LRI Children's Hospital

Paediatric Acute Venous Thromboembolism and Anticoagulation in Paediatric Patients

Staff relevant to:	All nursing and medical staff working in the Children's Hospital
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Contents

1. Introduction and who this standard operating procedure (SOP) applies to

This guideline advises on the prevention, investigation and management of venous thromboembolism (VTE) in paediatric patients.

Venous thrombo – embolism (VTE) is increasingly recognised in paediatric practice. With advances in neonatal and paediatric critical care medicine thrombotic events have become increasingly recognised. Events are associated with a risk of mortality and significant morbidity which is increased if diagnosis is delayed, or appropriate treatment is not given. The commonest age groups for VTE are neonates and teenagers, and this reflects the pattern of associated underlying disease and interventions. The most common precipitating factor is the presence of a central venous device.

Although there remains limited direct evidence in children, there is very strong indirect evidence from adults that symptomatic VTE requires treatment. The current drugs used to anticoagulate paediatric patients consist of unfractionated heparin (UFH), Low Molecular Weight Heparin (LMWH), Warfarin and more recently the direct thrombin inhibitor Rivaroxaban has been licensed for use in paediatric patients. Thrombolysis should be considered in paediatric patients with submassive Pulmonary Embolism (PE) however in most cases the risk of thrombolysis often outweighs the benefit.

The use of Anti thrombin concentrate has increased in recent years in the management of VTE in children. The most used indication is to facilitate attainment of therapeutic heparin activity. There is little evidence of clinical benefit and perhaps evidence of clinical harm. It should therefore not be routinely used and should be discussed with a haematologist.

Related Documents:

Venous Thromboembolism (VTE) Prophylaxis in Children UHL Childrens Hospital Guideline

Stroke UHL Childrens Guideline

Thrombolysis Paediatric Intensive Care UHL Guideline

Warfarin Dosing Paediatric Cardiology UHL Guideline

2. Standards and Procedures

2.1 Prevention

Medical and surgical patients who are temporarily at an increased risk of thrombosis can be risk stratified to identify those at highest risk. All paediatric patients admitted to Leicester Children's Hospital should undergo a VTE risk assessment within 24 hours of admission and every 3 days thereafter. The guideline is based on the key recommendations of the APAGBI comprehensive guideline published in 2018.

Please see; Venous Thromboembolism (VTE) Prophylaxis in Children UHL Childrens Hospital Guideline **for separate guidance**

Young women taking the Combined Oral Contraceptive Pill (COCP) should be advised to stop taking the pill at least 4 weeks prior to elective surgery and to use an alternative form of contraception which does not contain oestrogens.

If a child (excluding cardiac patients) is already on anticoagulation and requires surgery, the management of their anticoagulation should be discussed with a consultant or SpR in Haematology. If non urgent email the haematology registrars via; haematologyreferralsmailbox@uhl-tr.nhs.uk. For cardiac patients this is managed by cardiology team.

Anticoagulation is sometimes required for children who have had cardiac surgery to prevent thrombosis. The decision to anticoagulate is based on the child's individual risk factors including the type of surgery undertaken and is made by the consultant cardiologist involved

2.2 Diagnosis of VTE

Since thrombotic events are rare in children a high index of suspicion in certain clinical scenarios is required. Accurate and prompt diagnosis is vital to allow early intervention if a thrombotic event is confirmed and to avoid unnecessary anticoagulation when an event can be excluded.

Clinical Presentation

Table 1(on the following page) includes the more common presenting features of a VTE at various sites. If a child presents with these features diagnostic imaging should be requested to investigate further.

Table 1

Clinical features (not all features may be present)	Additional suspicious features	Site of thrombus
CVL dysfunction, limb or facial swelling distal to CVL insertion site, new superficial collateral vein development adjacent to CVL insertion site	Recurrent CVL sepsis	CVL related DVT
Pain, swelling, redness of a limb	New superficial collateral vein development. On an Oestrogen containing oral contraceptive pill	Limb DVT
Abdominal pain +/- fever without other explanation		Mesenteric/portal vein
Unexplained hypoxia, sudden cardiovascular collapse, acute pleuritic chest pain, dyspnoea, haemoptysis	Presence of CVL Post cardiac surgery On an Oestrogen containing oral contraceptive pill	Pulmonary
Infant with haematuria, flank mass or thrombocytopenia		Renal vein
Swelling and cyanosis of head and upper thorax, prominent collateral veins		SVC
Patients with mechanical valve prostheses demonstrating any sort of circulatory or respiratory symptoms		Request specialist paediatric cardiology advice as? thrombus on prosthetic valve
Acute headache, visual impairment, seizures		Cerebral sinovenous thrombosis

Laboratory Investigations

D – dimer is used in adult patients as part of the investigation of VTE. This practise has not been validated in children and d-dimer should not generally be used

Diagnostic Imaging

- USS is recommended for the initial assessment of the peripheral upper limb, axillary, subclavian and internal jugular veins but may be relatively insensitive for the detection of central intra-thoracic VTE
- Contrast MRV or CT is recommended for assessing the central veins for VTE
- Doppler US is recommended to assess the LL venous system for VTE. If the US is normal and the clinical suspicion of VTE remains high this should be repeated after a week to assess for proximal progression of any calf vein thrombus.
- MRV should be considered in children with suspected proximal extension of femoral VTE
- PE – CTPA
- Intracardiac - Cardiac ECHO
- Cerebral sinovenous thrombosis – CT head (may require GA for small children. If not conclusive may require MRI with MRV

Management

Anticoagulation is to prevent death, thrombosis progression, embolization and to reduce the risk of post thrombotic syndrome. The decision to anticoagulate however, must weigh up the risks of the above against the risk of bleeding.

Duration of anticoagulation depends on the risk of recurrence which is largely determined by the presence of ongoing risk factors for VTE. Some situations will require lifelong anticoagulation such as recurrent idiopathic VTE, cardiac patients and children with antiphospholipid syndrome. The duration of anticoagulation of non – cardiac indication should be discussed with a haematologist. Duration rarely needs to exceed 3 months for a provoked event.

The choice of anticoagulant used will depend on the individual case see section 2 re types of anticoagulation, discuss with a haematologist if any doubt.

Thrombolysis for massive and sub massive thrombus should be the result of a multidisciplinary discussion and requires informed consent of the child's parents/carers. It requires expertise and careful monitoring of the patient, both clinically and using a combination of laboratory and radiology tests. **Do not** undertake thrombolysis if you have no previous experience of the use of thrombolytic drugs. This should be undertaken by a consultant only.

See Thrombolysis Paediatric Intensive Care UHL Guideline

Central Venous Device

Investigation of a blocked CVL; A chest X-Ray is recommended to visualize the CVL position. A contrast linogram is recommended to determine potential occlusion at the tip of the CVL and presence of retrograde flow.

Surveillance for asymptomatic VTE is not recommended.

Doppler USS, conventional venography or contrast enhanced MRV may be required to exclude large vessel thrombosis.

If the line is functioning it may be possible to retain the line and treat with anticoagulation especially if venous access is difficult. However, if symptoms fail to resolve after several days of anticoagulation or the line is non-functioning it should be removed, 3-5 days after anticoagulation due to the theoretical risk of potentially inducing a PE or paradoxical stroke

Adjuvant therapy

Post thrombotic syndrome (PTS) occurs in 10 – 20% of children who have a limb thrombosis. PTS refers to chronic insufficiency characterised by pain, swelling and discolouration of the limb which may occur years after the initial thrombosis. In severe cases skin ulceration can occur which is a very difficult to manage. In adults there is good evidence that wearing compression stockings for 2 years following the lower limb DVT significantly reduces the risk of post thrombotic syndrome.

