purpura fulminans.

Venous Thrombosis

Venous thrombi constitute about 65-75% of all neonatal thrombotic events. Over 80% are central line related. Umbilical venous catheters must be correctly placed (in the IVC - not in the portal veins) and used for as short a period as possible.

Clinical presentation will depend on thrombus location, but in general occurs with loss of catheter patency, swollen, painful and discoloured limb. Superior vena caval obstruction presents with swelling of the face and neck and chylothoraces. Pulmonary thromboembolism presents with respiratory compromise. Renal vein thrombosis presents as a palpable flank mass, haematuria, proteinuria, renal impairment and thrombocytopenia. Oedematous, cold, discoloured lower limbs may indicate extension of the thrombus into the IVC. Portal vein thrombosis is often difficult to identify by clinical means. An USS of the portal system may be considered if there is unexplained thrombocytopenia in a sick neonate.

Management:

Remove the indwelling catheter. Precious lines can be salvaged by anticoagulation but this is beyond the scope of this guideline and must be discussed with Paediatric/Coag Haematology.

1. Doppler ultrasound and discuss with radiology regarding contrast venogram.
2. Small thrombi related to catheters/obvious cause with no family history of venous thrombo-embolic disease may not need thrombophilia screening blood tests.
3. Extensive skin necrosis occurs in Protein C or S deficiency. This is termed purpura fulminans and is a medical emergency. Check Protein C and S in the baby (1 paediatric coagulation bottle for this specific test) and contact the Coagulation Haematology team for Protein C concentrate and advice.
4. Extensive thrombi, those arising without any obvious cause and in patients with a family history of venous thromboembolic disease may warrant further testing. Contact Paediatric Haematology or Coagulation Haematology team.
5. Monitor limb swelling, temperature and discoloration.
6. Monitor renal function and blood pressure if renal vein thrombosed, arrange nephrology referral.
7. Anticoagulation: Consider for any extensive deep vein thrombosis, renal vein thrombosis with IVC extension or renal failure. Start low molecular weight heparin. LMWH is preferred in neonates due to reduced risk for bleeding, no need for venous access and reduced monitoring requirements. Use unfractionated heparin (UFH) if LMWH is unavailable, or in cases where there may be a need to stop...
the anticoagulation or reverse the effects quickly (e.g., patient requiring surgery or bleeding) and in renal failure (LMWH is excreted by kidneys). Please see the LMWH and heparin guidelines in part (B). If the thrombus is large consider using antithrombin/FFP as an adjunct to heparin.

8. Treat for 3 months then stop. If VTE occurs after this then restart anticoagulation and consider continuing for life.

9. Thrombolytics are rarely indicated in venous thromboembolism.

**Arterial Thrombosis**

Arterial thromboses account for 25-35% of all neonatal thromboses and are almost exclusively secondary to indwelling arterial catheters. UA catheters should always be appropriately placed at T6-T10 or between L3-L5. Careful monitoring of colour, temperature, capillary refill time and pulses are important for early detection.

**Management**

1. Remove any indwelling catheter.
2. Anticoagulation: 70% of thrombi will resolve with anticoagulation alone. Use LMWH or UFH, please see the guidelines for LMWH and UFH.
3. Thrombolysis should be considered if thrombus is limb life or organ threatening. Start alteplase (t-PA) at 0.3-0.5mg/kg/hour for 6 hrs. Give FFP 10-20ml/kg at least 30 minutes prior to starting thrombolytic therapy. Monitor fibrinogen and aim to keep above 1g/l (please see the t-PA guideline).

Contraindications for thrombolysis:
- Active bleeding.
- General surgery within the previous 10 days or neurosurgery in the previous 3 weeks.
- Infants <32 weeks (relative contraindication)

**Stuck long lines:** Reported between 1 and 12% in older children and adults, no neonatal data available. Venospasm is the main cause for difficulty in removal although other causes include infection, fibrin formation and endothelial thrombosis. It usually occurs in medium sized veins especially basilic and cephalic veins.

**Management:**

1. Firm but gentle traction and tape down securely, release and try again after 20-30 minutes, repeat 4 hourly.
2. If unsuccessful try warm compresses to entire limb and gentle massage and milking of the skin overlying the vein (Kim et al)
3. Infusion of warm 0.9% Sodium Chloride in a line distal to long line, it should not be warm to touch.
4. Consider radiological examination to delineate knots.
5. Surgical cut-down may be needed if unsuccessful.
6. Consider using Urokinase 5000U/kg/hour IV or t-PA 0.1mg/kg/hr for 12-24 hours (E Chalmers personal communication).

**Congenital Prothrombotic disorders:**

Complete absence of Protein C or S warrants life long anticoagulation but testing for the other disorders does not alter management and current UK guidance is not to test.

Ref
Clinical guidelines for testing for heritable thrombophilia, British Journal of Haematology 2010, (149), pp 209–220
Paediatric Cardiology

Indications for use of aspirin in children (plus see tables below):

- Anti-inflammatory action – treatment of
  - Acute pericarditis
  - Kawasaki disease (acute phase)
  - Acute rheumatic fever

- Anti-platelet therapy – treatment of
  - Kawasaki disease (convalescent phase)
  - Systemic-pulmonary shunt
  - Chronic cyanosis (e.g. cavopulmonary shunt, Eisenmenger syndrome – relative indication)
  - Prosthetic valve with history of embolism despite anticoagulation (added therapy)

If aspirin cannot be used (e.g. allergy), consider the use of other agents such as dypridamole or clopidogrel (limited data in children).

In the event of development of chicken pox, herpes, influenza, rubella, or other severe flu-like febrile illness, the clinician will determine whether the risks / benefits of continuing aspirin vs the small risk of Reye’s syndrome. Parents should be instructed to telephone to ask for advice in this situation. Patients on aspirin should not have Fluenz nasal immunisation – instead they should have the injected flu vaccine. Also consider varicella vaccination.

Patients on aspirin for a B-T shunt should not have therapy discontinued, even during a febrile illness; however patients with a weaker indication for aspirin (e.g. chronic cyanosis with a cavopulmonary shunt, Kawasaki disease) should discontinue aspirin temporarily during the feverish phase of an illness. The consultant may consider use of dypridamole or clopidogrel during this period (NB the data sheet for clopidogrel also advises discontinuation during chicken pox, etc).

 Devices, Patches and Stents

<table>
<thead>
<tr>
<th>Indication</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD device</td>
<td>Aspirin 3-5 mg/kg once daily, usual maximum 75 mg once daily*</td>
<td>6 months</td>
</tr>
<tr>
<td>ASD surgical closure</td>
<td>Suture closure or patch closure with pericardium or Goretex – no antithrombotic therapy needed, unless other indication (e.g. supraventricular arrhythmia, pro-thrombotic condition, identified post-op thrombosis); Dacron patch closure – Aspirin 3-5 mg/kg once daily, usual maximum 75 mg once daily*</td>
<td>6 months</td>
</tr>
<tr>
<td>VSD device</td>
<td>Aspirin 3-5 mg/kg once daily, usual maximum 75 mg once daily*</td>
<td>6 months</td>
</tr>
<tr>
<td>Aortic stent</td>
<td>Aspirin 3-5 mg/kg once daily, usual maximum 75 mg once daily*</td>
<td>6 months</td>
</tr>
<tr>
<td>Pulmonary artery stent</td>
<td>Aspirin 3-5 mg/kg once daily, usual maximum 75 mg once daily*</td>
<td>6 months</td>
</tr>
<tr>
<td>PDA device</td>
<td>Not indicated</td>
<td></td>
</tr>
</tbody>
</table>
*NB* – there may be individual clinical reasons to extend treatment, to supplement with other antiplatelet agents (e.g. clopidogrel), or to use formal anticoagulation. Aspirin dose of 150 mg or 300 mg may be used in older adolescents.

See section 6.1.1 for advice regarding use of aspirin during intercurrent illness.

### Valve replacement

<table>
<thead>
<tr>
<th>Indication</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue valve (tricuspid, mitral, aortic)</td>
<td>Aspirin 3-5 mg/kg once daily, usual maximum 75 mg once daily*</td>
<td>6 months</td>
</tr>
<tr>
<td>Tissue RV-PA conduit or pulmonary valve</td>
<td>Aspirin 3-5 mg/kg once daily, usual maximum 75 mg once daily*</td>
<td>6 months</td>
</tr>
<tr>
<td>Prosthetic valve (any type including mitral or aortic)</td>
<td>Warfarin – target INR 3.0 ± 0.5 (i.e. range 2.5-3.5)**</td>
<td>Indefinite</td>
</tr>
</tbody>
</table>

*NB* – there may be individual clinical reasons to extend treatment, to supplement with other antiplatelet agents (e.g. clopidogrel), or to use formal anticoagulation. Aspirin dose of 150 mg or 300 mg may be used in older adolescents.

See section 6.1.1 for advice regarding use of aspirin during intercurrent illness.

**NB:**

- In high-risk AVR or MVR patients (e.g. small valve or increased risk of thrombosis), a target INR of 3.5 may be used (range 3 – 4) – this needs to be clearly specified in the medical notes and in the INR booklet.

- Our unit experience tells us that an upper range of 4 has been used without adverse incidents in the past.

- AHA guidelines recommend a target INR of 2.5 (range 2.0 – 3.0) for aortic valve replacement with a Starr-Edwards valve or a tilting disk valve (other than Medtronic-Hall) with no other risk factors (reference *Circulation* 2013;128:2622-2703). Based on our local experience, this unit will continue to have a target INR of 3.0 in all prosthetic paediatric aortic valves.

### Cavopulmonary shunt / Fontan

<table>
<thead>
<tr>
<th>Indication</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glenn / superior cavopulmonary shunt</td>
<td>Aspirin 3-5 mg/kg once daily, usual maximum 75 mg once daily*</td>
<td>To continue until Fontan / TCPC**</td>
</tr>
<tr>
<td>Fontan / TCPC</td>
<td>Warfarin – target INR = 2.5 ± 0.5 (i.e. range 2-3)</td>
<td>Indefinite***</td>
</tr>
</tbody>
</table>

*NB* – See section 6.1.1 for advice regarding use of aspirin during intercurrent illness.

**NB** – There may be individual clinical reasons to extend treatment, to supplement with other antiplatelet agents (e.g. clopidogrel), or to use formal anticoagulation.

***NB** – Some patients may be treated with aspirin rather than warfarin – the reasons for this should be clearly stated in the surgical summary and the local patient record. AHA guidelines support the use of aspirin alone in uncomplicated Fontan patients, and Warfarin in patients with adverse risk factors (see *Circulation* 2013;128:2622-2703).
Other indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD surgical patch with Dacron (pericardial / Goretex patch will not normally be given aspirin)</td>
<td>Aspirin 3-5 mg/kg once daily, maximum 75 mg daily</td>
<td>6 months</td>
</tr>
<tr>
<td>Kawasaki disease</td>
<td>Refer to AHA or UK guidelines</td>
<td>Refer to AHA or UK guidelines</td>
</tr>
<tr>
<td>Line related venous or arterial thrombosis</td>
<td>Clexane (infant) or warfarin (older child; target INR 2.5 (range 2-3)</td>
<td>3 months, with levels maintained in the treatment range</td>
</tr>
<tr>
<td>Modified Blalock-Taussig shunt</td>
<td>Aspirin 3-5 mg/kg once daily, usual maximum 75 mg once daily</td>
<td>To continue until next definitive surgery; treatment to continue with febrile illness</td>
</tr>
<tr>
<td>Pulmonary arterial hypertension (idiopathic, genetic or familial)</td>
<td>EITHER Aspirin 3-5 mg/kg once daily, usual maximum 75 mg once daily* OR Warfarin – target INR 2.0 (range 1.5-2.5)</td>
<td>Indefinite</td>
</tr>
<tr>
<td>Pulmonary arterial hypertension (Eisenmenger syndrome)</td>
<td>EITHER Aspirin 3-5 mg/kg once daily, usual maximum 75 mg once daily* OR Warfarin – target INR 1.8 (range 1.5-2.1)</td>
<td>Indefinite</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>Aspirin 3-5 mg/kg once daily OR Warfarin – INR target 2.5 (range 2-3)</td>
<td>Continue until fractional shortening &gt;25%, and/or not deemed high risk of LV thrombosis</td>
</tr>
<tr>
<td>Post L heart electrophysiology ablation</td>
<td>Aspirin 3-5 mg/kg once daily, usual maximum 75 mg once daily*</td>
<td>3 months</td>
</tr>
</tbody>
</table>

*NB – there may be individual clinical reasons to extend treatment, to supplement with other antiplatelet agents (e.g. clopidogrel), or to use formal anticoagulation. Aspirin dose of 150 mg or 300 mg may be used in older adolescents.