In older children with lower limb DVT below knee fitted graduated elastic compression stockings should be prescribed. It is essential that they are fitted correctly to avoid skin irritation.

Thrombophilia Screening

Venous thromboembolic events in children are usually associated with underlying clinical conditions such as central venous lines, sepsis, cancer and cardiac diseases. Idiopathic events in children are rare.

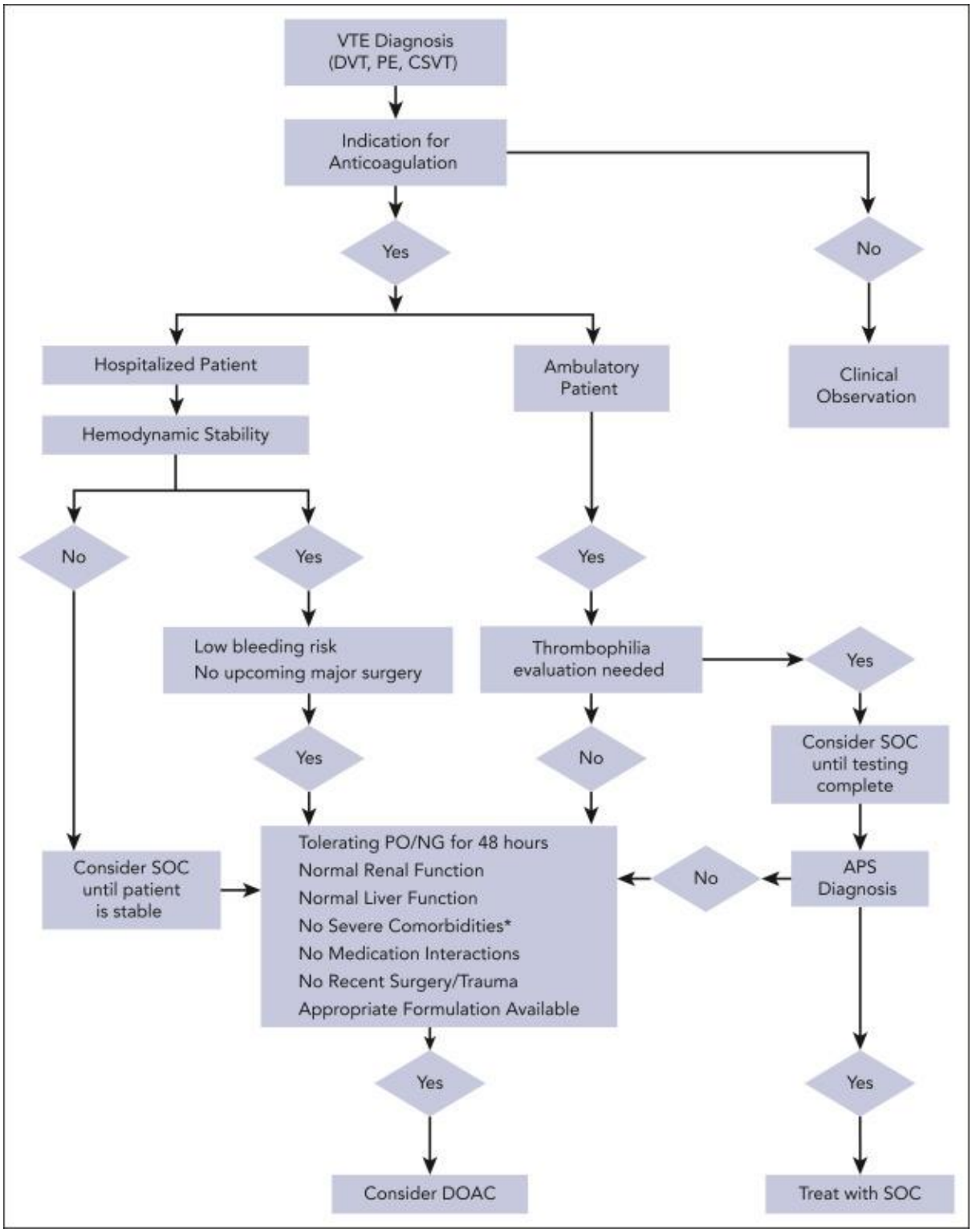
Several inherited conditions that can increase the risk of a thrombosis have been described. The well-established characterised and accepted inherited thrombophilia are deficiencies of antithrombotic, protein C and protein S, activated protein C resistance/factor V Leiden mutation and prothrombin G20210A mutation.

Given the low prevalence of thrombosis in childhood even if a child carries a mutation for one of these conditions in the absence of other risk factors, they are very unlikely to have a VTE. It is generally not helpful to screen asymptomatic children who have a family history of VTE even if a thrombophilia defect is found in a relative.

Testing of children for thrombophilia defects is discouraged since management is rarely affected by the knowledge of a defect. Homozygous protein C, protein S, antithrombin deficiency usually presents with severe clinical manifestations, such as purpura fulminans or idiopathic extensive large vessel thrombosis. Testing is justifiable in these limited situations as specific replacement therapy is indicated.

See below a helpful Algorithm for management of Paediatric VTE;

Algorithm for pediatric VTE Anticoagulation Management:



*indicates severe liver or renal dysfunction, short gut syndrome, severe thrombocytopenia, ICH, or postoperative or severe trauma. VTE, venous thromboembolism; SOC, standard of care; DOAC, direct oral anticoagulant; NG, nasogastric; PO, by mouth.

2.3 Unfractionated heparin in the treatment of thrombosis

Continuous infusion unfractionated heparin is used both as prophylaxis and treatment of thrombosis. It has a short half-life, and its anticoagulant effects can be rapidly reversed. It is therefore used in children who require anticoagulation but are at high risk of bleeding, or where multiple surgical interventions may be necessary. Such children for example will include post-operative cardiac and other PICU patients.

Usage of UFH is associated with bleeding, even at therapeutic levels of heparin; the response to UFH can be very variable, so that a wide range of dosages may be required to maintain therapeutic anticoagulation.

The laboratory monitoring of UFH can be difficult and is usually done using the APTT ratio or Heparin assay: the correlation between the two tests (and with plasma heparin levels) is not good. Several assessments have found that use of anti-Xa-based (Heparin assay) management results in more rapid attainment of target values with fewer rate adjustments as compared to the APTT.

APTT lacks sensitivity;

- Lupus anticoagulant or clotting factor deficiency may prolong APTT, this may falsely raise the APTT in the target range even if suboptimal heparin levels
- Coagulation factors and fibrinogen are frequently elevated due to acute phase response
- Similarly, acquired anti- thrombin deficiency in critically ill patients, sometimes contributes to a higher than expected dose of UFH
- Also, FVIII levels increase in an acute thrombotic event

All making APTT less sensitive to UFH and leading to the incorrect assumption that heparin levels are inadequate.

Occasionally situations occur in which the anti Xa (Heparin Assay) activity will not accurately reflect the amount of UFH effect present (See table below), in this situation both tests should be used and the clinical scenario individually assessed (and discussed with haematology if appropriate) to make the decision re dose changes.

Table 1: Situations impacting measured anti-Factor Xa or aPTT results

	Influencing Factors	anti-Factor Xa	aPTT
Preanalytic	Diurnal Variation	↕	↕
	High Citrate Conc. in Tube	↔	↑
	Poor Blood Sampling	↑	↑
	Underfilled Tubes	↔	↑
	Prolong time (> 2 hours) to sample analysis	↓	↓
	Inadequate centrifugation (inadequate platelet removal)	↓	↓
	Gross Hemolysis in Sample	↓	↔
Analytic	Reagent Issues	↕	↕
	Coagulometer	↕	↕
Biologic	AT Deficiency	↓*	↓
	Increase acute phase reactants (↑FVIII, ↑Fibrinogen)	↔	↓
	Increased Heparin binding proteins	↓	↓
	Obesity (↑ Vd)	↓	↓
	Impaired Renal Function (↓ Elimination)	↑	↑
	Liver Disease (↓ Clotting Factors)	↔	↑
	Consumptive coagulopathy	↔	↑
	Lupus Anticoagulant	↔	↑
	Decreased in specific clotting factors (Factor IX, XI, XII, prekallikrein)	↔	↑
	Elderly	↔	↑
	Recent use of other anti-Xa agents (LMWH, Fondaparinux, DOAC)	↑	↔
	Triglyceride > 360 mg/dl	↑	↔
	T Bili > 6.6 mg/dl	↓	↔
	COVID-19	↔	↑

Commencing UFH:

- Check base line full blood count, coagulation screen, serum urea and creatinine before starting heparin.
- Maintain platelet count >50 $x10^9$/l and fibrinogen >1g/l for full dose heparin to be given.
- If PT and/or APTT abnormal, or renal impairment, then discuss heparinisation with haematologist. Heparin undergoes renal clearance: impaired renal function will often necessitate reduced doses of heparin therapy.
- Use Heparin 1000units in 1ml preparation (available as 1ml, 5ml, 10ml or 20ml ampoules)
- **Loading dose:** 75units/kg over 10 minutes. **Omit loading dose** if perceived increased bleeding risk, central nervous system pathology, arterial ischaemic stroke or cerebral sinus vein thrombosis.
- Followed by **continuous infusion** ; <1yr age 25 units/kg/hr
  ; >1 yr age 20 units/kg/hr
- Adjust according to Heparin assay result

Monitoring on UFH

Obtain a venous blood sample in citrate tube for Heparin Assay level 3 - 4 hours after starting heparin. Heparin assay (anti Xa) is run in fast-track level 4 Sandringham. The sample should be walked to fast track not podded as this can activate the sample and give an inaccurate result.

Ideally this sample should be taken by venepuncture and not from a line or squeezed from a heel prick all of which can affect the integrity of the sample. However, if venepuncture is not possible and sample is taken from a line then; the line should not contain heparin and after a flush a good discard needs to be taken so not to dilute the sample. See Appendix 1 for advice.

Check FBC once daily or more frequently if clinically indicated.

See Appendix 2 for UFH monitoring chart (available from print room)

Heparin Assay Therapeutic range = 0.30 - 0.70 units/ml

Heparin Assay(units/ml)	Hold (minutes)	Dose Change	Repeat Heparin Assay
<0.20 Consider drug administration problem and check Heparin assay sample integrity – bolus 50 units/kg and increase by 20% **after consultant discussion**	No	Increase by 20%	4 hours after change
0.20-0.29	No	Increase by 10%	4 hours after change
0.30- 0.7	No	No change	Once daily
0.71-1.0	No	Decrease by 10%	4 hours after change
1.1-1.4	30mins	Decrease by 10%	4 hours after restarting
>1.4 Consider sample contamination **and discuss with consultant**	60 mins	Decrease by 20%	4 hours after restarting

Under or Over Anticoagulation

Discuss problems of persistent under- or over-coagulation with haematology consultant or registrar. The commonest causes of under anticoagulation are;

A sampling issue: It is essential that the sampling of the Heparin assay is done accurately as the result determines the amount of heparin the patient is on. If you are struggling to see an increase in the Heparin assay result despite increasing the units, please go to **Appendix 1** for advice.

Or "heparin resistance" may be due to physiological antithrombin deficiency as seen in neonates, which is often overcome by increasing the dose of Heparin or as a secondary event in children with protein losing conditions such as chylothorax or nephrotic syndrome and may require consideration of antithrombin supplementation.

Procedures

The infusion should be discontinued 6 hours pre – operatively and the heparin assay checked 2 hours prior to surgery to ensure the patient is no longer anti-coagulated.

The optimal time to recommence heparin post – surgery or an invasive procedure depends on the type of surgery, the bleeding risk and the underlying thrombotic risk.

Monitoring for HIT

Heparin induced thrombocytopenia (HIT) is rare but a serious adverse effect of heparin. The greatest risk period is between days 4 -14 of treatment. However, if the patient has been recently exposed to heparin HIT can occur much more rapidly. This includes exposure to heparin line flushes.

- If exposed to heparin within the previous 100 days
  Check FBC within 24 hours of starting the heparin, then on alternate days until day 14.
- If not exposed within the last 100 days
  Check FBC on alternate days from days 4 -14 of starting heparin

Reversal of UFH

If anticoagulation needs to be discontinued for clinical reasons, termination of heparin infusion will usually be sufficient because of the rapid clearance of heparin. If immediate reversal of heparin is required, consider protamine sulphate infusion.

Time from last dose of Heparin in minutes	Dose of Protamine mg
<30 minutes	1mg per 100 units of Heparin received
30 – 60 minutes	0.75 mg per 100 units of Heparin received
61 – 120 minutes	0.5mg per 100 units of Heparin received
>120 minutes	0.25 mg per 100 units of Heparin received

• Maximum dose of protamine sulphate is 50 mg (except for cardiopulmonary bypass).

2.3 Low Molecular Weight Heparin

Low Molecular Weight Heparins (LMWH) have become widely used in adult medicine and their use has increased greatly in paediatrics over the last 10-15 years. LMWHs are administered subcutaneously, have a relatively long half-life and in adults give reliable therapeutic results with standard doses without laboratory monitoring.

In children, there are variations in pharmacokinetics between individuals, often age-related, which have led to laboratory monitoring to achieve therapeutic anticoagulant levels being standard practice. Most children will need twice daily injections of LMWH because of shorter drug half-lives and increased clearance compared with the once daily injections given to adults.

In general, LMWH delivers more reliable anticoagulation than UFH but its long duration of action may also be a disadvantage if reversal of anticoagulation is required. In addition, there is no good reversal agent, though protamine sulphate can be given (as per BNFc for dose) and will reverse some of the anticoagulant effect. Patient selection is therefore important, with UFH being more appropriate for children at high risk of bleeding, who need to achieve therapeutic heparin levels rapidly or who require multiple procedures.