See section 6.1.1 for advice regarding use of aspirin during intercurrent illness.

References:
2. Valvular and Structural Heart Disease. *Chest* 2008; 133: 593S - 629S.
The Cancer Patient/General Paediatrics

This covers medical and surgical in-patients over the age of 1 and under 18 who are not critically unwell on an intensive care unit and have normal cardiac anatomy.

The common scenarios are

1) Central Venous Sinus Thrombosis
2) Lower limb DVT
3) PE
4) Upper limb DVT and Hickman/Portacath associated thrombi
5) Extrinsic compression due to tumour
6) Thromboprophylaxis

In cancer patients all of the above can be exacerbated and/or precipitated by asparaginase

For all of the above LMWH is the anticoagulant of choice. Check renal function, FBC and clotting screen before use

See Section B for dosing

Children can be discussed with Paediatric/Clotting Haematology

1) Central Venous Sinus Thrombosis

Discuss with Paediatric Neurology

Predisposing Factors
Iron deficiency, microcytic anaemia, dehydration, local (usually middle ear area) infection, asparaginase

Present with lethargy, anorexia headache, vomiting, seizures, focal signs or coma.

MRI investigation of choice due to lack of radiation but CT angiogram has fewer artefacts and is easier to arrange as an emergency

Treat for 3 months if there is a clear precipitating cause and 6 months if no cause identified. Small intracranial haemorrhages are not contraindications to anticoagulation. In a massive bleed resulting in local mass effect or intraventricular haemorrhage it is reasonable to withhold anticoagulation

2) Lower limb DVT

Rare in children. Discuss with Paediatric/Clotting Haematology

Separate into “above” and “below knee” based on Doppler report and “idiopathic/spontaneous” or “secondary/precipitated” based on history

Predisposing factors
Obesity, immobility, malignancy, smoking, age (amongst others), asparaginase

Present with lower limb swelling, pain and erythema.
Doppler angiogram of lower limbs the investigation of choice. Do not test D-Dimers

Treatment of below knee: either re-scan in 7 days or treat for up to 3 months (min 6 weeks) anticoagulation

Treatment of above knee
  Precipitated – 3 months of anticoagulation
  Idiopathic – 6 months of anticoagulation

3) PE

Rare in children. Discuss with Paediatric/Clotting Haematology

Predisposing factors
Obesity, immobility, malignancy, smoking, age (amongst others), asparaginase

Present with chest pain, shortness of breath, hypoxia.

CTPA is the initial investigation of choice. Do not test D-Dimers

Treat with 6 months of anticoagulation.

4) Upper limb DVT and Hickman/Portacath associated thrombi

Common in cancer patients (2.7% of ALL patients in Cardiff). Discuss with Paediatric/Clotting Haematology

Predisposing factors
Central line, dehydration, cancer, asparaginase.

US is the investigation of choice. MRI/MRV may be required for central veins

Treat by removing the line and anticoagulate for 3 months. “Precious” lines may remain in-situ but will management must be discussed with Paediatric/Clotting Haematology

5) Extrinsic compression due to tumour

Common in cancer patients. Discuss with Paediatric/Clotting Haematology

Predisposing factors
Central line, dehydration, cancer, asparaginase

US is the investigation of choice to demonstrate occlusion. Tumour will be imaged as part of staging.

Responding tumours with thrombus present at diagnosis may only need 3 months of anticoagulation beyond signs of the tumour shrinking. Relapsed/refractory tumours may need long term anticoagulation
6) Thromboprophylaxis

NICE Clinical Guidance 92 does not apply to people under the age of 18

General preventative measures in all children (both medical and surgical cases) are adequate hydration, early mobilisation post-operatively and removal of central lines as soon as they are no longer required.

Physical methods of prevention such as compression stockings should be considered in older children

Pharmacological methods of prevention have no evidence base at the moment. In general we would not recommend using thromboprophylaxis in unselected cases (ie no blanket use in all children).

All surgical patients (from neonates to geriatrics) at UHW are subject to preoperative thromboprophylaxis risk assessment, a copy of which is in Appendix C. Remember that this is a guideline and there may be specific circumstances in which thromboprophylaxis may be necessary but we have not foreseen. There is no validated scoring system to assess risk for children. A scoring system has been developed for PICU and pre-operative patients. Retrospective analysis/audit of VTE in children at UHW has suggested the current guideline. We will audit this in the future

In post-pubertal girls on the contraceptive pill undergoing surgery consideration should be given to stopping 4 weeks prior to surgery. Beware, unwanted pregnancy could be a consequence, please advise use of alternative contraception and document this.

See Cardiology paragraphs in Section A for specific cardiac conditions such as mechanical valves.

B) Safe Use of Medicines

Low molecular weight heparin (LMWH)

Prior to therapy:

1. Exclude contraindications (see BNF for Children)
2. Measure full blood count and keep platelets >50,000, and check clotting screen
3. Measure renal function and be cautious in renal impairment (see below and discuss with haematology)
4. Obtain blood group and cross match
5. Ensure adequate supply of blood products available for patients
6. Ensure adequate supply of protamine sulphate available
7. Perform cranial ultrasound scan in neonates

LMWH (enoxaparin):

- Neonate: 1.5 – 2 mg/kg
- 1 - 2mo age: 1.5mg/kg
- >2mo age: 1.0 mg/kg.

During therapy:

Phone laboratory to discuss timing of anti-Xa levels. Samples can be frozen and defrosted for a routine run. Prior to the assay the instrument (automated coagulation machine) must be purged/cleaned. This takes several hours and may mean the rest of the hospital will not be able to get coagulation results. Be careful what you call “urgent” results

Target anti-Xa is 0.5-1iu/ml

Administer 4 to 5 doses (2 to 3 days worth) before checking levels.

Do NOT use insulons or other S/C devices to administer doses – they cause marked variation in total drug dose delivered

Measure anti Xa 4 hours after dose and adjust according to table:

<table>
<thead>
<tr>
<th>Anti Xa</th>
<th>Hold next dose</th>
<th>Dose change</th>
<th>Repeat Xa level?</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.35U/ml</td>
<td>no</td>
<td>Increase by 25%</td>
<td>4h after 4 doses</td>
</tr>
<tr>
<td>0.35-0.49U/ml</td>
<td>no</td>
<td>Increase by 10%</td>
<td>4h after 4 doses</td>
</tr>
<tr>
<td>0.5-1.0U/ml</td>
<td>no</td>
<td>no</td>
<td>1 week later, then monthly while receiving enoxaparin (4h after am dose)</td>
</tr>
<tr>
<td>1.1-1.5U/ml</td>
<td>no</td>
<td>Decrease by 20%</td>
<td>Before next dose</td>
</tr>
<tr>
<td>1.6-2.0U/ml</td>
<td>3h</td>
<td>Decrease by 30%</td>
<td>Before next dose, then 4h after next</td>
</tr>
<tr>
<td>&gt;2.0U/ml</td>
<td>Until Xa ≤ 0.5</td>
<td>Hold then decrease by 40%</td>
<td>Before next dose, If not≤ 0.5, repeat q12h</td>
</tr>
</tbody>
</table>

Levels are routinely run on Monday/Wednesday/Friday. Non-urgent samples can be frozen and analysed at a more convenient time. For urgent samples discuss with the on call coagulation team or paediatric haematology

Side effects and precautions: Bleeding
Use unfractionated heparin (UFH) in renal failure as LMWH is excreted by the kidneys.
It may be possible to switch to LMWH once anticoagulation established – discuss with haematology
Monitor for Thrombocytopenia. Check FBC on day 8 of therapy.
Avoid NSAIDS or anti-platelet drugs

Duration of therapy: Has been used for a short course 10-14 days. For extensive deep vein thrombosis heparin has been used for 3 – 6 months.

The child’s carer will be competency assessed prior to discharge to ensure safe home administration of LMWH. Written instructions will be given to the carer on how to administer (see Appendix A for documents)

Unfractionated Heparin (UFH)

Prior to therapy:
1. Exclude contraindications (see BNF for Children)
2. Measure full blood count and keep platelets >50,000, and check clotting screen
3. Measure renal function and be cautious in renal impairment (see below and discuss with haematology)
4. Obtain blood group and cross match
5. Ensure adequate supply of blood products available for patients
6. Ensure adequate supply of protamine sulphate available on the unit
7. Perform cranial ultrasound scan in neonates

During Therapy

\[ \text{APTRR} = \frac{\text{patient's APTT}}{\text{mid point of normal range}} \]

For example, if the APTT is 32 seconds and the range is 26 to 38 seconds:

\[ \text{APTRR} = \frac{32}{(38-26)/2 + 26} = \frac{32}{(6 + 26)} = \frac{32}{32} = 1 \]

Maintain APTT between 60 and 85 seconds. This corresponds to an APTTR 1.5 to 2.5. Give by IV route

Loading dose: 75 U/kg over 10 minutes } Check with BNFc

Maintenance: 10 – 20 U/kg/hr (higher doses may be needed) } Check with BNFc

Check APTT 6 – 8 hours after starting therapy.
If APTT ratio is LOW – increase maintenance dose by 10-20% and recheck APTT ratio 4-6 hours later.
If APTT ratio is >2 and ≤3, reduce the maintenance dose by 10% and recheck APTT ratio 6-8 hours later.
If APTT ratio is >3, stop heparin for 1 hour, then restart at a reduced maintenance dose (reduce by 20%).
NB – if maintenance doses of >35 U/kg/hour are required it may be appropriate to accept slightly lower APTT ratios.
If bleeding develops then stop the infusion and inform a senior. Consider protamine sulphate. Administer protamine sulphate as follows (based on total amount of heparin received in last 2 hours):

<table>
<thead>
<tr>
<th>Heparin (time since last dose, minutes)</th>
<th>Protamine Sulphate Dose (per 100 units of heparin received)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 30</td>
<td>1 mg</td>
</tr>
<tr>
<td>30 – 60</td>
<td>500 – 750 micrograms</td>
</tr>
<tr>
<td>60 – 120</td>
<td>375 – 500 micrograms</td>
</tr>
<tr>
<td>Greater than 120</td>
<td>250 – 375 micrograms</td>
</tr>
<tr>
<td>Max Dose</td>
<td>50 mg</td>
</tr>
<tr>
<td>Infusion rate</td>
<td>Infuse over 10 minutes (max rate 5 mg/minute)</td>
</tr>
</tbody>
</table>

**Warfarin**

Procedure and process of prescription and parent competency assessment shall be done as per the All Wales Paediatric Warfarin Care Pathway and prescribed on the all Wales Paediatric In-Patient Warfarin Treatment Chart.

Copies of these documents are given in Appendix B
Tissue-type plasminogen activator (rt-PA)

Most often used in neonates to treat life or limb threatening thrombosis.

Paediatric Cardiology use it to treat limb ischaemia following femoral puncture (& thrombosis) for catheterisation

Also indicated in massive pulmonary embolism where there is systemic hypotension

Treatment of neonatal thrombosis is still controversial. The evidence based for the management of neonatal thrombosis is very limited and is mostly based on case series and extrapolated adult literature. Tissue type plasminogen activator (t-PA) has been used to treat both neonatal arterial and venous thrombosis. Consider t-PA for the following Indications:

Any limb, life or organ threatening condition secondary to thrombosis.

<table>
<thead>
<tr>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral renal vein thrombosis with impending renal failure</td>
</tr>
<tr>
<td>Arterial thrombosis with impending loss of limb</td>
</tr>
<tr>
<td>(femoral, iliac, axillary arterial thrombosis)</td>
</tr>
<tr>
<td>Extensive aortic or vena caval thrombosis</td>
</tr>
<tr>
<td>Intracardiac thrombosis compromising systemic or pulmonary circulation</td>
</tr>
</tbody>
</table>

Absolute contraindications for use:
1. Active bleeding at any site
2. Any General Surgery in the past 10 days or Neurosurgery in the last 3 weeks

Relative contraindications for use:
3. Thrombocytopenia (<50,000)
4. Low fibrinogen concentration (<100mg/dl)
5. Preterm <32 weeks

Prior to initiating therapy
1. Exclude contraindications
2. Ensure good venous access for drug administration and for monitoring purposes
3. Measure full blood count, fibrinogen
4. Obtain blood group and cross match
5. Notify blood bank to ensure FFP and cryoprecipitate are available.
6. Notify Pharmacy to ensure tranexamic acid is available
7. Perform cranial ultrasound scan in neonates
8. Ensure adequate venous access
9. Stop heparin infusion 3 hours prior to therapy
10. In Neonates give FFP 10-20ml/kg at least 30mts prior to starting thrombolytic therapy. (ACCP guidelines) to provide some plasmin for the drug to activate
11. In older children transfer to PICU or HDU prior to initiating therapy.
Dose Regimens -

there is no Trial data to support one over the other.