<u>Commencing treatment with LMWH:</u>

- Check base line full blood count, coagulation screen and renal function before starting LMWH, if abnormal discuss with a haematologist
- Abnormal renal function will require dosing adjustment or may be contraindicated
- Maintain platelet count >50 x10 9/L and fibrinogen >1g/l for full dose heparin to be given
- Dalteparin is the LMWH used in paediatrics and is administered subcutaneously
- Dose of Dalteparin :
    - Neonate 150 units/kg
    - Child < 2 years 150 units/kg twice daily
    - 2 - 7 yrs 125units/kg BD
    - 8 -18 yrs 100units/kg/ BD (consider over the age of 12yrs 200units/kg/OD depending on bleeding risk and clinical context)

<u>Monitoring of LMWH</u>

- Obtain a venous blood sample in citrate tube for Heparin Assay level 3 - 4 hours after starting heparin. Heparin assay (anti Xa) sample is run in fast-track level 4 Sandringham. The sample should be walked to fast track not podded in the shoot as this can activate the sample and give an inaccurate result.

- Ideally this sample should be taken by venepuncture and not from a line or squeezed from a heel prick all of which can affect the integrity of the sample. However, if venepuncture is not possible and sample is taken from a line then; the line should not contain heparin and after a flush a good discard needs to be taken so not to dilute the sample. See Appendix for advice.

- **When to repeat levels**:

- If a dose change is made, then the Heparin assay (anti Xa) must be checked no sooner than after the 3rd dose post the dose change
- In unstable in patients' (PICU/CICU) level should be taken weekly once in range
- In stable ward patients the level can be less frequent i.e. 2-3 weekly once in range
- On discharge a level should be taken every 4 –6 week
- Levels are recommended in children <16 yrs, Crcl <30ml/min

NB: if transitioning from UFH to LMWH the UFH infusion should be stopped at least 4 hours prior to commencement of LMWH.

For UHL **BD dosing**: Therapeutic range 0.4 – 1.0

Heparin Assay (units/ml)	Hold next dose	Dose change	Repeat Heparin Assay
<0.30 consider drug administration problem and check Heparin assay sample integrity	No	Increase by 25%	3-4 hours after 3rd dose since dose change
0.30-0.39	No	Increase by 10%	3 –4 hours after 3rd dose since dose change
0.4 – 1.0	No	No change	Weekly if unstable pt on PICU/CICU, every 2-3 weeks on ward and on discharge every 4-6 weeks
1.1 – 1.5	Omit next dose	Decrease by 20%	3-4 hours after 3rd dose since dose change
1.6 – 2.0	Omit next 2 doses	Decrease by 30%	3-4 hours after 3rd dose since dose change
>2.0 consider contamination with Heparin	Until Heparin assay <0.4	Decrease by 40%	3-4 hours after 3rd dose since dose change

For UHL **OD dosing**: Therapeutic range 0.6 – 1.2

Heparin Assay (units/ml)	Hold next dose	Dose change	Repeat Heparin Assay
<0.35 consider drug administration problem and check Heparin assay sample integrity	No	Increase by 25%	3 –4 hours after 3rd dose since dose change
0.36-0.59	No	Increase by 10%	3 –4 hours after 3rd dose since dose change
0.6 – 1.2	No	No change	Weekly if unstable pt on PICU/CICU, every 2-3 weeks on ward and on discharge every 4-6 weeks
1.3 – 1.5	Omit next dose	Decrease by 10%	after 3rd dose since dose change
1.6 – 2.0	Omit next 2 doses	Decrease by 20%	3 –4 hours after 3rd dose since dose change
>2.0 consider contamination with Heparin	Until Heparin assay <0.60	Decrease by 40%	3 –4 hours after 3rd dose since dose change

See Appendix 3 for LMWH monitoring charts (available from print room)

Under or Over Anticoagulation

Discuss problems of persistent under- or over-coagulation with haematology consultant or registrar. The commonest causes of under anticoagulation are;

A sampling issue: It is essential that the sampling of the Heparin assay is done accurately as the result determines the amount of heparin the patient is on. If you are struggling to see an increase in the Heparin assay result despite increasing the units, please go to **Appendix 1** for advice.

Or "heparin resistance" may be due to physiological antithrombin deficiency as seen in neonates, which is often overcome by increasing the dose of Heparin or as a secondary event in children with protein losing conditions such as chylothorax and nephrotic syndrome and may require consideration of antithrombin supplementation.

Procedures

If surgery is required for a patient receiving LMWH, it is recommended that 2 doses of heparin are omitted prior to surgery, i.e. the morning dose is given on the day before surgery.

Generally, LMWH should not be restarted until at least 8-12 hours post op. Epidural catheters should be removed at least 4 hours prior to a LMWH dose.

For children on prophylactic LMWH, doses should be avoided for 12 hours prior to surgery and Invasive procedure including lumbar puncture and epidurals.

Monitoring for HIT

Heparin induced thrombocytopenia (HIT) is rare but a serious adverse effect of heparin. The greatest risk period is between days 4 -14 of treatment. However, if the patient has been recently exposed to heparin HIT can occur much more rapidly. This includes exposure to heparin line flushes.

- If exposure to heparin within the previous 100 days
  Check FBC within 24 hours of starting heparin
- If not exposed within last 100 days
  Routine monitoring not required.

Reversal of LMWH

Reversal of LMWH is difficult. The half-life is longer than UFH. The only antidote is protamine, but it does not completely reverse the effect of LMWH. Plans for reversal are best discussed with a haematologist.

The dose required depends on the amount of LMWH administered and the time elapsed since last dose.

Suggested doses:

- If protamine is given within 8hours of LMWH, give 1mg protamine/mg of LMWH given in last dose.
- If protamine given > 8 hours of LMWH, give 0.5mg protamine/mg of LMWH given in last dose. Do not use same regimen as for UFH.

Outpatients on LMWH

For children who need to continue LMWH anticoagulation on discharge it is essential that parents are given detailed information including practicalities of administration, bleeding risk and planned length of duration.

Arrangements must be made for the continued supplies of heparin from a hospital or from the GP as well as any further monitoring required. The discharge plan must include the intended length of time of anticoagulation. For more complex cases and where duration cannot yet be decided please refer to paediatric haemostasis clinic via the haemophilia centre mailbox.

2.4 Warfarin

Warfarin is an effective, oral anticoagulant which works through interference with the carboxylation of vitamin K dependent clotting factors. Therapeutic monitoring of warfarin is carried out using the INR (Internationalised Normalised Ratio): a commonly used therapeutic range is 2-3, with higher ranges used in specific circumstances, e.g. mechanical mitral valve replacement.

Most patients requiring Warfarin will be cardiac and are referred to the cardiology anticoagulation team for monitoring and dosing via the cardiology team pathways. Please refer to Warfarin Dosing Paediatric Cardiology UHL Guideline

For adolescent and adult females of childbearing age with mechanical valves please refer to the Warfarin Dosing Paediatric Cardiology UHL Guideline

If the patient requiring Warfarin is non cardiac, please follow this guidance and refer to paediatric thrombosis via the haemophilia centre mailbox with; patient's details and contact numbers, indication for warfarin and the team/consultant who made the decision re initiation, the INR range and plan for blood tests i.e. if they have a home device or day case and duration of treatment.