Case series evidence favours the low dose regimen as less likely to cause severe bleeds

High Dose:
Give a loading dose of 0.1mg/kg, followed by an infusion of 0.3-0.5mg/kg/hr over 6 hours.

Low dose:
Give 0.1mg/kg/hr for 4 hours. Once the infusion is complete, start UFH (protocol as above) and continue until next rt-PA infusion.

Perform ultrasound scan of thrombosed vessel at the end of infusion and if recanalisation is not complete. Up to four additional doses of t-PA can be given at intervals of 12-24 hours.

During therapy:

1. No intramuscular injections during therapy
2. Minimal manipulation of the patient i.e. no bathing, physiotherapy
   Avoid concurrent use of coumadin or antiplatelet agents (ie. NSAIDS, Aspirin, persantin).
3. No urinary catheterisation, rectal temperatures or arterial punctures
4. Blood samples from a superficial vein or indwelling catheter. If blood sampling is difficult, insert an indwelling catheter for blood samples prior to thrombolytic therapy
5. Monitor fibrinogen level 1 and 4 hour after each t-PA infusion. Expect a 20-50% drop in fibrinogen levels. Maintain fibrinogen level >1g/l with FFP or cryoprecipitate or fibrinogen concentrate infusion
6. Maintain platelet count >100x10^9/L
7. Do not give intramuscular injections and do not do procedures like urinary catheterisation, rectal temperatures, arterial punctures etc.
8. Minimal handling of patient
9. Perform daily cranial ultrasound scan
10. If a patient has received thrombolytic therapy for more than 6 hours, consider treating with heparin alone for 24 hours before reinstituting thrombolytic therapy. There may be ongoing thrombolysis even in the absence of continued administration of the thrombolytic agent

LMWH of choice is enoxaparin

**Children over 1 month old**

Enoxaparin (Clexane®) multidose vial will be supplied to patients whose dose is less than 40mg, for 20mg doses the 20mg Clexane® pre-filled syringes may be used

Clexane® pre-filled syringes may be used for doses of 40mg and above if measurable.

Enoxaparin (Clexane®) multidose vial - Vials containing 300 mg enoxaparin (equivalent to 30,000 IU anti-Xa activity) in 3.0 ml [avoid in neonates].

**Neonates**

Ward preparation: Clexane® pre-filled syringe 20mg in 0.2ml

As the dose of enoxaparin is small, some of the dose maybe lost in the needle. To minimise this please follow the instructions below:

1. Inject 0.2ml (of a 20mg in 0.2ml) syringe into a 1ml syringe
2. Dilute to 1ml using water for injection to give a 20mg in 1ml solution
3. Calculate the quantity required for the injection e.g. quantity required for injection = dose / 20
4. Expel the unwanted quantity from the syringe
5. Use immediately e.g. if dose prescribed is 6mg, volume for injection of diluted enoxaparin is 6/20= 0.3ml

<table>
<thead>
<tr>
<th>Enoxaparin dose</th>
<th>Volume of diluted solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>2mg</td>
<td>0.1ml</td>
</tr>
<tr>
<td>3mg</td>
<td>0.15ml</td>
</tr>
<tr>
<td>4mg</td>
<td>0.2ml</td>
</tr>
<tr>
<td>5mg</td>
<td>0.25ml</td>
</tr>
<tr>
<td>6mg</td>
<td>0.3ml</td>
</tr>
<tr>
<td>7mg</td>
<td>0.35ml</td>
</tr>
<tr>
<td>8mg</td>
<td>0.4ml</td>
</tr>
<tr>
<td>9mg</td>
<td>0.45ml</td>
</tr>
<tr>
<td>10mg</td>
<td>0.5ml</td>
</tr>
<tr>
<td>12mg</td>
<td>0.6ml</td>
</tr>
</tbody>
</table>

Pharmacy will provide ready made syringes of 20mg in 1ml for dose adjustment on discharge.

**Prior to discharge:**

- Patient/Carer counselled and assessed with regard to risks and benefits of LMWH
- Patient/Carer has undergone training in administration of correct dose and is competent (see appendix for teaching pack)
- If not competent to self/carer administer may need to attend Ward/Outpatient or have community nurse administer
- Document clearly in clinical notes and in hand held records, current enoxaparin dose and when next anti Xa level is due and who is giving it
- Prescribe the dose as “x mg s/c twice per day for y weeks” on the TTH
- Inform Haematologist of discharge of patient
- Check FBC on day 8

Appendix A

Enoxaparin – Preparation Guidelines
Child Health Directorate

Procedure for the home administration of subcutaneous Clexane by parent/carer using multi-dose vial or pre-filled syringe

Clexane dose …………………
Preparation used (mg/ml) ……………….1
Amount to be given (ml) ………………..
Storage requirements …………………………………………………………………… ………

Equipment
- Work surface e.g. plastic tray
- Kitchen roll or clean tea towel
- Anti-bacterial wipes x 2
- Gauze square or clean tissue
- Disposable gloves – optional (parent choice)
- Cold (ethyl chloride) spray – optional (patient choice)
- Clexane:
  - Babies < 1 month: Pharmacy prepared 20mg/ml pre-filled syringes
  - All other Babies & Children: Multi-dose vial with pharmacy label containing your child’s details and:
    - 1ml syringe
    - Orange needles (5/8” length) x 2