Initiation

- Obtain a baseline LFT and Coagulation screen prior to commencing Warfarin therapy
- Consider drugs and feeding regimens which may interfere with anticoagulant effect or control e.g. concurrent medication (regular and intermittent), TPN, oral types of feeds etc. If the child is on drugs which potentiate warfarin the loading dose may need adjusting
- The loading period is approximately 3 – 5 days for most patients before a stable maintenance phase is achieved
- Commence Warfarin on day 1 or 2 of heparin therapy or as soon as able to take oral medication, heparin should be continued for at least 5 days if new diagnosis of thrombosis. If thrombosis is extensive it may need to be longer
- When INR has been >2 for 2 consecutive days then the Heparin can be stopped

Warfarin should be prescribed on a separate sheet; 'Paediatric Warfarin prescription sheet' Appendix 4

Measure INR Day 2 – 6		
If your response is an INR of		
INR	1.1-1.4	Repeat loading dose
INR	1.4-1.9	50% of loading dose
INR	2.0-3.0	50% of loading dose
INR	3.0-4.0	25% of loading dose
INR	>4.5	Omit dose until INR less than 4.5 then restart at 50% less than previous dose.
If INR not greater than 1.5 on day 4 contact consultant haematologist for help.		

Long term control – day 6 onward		
INR	1.1-1.4	Increase by 20% of dose
INR	1.4-1.9	Increase by 10% of dose
INR	2.0-3.0	No change
INR	3.1-4.0	Decrease by 10% dose
INR	4.1-4.5	Decrease by 20% dose
INR	>4.5	Hold dose, check INR daily until INR <4.5 then restart at 20% less than previous dose.

Reversal of Warfarin therapy:

There are situations when the anticoagulant effect of warfarin needs reversal. The INR may fluctuate due to changes in medication, diet, clinical status or compliance and over anti-coagulation may result.

A child on warfarin may develop bleeding even with a therapeutic INR. Warfarin reversal may be necessary prior to surgery or another clinical intervention.

The urgency of reversal is dependent on the clinical situation and the prolongation of the INR;

If the patient is a cardiology patient i.e. a mechanical heart valve, then the patient must be discussed with cardiology consultant before any warfarin reversal. **If warfarin is inappropriately reversed it can be very difficult to get these patients back in range.**

Please refer to Warfarin Dosing Paediatric Cardiology UHL Guideline C197/2016

- All other anticoagulated/bleeding patients on warfarin should be discussed with a haematologist, as should those patients on warfarin requiring a surgical intervention. Vitamin K may be indicated, but not always.

Emergency Reversal Of Warfarin in a bleeding patient:

- Fresh Frozen Plasma/Octaplex is relatively ineffective in the urgent, temporary reversal of Warfarin.
- Prothrombin Complex Concentrate (Beriplex) is the treatment of choice and should always be prescribed after discussion with a Haematologist.
  Recommended dose: 15-50 units/kg depending on the INR and clinical situation.

2.5 Rivaroxaban

Is a direct oral anticoagulant used in the 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.

Initiation of Rivaroxaban;

- Check baseline clotting, renal and liver function
- **Initiate after at least 5 days of parenteral anticoagulation**
- **Conversion: start 0-2 hrs before the next dose of LMWH or at the time of discontinuing continuous UFH**
- **Rivaroxaban should be taken with food**
- **Check drug interactions**
- For patients with body weight of at least 2.6 kg - 30 kg only the oral suspension should be used
- Do not split Rivaroxaban tablets or use Rivaroxaban tablets of lower strength to provide doses for children with body weight below 30 kg
- For patients with body weight of at least 30 kg, Rivaroxaban oral suspension or tablets of 15mg or 20 mg strength can be administered once a day.

Recommended dose for Rivaroxaban in paediatric patients from full-term neonates (following at least 10 days of oral feeding and weighing at least 2.6 kg) to children less than 18 years of age:

Weight Dose (1 mg Rivaroxaban = 1 ml of suspension) as per BNFc

- Dosing as per BNFc
- Rivaroxaban is not recommended in patients receiving concomitant systemic treatment with azoleantimycotics (such as ketoconazole, itraconazole, voriconazole and posaconazole) or HIV protease inhibitors (e.g.ritonavir)
- These active substances are strong inhibitors of both CYP3A4 and P-gp and therefore may increase rivaroxaban plasma concentrations to a clinically relevant degree (2.6 fold on average) which may lead to an increased bleeding risk

- Other haemorrhagic risk factors, as with other antithrombotics, rivaroxaban is not recommended in patients with an increased bleeding risk such as:

  • congenital or acquired bleeding disorders
  • uncontrolled arterial hypertension
  • vascular retinopathy
  • bronchiectasis or history of pulmonary bleeding
  • coagulopathy and liver disease

- Rivaroxaban is not licenced in patients with prosthetic heart valves.

Rivaroxaban is not recommended in children 1 year or older with moderate or severe renal impairment (glomerular filtration rate < 50 mL/min/1.73m2), as no clinical data is available.

Rivaroxaban is not recommended in children younger than 1 year with serum creatinine results above 97.5th percentile, as no clinical data are available. Please see so that percentile can be estimated; Xarelto 1 mg/mL granules for oral suspension - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

Dosing recommendations before and after invasive procedures and surgical intervention

If an invasive procedure or surgical intervention is required, Rivaroxaban should be, if possible, stopped at least 24 - 48 hours before the intervention depending on the bleeding risk and clinical judgement of the physician. If the procedure cannot be delayed the increased risk of bleeding should be assessed against the urgency of the intervention. If a bridging plan is required contact the haematology mailbox or discuss with Haematology Specialist registrar on call.

Rivaroxaban should be restarted as soon as possible after the invasive procedure or surgical intervention provided the clinical situation allows and adequate haemostasis has been established as determined by the treating physician.

Effect of Rivaroxaban on blood tests and monitoring

- Regular monitoring is NOT required whilst on rivaroxaban
- Weight should be monitored regularly, and dose adjusted accordingly
- If required Rivaroxaban levels can be done (sample sent to special haematology – call first with patient details and reason for testing)
- If there are concerns about bleeding, please monitor FBC and clinically.

Rivaroxaban can prolong PT, aPTT and INR, especially if these tests are done 1-3 hours after dose. BUT the results have no correlation to rivaroxaban levels and should NOT be used for monitoring.

Reversal of anticoagulation in case of an emergency:

Rivaroxaban is a highly selective direct inhibitor of factor Xa. It has no direct inhibitory activity against thrombin or platelets. Rivaroxaban has a half-life of 5 to 13 hours (depending on age and may be prolonged in severe renal insufficiency).

There is currently NO REVERSAL agent for rivaroxaban – See Appendix 5

Management of bleeding – for flow sheet see Appendix 5

Should a bleeding complication arise in a patient receiving rivaroxaban, the next rivaroxaban administration should be delayed, or treatment should be discontinued as appropriate. Rivaroxaban has a half-life of approximately 5 to 13 hours in adults. The half-life in children estimated using population pharmacokinetic (popPK) modelling approaches is shorter.

Management should be individualised according to the severity and location of the haemorrhage. Appropriate symptomatic treatment could be used as needed, such as mechanical compression (e.g. for severe epistaxis), surgical haemostasis with bleeding control procedures, fluid replacement and haemodynamic support, blood products (packed red cells or fresh frozen plasma, depending on associated anaemia or coagulopathy) or platelets.

If bleeding cannot be controlled by the above measures, administration of a specific procoagulant reversal agent should be considered, such as **prothrombin complex concentrate (PCC), activated prothrombin complex concentrate (APCC) or recombinant factor VIIa (r-FVIIa).** This should be discussed with Haematology specialist registrar on call.

Protamine sulphate and vitamin K are **not expected** to affect the anticoagulant activity of rivaroxaban. There is limited experience with tranexamic acid and no experience with aminocaproic acid and aprotinin in adults receiving rivaroxaban. There is no experience on the use of these agents in children receiving rivaroxaban. There is neither scientific rationale for benefit nor experience with the use of the systemic haemostatic desmopressin in individuals receiving rivaroxaban.

Missed doses

Once a day regimen: a missed dose should be taken as soon as possible after it is noticed, but only on the same day. If this is not possible, the patient should skip the dose and continue with the next dose as prescribed. The patient should not take two doses to make up for a missed dose.

Two times a day regimen: a missed morning dose should be taken immediately when it is noticed, and it may be taken together with the evening dose. A missed evening dose can only be taken during the same evening, the patient should not take two doses the next morning.

Three times a day regimen: the three times daily administration schedule with approximately 8-hour intervals should simply be resumed at the next scheduled dose without compensating for the missed dose.

Converting from Rivaroxaban to Vitamin K antagonists (VKA):

There is a potential for inadequate anticoagulation during the transition from Rivaroxaban to VKA. Continuous adequate anticoagulation should be ensured during any transition to an alternate anticoagulant. It should be noted that Rivaroxaban can contribute to an elevated INR. Children who convert from Rivaroxaban to VKA need to continue Rivaroxaban for 48 hours after the first dose of VKA. After 2 days of co-administration an INR should be obtained prior to the next scheduled dose of Rivaroxaban. Co-administration of Rivaroxaban and VKA is advised to continue until the INR is ≥ 2.0. Once Rivaroxaban is discontinued INR testing may be done reliably 24 hours after the last dose.

2.6 Paediatric VTE and Malignancy

The aetiology of VTE in children with cancer is multifactorial and includes genetic predisposition (thrombophilia), disease-related factors; activation of coagulation, reduced fibrinolysis, secretion of cytokines and clotting factors by cancerous cells, tumours with mass effect impairing blood flow, renal tumours with vascular invasion and treatment-related factors including use of CVC, surgery, and chemotherapy.

CVL-related thrombosis

The decision to anticoagulate a child with a CVL-related thrombosis is influenced by the presence of symptoms, the risk of progression or embolisation and the desire to reduce the risk of post-thrombotic syndrome. If the CVL is still required, in a good position and functioning, current evidence does not favour removal if anticoagulation is given.

If the line is to be removed, it is advised to give 2–5 days of anticoagulation. Whilst this approach lacks evidence, it may avoid delays in initial anticoagulation.

Once removed, the optimal duration of anticoagulation is not defined, although it has been suggested that children with uncomplicated events and rapid resolution of thrombosis following CVL removal could be managed with a shorter course 6 weeks (as per KIDS DOTT (does exclude children with cancer).

Anticoagulation according to standard VTE protocols is recommended for cerebral venous thrombosis (CVT) in children with cancer and should be given for a minimum of 3 months. Anticoagulation is not contraindicated in the presence of intracranial haemorrhage (ICH) unless the risk of further bleeding is considered to outweigh the potential benefits of treatment

Children with VTE unrelated to CVLs should receive anticoagulation for an initial period of 3 month. Continuation of treatment beyond 3 months should be considered in patients with active cancer or other ongoing risk factors.

Incidental VTE

Children with cancer who are found to have incidental VTE should be considered for systemic anticoagulation as per protocols for symptomatic disease. However, if the thrombosis is solely CVL-related, then it is reasonable to withhold anticoagulation initially and monitor the patient. If anticoagulation is not initially given, incidental VTE should be monitored, and anticoagulation commenced if there is extension of the thrombosis, or the child becomes symptomatic.

LMWH is the anticoagulant of choice for VTE in children with malignancy.

Procedures

Children with normal renal function on LMWH, the last therapeutic dose should be given 24 hours prior to an invasive procedure and last prophylactic dose 12 hours prior.

LMWH should be restarted no sooner than 4-6 hours after a procedure

For children on warfarin, last dose should be given 4-5 days prior to an invasive procedure. Bridging anticoagulation with LMWH when INR becomes sub therapeutic will be required for individuals within 1 month of a VTE. This should be considered for up to 3 months is those judged to be high risk of recurrence.

Anticoagulation and Thrombocytopenia & Coagulopathy

Therapeutic anticoagulation may be continued while the platelet count is >50

If <50 in an individual with a life-threatening or recent thrombosis (within 1 month or 3 months in individuals with high risk of recurrence) should be managed with platelet transfusion support, to maintain platelet count >50 and continuation of therapeutic anticoagulation.

Or consider reducing the dose to 50% when plt count is between 25 – 50 and temporarily interrupting anticoagulation when <25.

Correct coagulopathies and maintain fibrinogen level >1g/l in children on anticoagulation.

Investigations: Coagulation screen

FBC, blood film and PT, APTT and fibrinogen should be performed on all patients with suspected malignancy – if abnormal additional tests and management should be discussed with a haematologist

If Fibrinogen is <1 g/l, fibrinogen replacement should be administered for surgical procedures and in those with bleeding complications/at risk of haemorrhage

Consider the use of topical and/or systemic tranexamic acid in patients who are bleeding as per BNFc

Factor VIII and Von Willebrand factor antigen and activity assays should be performed on all patients with an abdominal mass suspicious for Wilms tumour

In patients at high risk of vaginal bleeding due to severe thrombocytopenia, progestogens (Medroxyprogesterone) should be considered for initial management suppression dose as per BNFc.

Paediatric Acute Lymphblastic Leukaemia (ALL) and Thrombosis – as per current trial; ALLTogether 1

Venous thromboembolism (VTE) is a common and impactful complication for patients with acute lymphoblastic leukaemia (ALL).

Management

For patients with symptomatic or asymptomatic radiologically confirmed VTE, LMWH at therapeutic doses is recommended for a minimum of 3 to 6 months (6 weeks for asymptomatic CVL-related DVT) AND continue throughout asparaginase (and erwinase) treatment (including 3 weeks after the last dose). Beyond this point, decisions regarding ongoing anticoagulation should be individualised according to risk of recurrent VTE, risk of bleeding & the presence or absence of remission.

For patients with acute VTE at high concurrent bleeding risk (e.g. CVT with intracerebral bleeding) an unfractionated heparin infusion may initially be an option due to shorter half-life than LMWH and reversibility with protamine if needed. Reduced dose LMWH is an acceptable alternative. For these patients at very high risk of bleeding and thrombosis, suggest checking and maintaining fibrinogen >1.5 g/L in the acute phase.

Heparin assay level should be done frequently at LMWH initiation and at least once per week during asparaginase (or Erwinase) containing parts of the protocol including 3 weeks after each dose. For patients with a stable anti-Xa level not receiving asparaginase, once per month monitoring is reasonable.

If renal function is normal, therapeutic dose LMWH should be omitted 24h before invasive procedures including lumbar punctures and recommenced 6h after.

VTE post Asparaginase and Erwinase

For patients with a clinically significant VTE (such as CVT, PE or proximal DVT), we would recommend withholding PEGylated asparaginase (and Erwinase) for at least 4 weeks after the VTE event as the risk of VTE related death and recurrence are particularly high in this time frame and likely to outweigh the benefits of asparaginase. Beyond that point, in patients who have clinically improved, re-exposure to asparaginase can be considered safe and feasible with therapeutic or intermediate dose anticoagulant continuation (for at least 2-3 weeks after each asparaginase). In patients with CVT, repeat neurological imaging may be helpful prior to re-exposure to asparaginase to confirm stabilisation or improvement of the thrombosis.