Preparing the injection
1. Wash work surface with hot water and detergent. Dry with kitchen roll or tea towel.
2. Collect equipment together.
   Check that your child’s name and Clexane dose are correctly printed on the pharmacy label.
3. Wash and dry hands thoroughly. Use kitchen roll or tea towel for drying. Put gloves on (optional).
   For multi-dose vial with pharmacy label containing your child’s details: Go to 4
   For Pharmacy prepared 20mg/ml syringes: Go to 12
5. Open needle packet. Attach sheathed needle to syringe. Return to tray.
6. Open anti-bacterial wipe x 1 and clean surface of multi-dose vial. Allow surface to dry for 30 seconds.
7. Insert needle into rubber surface and invert vial (turn upside-down) so that needle tip remains beneath surface of liquid.
   Pull syringe plunger downward until ............ ml Clexane is drawn into syringe.
8. Turn vial back and pull syringe and needle from vial.
9. Carefully detach the needle from syringe, holding orange plastic at needle base.
   Do not touch metal shaft of needle.
10. Firmly attach a new needle to the syringe.
11. Hold the syringe with the needle pointing upward. Do not remove needle sheath.
   Have assistant and cold spray, gauze square or tissue in place before proceeding.

Giving the injection

1. Position your child comfortably and select injection site on upper leg.
   Avoid bruised or damaged skin.
2. Clean injection site with anti-bacterial wipe using gentle rubbing for about 5 seconds.
   Allow the skin to dry completely so that anti-bacterial solution is not injected (very stingy).
3. Remove the sheath from prepared syringe and ask assistant to direct a jet of cold spray onto the injection area. Direct spray away from eyes and face.
   The cold spray dries immediately on contact with the skin and will not contaminate cleaned area.
4. Holding syringe in your dominant hand, gently grip your child’s skin between thumb and forefinger of free hand, either side of the injection site.
5. Insert the needle about ½-way at an angle of 45 degrees.
6. Relax your hold on the skin and push the plunger quite slowly to inject all the Clexane.
   The Clexane is likely to leak from injection site if shot in very quickly.
7. Pull the needle straight out and dab the site with gauze or tissue.
   Hold for 30 seconds to prevent Clexane leaking out.
   Do not rub as this may irritate the skin.

Clearing up

1. Dispose of the syringe and needles into a special sharps bin.
2. Dispose of all waste and packaging with your normal household waste.
3. Return Clexane to a safe place for storage.
4. Wash and dry your hands at the end of procedure.

References


## Child Health Directorate

**Teaching check-list for the home administration of subcutaneous medication by parent or carer**

<table>
<thead>
<tr>
<th>Competence</th>
<th>Observe Date</th>
<th>Supervise Date</th>
<th>Assess Date</th>
<th>Assessor Sign</th>
<th>Parent/Carer Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has received written instructions and information</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Able to state reason for the treatment</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demonstrates good hand-washing technique</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prepares the medication correctly</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administers the medication using safe techniques for:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Positioning child</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Selecting injection site</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Cleaning site</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Administering cold spray</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Administering injection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Checking injection site</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disposes of equipment correctly</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Able to identify person to contact for professional advice if a problem occurs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Statement by parent or carer**

I have received teaching and information on how to give my child's medication by subcutaneous injection. I now feel able to give the injection safely at home. I know who to contact if any problems arise.

Parent/Carer name(s) ………………………………………………………………………

Signature(s) …………………………………………………………………………………

Date … / … / ………

Assessor name ………………………………………………………………………………

Signature …………………………………………………………………………………

Date … / … / ………
### Cardiff and Vale UHB: Paediatric Warfarin Care Pathway

**See overleaf for risk assessment and guidance for patient counselling**

**For indication, duration and target INR for warfarin treatment see paediatric in-patient warfarin chart.**

#### Section 1 – to be completed for patients commencing warfarin for the first time

<table>
<thead>
<tr>
<th>Action prior to initiation of warfarin</th>
<th>Health Board staff signature / date</th>
<th>Carer +/- patient signature / date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient/carer assessed with regard to risks and benefits of warfarin</td>
<td>Doctor</td>
<td></td>
</tr>
<tr>
<td>Patient/carer deemed able to comply with monitoring requirements</td>
<td>Doctor</td>
<td></td>
</tr>
<tr>
<td>GP contacted regarding risks vs benefits (see leaflet for guidance)</td>
<td>Doctor Not required (✓)</td>
<td></td>
</tr>
<tr>
<td>Patient/carer counselled with regard to risks and benefits of warfarin treatment</td>
<td>Doctor</td>
<td></td>
</tr>
<tr>
<td>Patient/carer involved in and agrees to decision to treat with warfarin</td>
<td>Doctor</td>
<td></td>
</tr>
<tr>
<td>Additional counselling provided – DVD/verbal/leaflet</td>
<td>Nurse/pharmacist</td>
<td></td>
</tr>
</tbody>
</table>

#### Section 2 – to be completed for ALL patients who will be taking warfarin when discharged

<table>
<thead>
<tr>
<th>Action prior to discharge</th>
<th>Health Board staff signature / date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient/carer assessed with regard to risks and benefits of continuing warfarin</td>
<td>Doctor</td>
</tr>
<tr>
<td>Patient has a completed anticoagulant pack</td>
<td>Nurse/pharmacist</td>
</tr>
<tr>
<td>Patient/carer has undergone appropriate training to use CoaguChek® machine</td>
<td>Nurse</td>
</tr>
<tr>
<td>Referral to INR monitoring service</td>
<td>Nurse/pharmacist</td>
</tr>
<tr>
<td>GP</td>
<td>Other</td>
</tr>
<tr>
<td>Name of person accepting patient for INR monitoring</td>
<td></td>
</tr>
<tr>
<td>INR &gt; 2 (or in range) for 2 consecutive days</td>
<td>Y / N</td>
</tr>
<tr>
<td>If No specific arrangements for monitoring</td>
<td></td>
</tr>
<tr>
<td>Arrangements for INR to be measured within 3 - 7 days of discharge (according to stability of patient)</td>
<td>Y / N Place Date/Time</td>
</tr>
<tr>
<td>Copy of pathway and warfarin prescription chart (all 3 to be completed)</td>
<td></td>
</tr>
<tr>
<td>a. FAXED to monitoring service on day of discharge</td>
<td>Nurse</td>
</tr>
<tr>
<td>b. Given to patient to give to monitoring service.</td>
<td></td>
</tr>
<tr>
<td>c. FAXED to GP on day of discharge</td>
<td></td>
</tr>
<tr>
<td>All INRs and warfarin doses recorded in yellow book (including INR on day of discharge and prescribed dose until date of next test)</td>
<td>Pharmacist/nurse/doctor</td>
</tr>
<tr>
<td>Patient/carer counselled with regard to risks and benefits of warfarin treatment</td>
<td>Pharmacist/nurse</td>
</tr>
</tbody>
</table>
Factors associated with an increased risk of bleeding for patients prescribed warfarin

Contact GP if concerns regarding suitability of patient for warfarin

- Uncontrolled hypertension (systolic pressure >180mmHg or diastolic pressure >100mmHg)
- Alcohol excess (acute or chronic)
- Liver disease
- Poor drug compliance or clinic attendance
- Bleeding lesions (e.g. gastrointestinal blood loss, recent cerebral haemorrhage)
- Bleeding tendency (coagulation defects, platelet count <100 x10^9)
- Concomitant use of non-steroidal anti-inflammatory drugs and certain antibiotics (see BNF/BNFc)
- Instability of INR control
- INR >3

Guidance for the counselling of patients who are commencing warfarin for the first time

Before starting warfarin, the following points should be discussed, in lay terms. Give plenty of opportunity for patients to ask questions.

Basic Information
- Why the warfarin has been prescribed
- Action of warfarin:
  - reduces the tendency of blood to clot
  - increases the tendency of a person to bleed
- When warfarin is prescribed it is believed that the beneficial effect in reducing the tendency to clot is outweighed by the increased tendency to bleed
- It depends on the inactivation of vitamin K. It is important to limit the amount of vitamin K in the diet
- Can be affected by many foods, drugs and alcohol. Care must be taken to monitor the effects of significant changes in diet or medication.
- For how long treatment will be needed
- The effects of warfarin must be measured by a blood test called the INR. Blood tests will be frequent to begin with, until the dose of warfarin is stable. The dose required to maintain the INR in the right range can vary between patients and in the same patient over a period of time

INR : International Normalized Ratio
- a measure of how quickly the blood clots when compared with samples from people not taking warfarin
- Higher INR means", "thinner" blood and more likely to bleed
- Lower INR means", "thicker" blood and more likely to clot
- Most people will have a dose of warfarin to maintain their INR between 2-3 (target 2.5). Some people will have a higher target range of 3-4 (target 3.5). Inform patient of their intended therapeutic range.
- Principles of dose modification (i.e. higher INR - reduce dose; lower INR - increase dose)

Complications:
- the patient should be advised of
- Symptoms of bleeding – see yellow book for examples (seek medical advice - GP or A&E)
- Symptoms of further clots (if appropriate) e.g. DVT, PE (seek medical advice - GP or A&E)
- Pregnancy – anticoagulant medicines may cause problems in pregnancy. If the patient is a female of childbearing age they should be advised to seek medical advice if they are planning a pregnancy or find they are already pregnant.

Taking warfarin:
- the patient should be informed of the following:
  - If taking the liquid - the strength is 1mg in 1ml
  - If taking tablets - the different colours and strengths of the tablets are (0.5mg - white, 1mg - brown; 3mg - blue; 5mg - pink)
  - The time the dose should be taken (early evening around 5pm)
  - What to do if a dose is missed (same day - take dose; if next day do not take extra that day but make a note in the yellow book and inform the clinic)
  - How to get more warfarin (prescription from GP)

Food/ drug interactions
- If should be assumed that starting or stopping ANY medicine may affect the INR. The yellow book should always been carried and shown to doctors, dentists and pharmacists involved in the prescription. The INR should be checked 3-4 days after a change in medication.
- Alcohol - Patients are advised to drink no more than two units a day and not to "save" the units for the weekend.
- Patients are advised to avoid cranberry juice which may increase the INR

Monitoring Clinic:
- Information should be provided regarding INR monitoring after discharge
- An appointment will be made with a monitoring clinic (either at the hospital or at the GP surgery)
- Importance of attending monitoring clinic (or telephoning result if a home monitor is being used)

NB patients receiving long-term warfarin should be reviewed by an experienced clinician at least annually to ensure that the benefits of continuing warfarin outweigh the risks associated with its use
## PAEDIATRIC IN-PATIENT WARFARIN TREATMENT CHART

Prescribe warfarin on the in-patient chart, write “see warfarin treatment chart” and attach this sheet securely to the chart. All doses must be given between 1400 – 1800 hours. If warfarin temporarily withheld write “OMIT” on this chart.

### Duration of warfarin for specific clinical indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Duration</th>
<th>Target INR (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary pulmonary hypertension</td>
<td>Long-term</td>
<td>1.8 (1.5 - 2.0)</td>
</tr>
<tr>
<td>Primary pulmonary hypertension</td>
<td>Long-term</td>
<td>2.5 (2.0 - 3.0)</td>
</tr>
<tr>
<td>Atrial arrhythmias</td>
<td>Long-term</td>
<td>2.5 (2.0 - 3.0)</td>
</tr>
<tr>
<td>Fontan TGA</td>
<td>Long-term</td>
<td>2.5 (2.0 - 3.0)</td>
</tr>
<tr>
<td>Distal cardiomyopathy</td>
<td>Long-term</td>
<td>2.5 (2.0 - 3.0)</td>
</tr>
<tr>
<td>DVT &amp; PE</td>
<td>3 months then</td>
<td>2.5 (2.0 - 3.0)</td>
</tr>
<tr>
<td>Recurrent VTE</td>
<td>Long-term</td>
<td>2.5 (2.0 - 3.0)</td>
</tr>
<tr>
<td>Prosthetic valve</td>
<td>Long-term</td>
<td>3.0 (2.5 - 3.5)</td>
</tr>
<tr>
<td>Other (specify)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### New/existing medicines which may affect INR (see RNFC)

### Induction of warfarin

- Obtain a baseline INR. Load as below and obtain daily INRs for the first 5 days. Patient to be dosed with the supervision of a paediatric cardiologist/paediatric haematologist for the first 5 days.
- If baseline < 1.5 the patient will need a lower loading dose. Review indication for warfarin and seek cardiologist or haematologist advice.
- Most patients will be commenced on low molecular weight or unfractionated heparin before warfarin.
- Continue until INR in target range for 2 consecutive days.