Routine clotting screens should not be performed prior to surgical procedures (or lumbar punctures) in patients with ALL in the immediate post-asparaginase period

VTE Prevention

Results if randomised trials do not justify a clear recommendation to perform a thromboprophylaxis either with LMWH subcutaneously or per ATIII substitution in all patients. It remains a clinical decision for the single patients with specific risk factors to evaluate the need of thromboprophylaxis based on an individual basis. As per paediatric VTE prophylaxis guideline and assessment.

3. Education and Training

None

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Review management of patients treated for VTE against guideline	Audit of patient notes	L Saunders	Annual	Children's Audit Meeting

5. Supporting References

1. BSH; Investigation, Management and Prevention of Venous Thrombosis in Children (b-s-h.org.uk)
2. Sheffield Childrens Hospital Guideline; Haemostasis-and-Thrombosis-Guidelines-for-Shared-Care-Centres-and-Community-Staff-for-M3-Patients.pdf
3. Birmingham childrens Hospital Guideline; Anticoagulation-protocol-March-2020.pdf (bwc.nhs.uk)
4. Guide to transitioning from the aPTT to anti-Xa assay to manage heparin infusions; **from The Anticoagulation Forum 1524-2020-04-29-101004.pdf (acforum-excellence.org)**

6. Key Words

Venous Thromboembolism, VTE, VTE prevention, VTE diagnosis, VTE management, VTE paediatric malignancy, Unfractionated Heparin, Low molecular weight heparin, Warfarin, Rivaroxaban, Children,

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The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

Contact and review details	
SOP Lead (Name and Title) L Sanders J Vujcikova S Wheeler	**Executive Lead** Chief Medical Officer
Details of Changes made during review: New document	

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Appendix 1: Guidance on Heparin Assay Testing using the Monovette system

- Ideally sample should be taken via venepuncture if the sample is taken from squeezing via heel or finger prick then this will activate the clotting system and give an inaccurate result

- A good 'flow' of blood is required for an accurate result

- If take via a central catheter there is a risk of heparin contamination or dilution of the sample post a flush if not enough blood is discarded

- The most accurate way of getting a 'good flow' of venous blood is using the monovette system

The Monovette System

Please use the Monovette system equipment for taking venous heparin samples on paediatric patients.

Prepare the baby/child for the venous sample.

Locate a patent vein

Apply the tourniquet

Use the monovette system to obtain the blood sample. Once you have successfully got a flashback of blood, ensure that you remove the end and allow the blood to flow down the tube and then re attach the end.

Once the end is re attached, connect the Citrate bottle to the blood adapter and obtain the sample, making sure that the bottle is filled up to the line.

The bottle must be filled to the line otherwise it cannot be tested. Also the sample should be hand delivered to the fast track lab for testing.

Appendix 2: Paediatric Therapeutic Unfractionated Heparin Monitoring Chart

PAEDIATRIC THERAPEUTIC UNFRACTIONATED HEPARIN MONITORING
(Based on Heparin Assay & Dose Adjustment)

To be used for patients on THERAPEUTIC doses of Unfractionated Heparin titrated according to Heparin assay (units/ml)
For ALL patients, heparin must be prescribed on the continuous infusion section of the drug chart.
For patients on CVVH & ECMO please continue to use respective existing paperwork.

Patient Name DOB			
S number		**Weight (kg)**	
Heparin indication			
Heparin assay target			
Length of treatment			

Prescription – please prescribe on drug chart – under dose section state "refer to Heparin Chart". To make up Heparin infusion:
Add 500 units/kg of Heparin up to 50 mls Sodium Chloride 0.9% 10 units/kg/h = 1ml/h
Loading dose 75 units/kg over 10 min,
Initial maintenance dose children < 1 year 25 units/kg/h
children > 1 year 20 units/kg/h; > 50kg 1000units/h

Heparin assay (units/ml)	Infusion change	Next Heparin level after
< 0.2	Consider drug administration problem and check Heparin assay sample integrity - Bolus 50 units/kg & increase by 20% **after consultant discussion**	4 hours (notify consultant for 2 consecutive Heparin levels < 0.3)
0.20 - 0.29	Increase by 10%	4 hours (notify consultant for 2 consecutive Heparin levels < 0.3)
0.30 - 0.70	**No change**	**4 hours ; after 2 consecutive heparin levels in range re-check every 24 hours**
0.71 – 1.0	Decrease by 10%	4 hours
1.1 - 1.40	Hold 30 min, decrease by 10%	4 hours
> 1.40	Hold 60 min, decrease by 20%	Repeat after 60 min hold + 4 hours
	- consider sample contamination (don't sample from the line used for Heparin infusion) - check if a sample is properly timed (3- 4h since recent bolus or rate change) - if no contamination risk, and correct timing, hold heparin infusion for 60 min and repeat Heparin level using peripheral blood draw; resume heparin infusion decreased by 20%	

PAEDIATRIC THERAPEUTIC UNFRACTIONATED HEPARIN MONITORING
(Based on Heparin Assay & Dose Adjustment)

Addressograph

MONITORING: "Heparin Assay" sample *must be filled to the line (green top bottle with citrate) * & *hand-delivered* (not podded) to a lab technician on Level 4 of Sandringham building within 2 hours of sampling, *Call 16525 before sending.*
Write UFH on form
Baseline Ix – FBC, APTT, PT; Maintain Plt > 50 x10^9/l and fibrinogen > 1g/l
Daily FBC; Alternate day potassium; Check "Heparin Assay" 3-4 hrs after each change in dose
Longer term - Check Plt weekly for the first month, if an abrupt drop of platelet count (around 50%) consider Heparin Induced Thrombocytopenia (HIT) **& discuss with Haematologists.**
PROPHYLAXIS with Heparin 10units/kg/h does NOT require regular monitoring of Heparin assay

Heparin assay record						Continuous infusion prescription							Additional bolus prescription			
Sample taken		Heparin assay	Dose change	Next sample		Date time	Infusion rate		Prescriber	Infusion check		Infusion holds, other (Plt, K levels)	Dose	Prescriber	Admin	
date	time	(units/ml)	Y/N	date	time		Units/kg/h	= mls/h		Sig 1	Sig 2				Sig1	Sig2

Appendix 3: Paediatric Therapeutic Low Molecular Weight Heparin (LMWH) Monitoring Charts

PAEDIATRIC THERAPEUTIC LOW MOLECULAR WEIGHT HEPARIN (LMWH) MONITORING
Dose Adjustment Chart

To be used for patients on THERAPEUTIC doses of LMWH on BD Dosing regimen titrated according to Heparin assay (units/ml)
For ALL patients, LMWH must be prescribed in the drug chart; usual choice is DALTEPARIN
LMWH needs to be stopped prior surgery, spinal, epidural procedure - placement or removal of epidural catheter

Patient Name			
Ward		**Weight (kg)**	
LMWH indication			
Heparin assay target			
Length of treatment			

Prescription – please prescribe on drug chart – under dose section state 'refer to LMWH Chart', Heparin assay to be taken 3-4 hours post dose
DALTEPARIN dose: subcutaneous administration (SC)
< 8 weeks and/or < 5kg 150 units/kg twice a day
> 8 weeks and > 5kg – 12 years 100 units/kg twice a day
over 12 years 200 units/kg ONCE a day
> 40kg consider adult dosing (max 18 000 units per dose)