### Loading and reloading of warfarin

For patients admitted on warfarin or newly warfarinised patients from day 5 see local paediatric maintenance dosing guidelines

### Day 1 - the recommended loading dose is 0.1 - 0.2mg/kg. In practice apply the following:

<table>
<thead>
<tr>
<th>Age group</th>
<th>Loading dose</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants (6 months - 1 year)</td>
<td>1-2mg</td>
<td>Check INR next day</td>
</tr>
<tr>
<td>Young children (1 - 5 years)</td>
<td>2-5mg</td>
<td>Check INR next day</td>
</tr>
<tr>
<td>Older children (5 - 12 years)</td>
<td>5-10mg</td>
<td>Check INR next day</td>
</tr>
<tr>
<td>Teenagers</td>
<td>8mg</td>
<td>Check INR next day</td>
</tr>
<tr>
<td>Adults</td>
<td>Use All Wales Adult Warfarin Chart</td>
<td></td>
</tr>
</tbody>
</table>

### Warfarin dose chart

<table>
<thead>
<tr>
<th>Date</th>
<th>INR result</th>
<th>Warfarin dose (mg)</th>
<th>Prescriber</th>
<th>Next test</th>
<th>Given by</th>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
</table>
Appendix B

SPECIAL CIRCUMSTANCES

- Reversal of warfarin for emergency surgery: discuss with haematologist
- Reversal of warfarin for patients with prosthetic heart valves: discuss with patient's cardiologist

DISCHARGE

- Use your local care pathway to ensure that accurate information is shared with the out-patient clinic and GP.
- Make arrangements for the patient to have his/her INR checked within seven days of discharge (three days if an interacting drug is being stopped or started).

MANAGEMENT OF A HIGH INR

If you are unsure, consult a haematologist (paediatric cardiologist or cardiac surgeon if the patient has a prosthetic heart valve). Patients with prosthetic heart valves should not be given intravenous vitamin K. (Reconsider if major bleeding)

INR in therapeutic range - patient bleeding.
- Investigate source of bleeding. Consider risk/benefit of stopping warfarin

INR < 6.0 but > 0.7 above target INR - no bleeding
- Reduce the dose following the local maintenance dosing guidelines

INR > 6 - no bleeding or minor bleeding from mucosae (nose, oropharynx, urinary tract, rectum, anus)
- Stop warfarin
- Restart when INR < 5.0
- Assess patient for their risk of bleeding: recent surgery/trauma, extensive bruising, minor mucosal bleeding
  If at high risk of bleeding give vitamin K 2mg orally
  Use Konakion® MM paediatric (phytomenadione 2mg in 0.2ml)
- Recheck INR after 24 hours, repeat dose of Vitamin K if INR is still too high

Major bleeding: Life or limb threatening bleeding, including intracranial haemorrhage
- Stop warfarin
- Give 250-500 micrograms/kg (max 10mg) vitamin K IV (1ml phytonadione 10 mg/ml - Konakion MM®)
  Give as an IV bolus over 3-5 minutes undiluted or diluted with 10-20ml glucose 5% to aid slow administration
- Give prothrombin complex concentrate (PCC - Factor II, VII, IX, and X concentrate) - dose to be advised by haematologist. Dissolve in water for injection as per manufacturer's guidance, using an aseptic technique.
  See local protocol for further details on administration, these should be provided with the prothrombin complex concentrate.
- Repeat INR within 1 hour of giving of PCC - consider further dose if INR remains >1.5 and patient still bleeding.
  Discuss with haematologist
- Consider risk/benefit of recommencing warfarin
SURGICAL THROMBOPROPHYLAXIS RISK ASSESSMENT
IS THE SURGICAL PATIENT POST-PUBERTAL or AGE > 13 YEARS?

Yes

No

Thromboprophylaxis is not required and the Risk Assessment is complete (sign below)

VENOUS THROMBOSIS RISK FACTORS

- Surgery involving pelvis / lower limb & total anaesthetic + surgical time >
- Acute surgical admission with inflammatory / intra-abdominal

- Total anaesthetic + surgical time >
- Active cancer / cancer treatment

- Pregnancy or < 12 weeks post-
- Personal or family history of DVT or

- Oestrogen containing contraceptive
- Hormone replacement therapy

- Expected significant reduced
- Critical care admission (planned or

- Age > 60
- Obesity (BMI > 30kg / m²)

- Varicose veins with phlebitis
- Dehydration

Unless contraindicated surgical patients should receive pharmacological and mechanical thromboprophylaxis

Note: although risk of VTE increases during adolescence, absolute risk remains low compared to adults. There is little evidence to support the use of specific modalities of thromboprophylaxis in non-adult surgical patients (clinical decision by surgeon on a case by case basis is advised)

Contraindication to enoxaparin thromboprophylaxis

- Concurrent use of anticoagulant (e.g. warfarin)

- Active bleeding or risk of bleeding

- Acute stroke / Uncontrolled hypertension (SBP > 180 mmHg)

- Thrombocytopenia: platelet count < 75 x 10⁹/l

- Heparin allergy / history heparin induced thrombocytopenia

- Severe renal disease (eGFR < 30ml/min)

- Inherited or Acquired bleeding disorder (e.g. liver disease)

- Lumbar puncture / epidural / spinal anaesthesia within past 4 hours or due in 12 hours

Contraindication to mechanical thromboprophylaxis

- Known or suspected arterial insufficiency

- Absent or weak foot pulses on palpation

- Peripheral or Sensory neuropathy

- Severe peripheral oedema

- New onset stroke

- Limb deformity preventing correct fit

- Local skin conditions e.g. ulcers, infection, recent skin graft, tissue paper skin, allergy to stocking material

Enoxaparin

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50 kg</td>
<td>20 mg daily</td>
</tr>
<tr>
<td>50 – 101 kg</td>
<td>40 mg daily</td>
</tr>
<tr>
<td>101 – 150 kg</td>
<td>40 mg twice</td>
</tr>
<tr>
<td>&gt; 150 kg</td>
<td>60 mg twice</td>
</tr>
</tbody>
</table>

Mechanical methods

- Anti-embolism stocking

- Intermittent pneumatic compression

- Foot impulse device

Prescribe pharmacological and mechanical thromboprophylaxis on the drug chart: YES

Clinician name: [Clinician name]

Clinician signature: [Clinician signature]

Bleep: [Bleep]