Heparin assay	Hold Next Dose	Dose Change	Repeat Heparin assay
< 0.30 (units/ml) consider drug administration problem and check Heparin assay sample integrity	**No**	**Increase by 25%**	**3-4 hours post next morning dose (consider drug administration problem)**
0.30 – 0.39	**No**	**Increase by 10%**	**3-4 hours post next morning dose**
0.4-1.0	**No**	**No change Therapeutic**	**Weekly if stable – 3 - 4 hours post morning dose;**
1.1 – 1.5	**Omit next dose**	**Decrease by 20%**	**3-4 hours post next morning dose**
1.6 – 2.0	**Omit next 2 doses**	**Decrease by 30%**	**3 -4 hours post next morning dose**
> 2.0 consider sample contamination with heparin	**Until Heparin assay < 0.4**	**Decrease by 40%**	**Trough level pre-next dose & if not <0.4 repeat twice a day (consider sample contamination with UFH from line)**

PAEDIATRIC THERAPEUTIC LOW MOLECULAR WEIGHT HEPARIN (LMWH) MONITORING
Dose Adjustment Chart

PROPHYLAXIS with LMWH Neonates – 12 years 100units/kg ONCE a day sc;
12 – 18 years 2500 – 5000 units ONCE a day sc (Heparin assay range 0.1-0.3 units/ml)

MONITORING: Heparin assay sample ***should be filled to the line (green top bottle with citrate)**
***walked (not podded) to a lab within 2 hours to fast track on level 4 Sandringham building**
***handed over to staff stating what it is. The sample will not be processed if more than 2 hours. Call 16525 before sending.**
Baseline FBC, APTT, PT, renal function (**AVOID LMWH in renal failure**, if Cr clearance < 30ml/min/1.73m^2 the use of UHF is preferred); if previous exposure to heparin, repeat FBC once at 24hours (watching for drop in platelets, however HIT is very rare)
Check Heparin assay 3-4 hrs after the next morning dose when a dose was altered;
Avoid administration LMWH if Plt > 50 x10^9/l and fibrinogen > 1g/l

Heparin assay record						ADMINISTRATION LMWH (Dalteparin)						
Sample taken		Heparin assay	Dose change	Next sample		Date time	Dose (units)		Prescriber	dose check		Dose holds, other (Plt, K levels)
date	Time (13-14:00)	(units/ml)	Y/N	date	time		(10:00)	(22:00)		Sig1	Sig2	

PAEDIATRIC THERAPEUTIC LOW MOLECULAR WEIGHT HEPARIN (LMWH) MONITORING
Dose Adjustment Chart

To be used for patients on THERAPEUTIC doses of LMWH on OD Dosing regimen titrated according to Heparin assay (units/ml)
For ALL patients, LMWH must be prescribed in the drug chart; usual choice is DALTEPARIN
LMWH needs to be stopped prior surgery, spinal, epidural procedure - placement or removal of epidural catheter

Patient Name			
Ward		**Weight (kg)**	
LMWH indication			
Heparin assay target			
Length of treatment			

Prescription – please prescribe on drug chart – under dose section state 'refer to LMWH Chart', Heparin assay to be taken 3-4 hours post dose
DALTEPARIN dose: subcutaneous administration (SC)
< 8 weeks and/or < 5kg 150 units/kg twice a day
> 8 weeks and > 5kg – 12 years 100 units/kg twice a day
over 12 years 200 units/kg ONCE a day
> 40kg consider adult dosing (max 18 000 units per dose)

Heparin assay	Hold Next Dose	Dose Change	Repeat Heparin assay
< 0.35 (units/ml) check Heparin assay sample integrity	**No**	**Increase by 25%**	**3-4 hours post next morning dose (consider drug administration problem)**
0.36 – 0.59	**No**	**Increase by 10%**	**3-4 hours post next morning dose**
0.60-1.20	**No**	**No change Therapeutic**	**Weekly if stable – 3 - 4 hours post morning dose;**
1.3 – 1.5	**Omit next dose**	**Decrease by 10%**	**3-4 hours post next morning dose**
1.6 – 2.0	**Omit next 2 doses**	**Decrease by 20%**	**3 -4 hours post next morning dose**
> 2.0 consider Heparin contamination	**Until Heparin assay < 0.4**	**Decrease by 40%**	**Trough level pre-next dose & if not <0.4 repeat twice a day (consider sample contamination with UFH from line)**

PAEDIATRIC THERAPEUTIC LOW MOLECULAR WEIGHT HEPARIN (LMWH) MONITORING
Dose Adjustment Chart

PROPHYLAXIS with LMWH Neonates – 12 years 100units/kg ONCE a day sc;
12 – 18 years 2500 – 5000 units ONCE a day sc (Heparin assay range 0.1-0.3 units/ml)

MONITORING: Heparin assay sample ***should be filled to the line (green top bottle with citrate)**
***walked (not podded) to a lab within 2 hours to fast track on level 4 Sandringham building**
***handed over to staff stating what it is. The sample will not be processed if more than 2 hours. Call 16525 before sending.**
Baseline FBC, APTT, PT, renal function (**AVOID LMWH in renal failure**, if Cr clearance < 30ml/min/1.73m^2 the use of UHF is preferred); if previous exposure to heparin, repeat FBC once at 24hours (watching for drop in platelets, however HIT is very rare)
Check Heparin assay 3-4 hrs after the next morning dose when a dose was altered;
Avoid administration LMWH if Plt > 50 x10^9/l and fibrinogen > 1g/l

Heparin assay record						ADMINISTRATION LMWH (Dalteparin)						
Sample taken		Heparin assay	Dose change	Next sample		Date time	Dose (units)		Prescriber	dose check		Dose holds, other (Plt, K levels)
date	Time (13-14:00)	(units/ml)	Y/N	date	time		(10:00)	(22:00)		Sig1	Sig2	

Appendix 4: Paediatric Warfarin Prescription Chart

Paediatric Warfarin Prescription Chart

Patient's addressograph

Hospital ……....	**Ward** ……..
Weight ……..	**Date weighed** ……...
Responsible Consultant ……	

Prescribing Information

Indication | **Target INR / range**

New / continuation *(delete as appropriate)* **Start date** | **Intended duration: LIFELONG** | **Other Months** ……

Date	INR	Machine number (if NPT used)	Warfarin dose	Prescriber's signature	Print name	Time given	Administered by	

Date	INR	Machine number (if NPT used)	Warfarin dose	Prescriber's signature	Print name	Time given	Administered by	

Discharge information

Warfarin dosing to be done by:-

☐ **East Midlands Congenital Heart Service** ☐ **Other (specify) ……**

INR testing done at:-

☐ **Home** ☐ **Hospital** ☐ **GP**

Tel no …… **……** *(Specify hospital)* **Tel no……** **……** *(Specify GP)* **Tel no ……**

If home testing: training done by: Name …… Date ……

NPT Machine Number ……

If hospital/GP: appointment arranged by: Name …… Date ……..

Warfarin counselling done ***(please tick box)*** ☐ **Name …….. Date ……..**

Appendix 5: Guidelines for management of bleeding with Rivaroxaban