Heparin Guideline

Reference: CG1020
Written by: Dr Jeanette Payne
Peer reviewer: Dr Emma Astwood
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Intended Audience

This guidance is to be used by any staff within the Trust when managing children on heparin anticoagulation

Purpose

This document contains background information and guidance for starting a child on heparin anticoagulation and for managing children who are already anticoagulated with heparin

Table of contents

1. Introduction
2. Indications
3. Contraindications
4. Types of Heparin
5. Investigations prior to starting heparin
6. Low Molecular Weight heparin (LMWH)
7. Unfractionated Heparin (UFH)
8. Adverse effects
9. Reversal of heparinisation
10. Switching between anticoagulants
11. Procedural interventions for patients on heparin
12. References

Appendix A Quick reference guide to heparin dosing
Heparin Guideline

1. Introduction

Heparin is an anticoagulant which is administered parenterally by the intravenous or subcutaneous route. Anticoagulation is achieved by complex formation with antithrombin and acceleration of the inhibitory effect of antithrombin on IIa and Xa which occurs to a varying degree depending on the particular type of heparin.

Heparins are used for the prophylaxis and treatment of venous and arterial thromboembolic disease. Onset of action is immediate so heparin is the anticoagulant of choice in the acute situation. Unfractionated Heparin (UFH) has been used traditionally and remains a commonly used anticoagulant but Low Molecular Weight Heparin (LMWH) has several advantages (see section 4) and has become the preferred choice in many clinical situations.

The following preparations are available at SC(NHS)FT.

Unfractionated Heparin:

**Heparin 1000 units in 1 ml - 1ml and 5ml ampoules**- this is the strength to use for intravenous heparin (loading and maintenance infusion) for anticoagulation

Heparin flushes for maintaining patency of venous and arterial catheters i.e not for anticoagulation are available in the following concentrations

- Heparin 100units in 1 ml (Hepflush)-
- Heparin 10units in 1 ml (Hepsal)

**Note that these vials all look very similar so it is imperative to double check the strength of heparin to ensure the correct dose is given**

**Low Molecular weight heparin** (administered subcutaneously)

Enoxaparin (clexane)  
- 20mg in 0.2ml
- 40mg in 0.4ml
- 60mg in 0.6ml
- 80mg in 0.8ml
- 100mg in 1 ml

Doses not available in one of the above pre-filled syringes can be made up in the aseptic department. Doses should be rounded up to whole mg wherever possible

Dalteparin (named patient use only and restricted use for patients transferred to SCH established on treatment)

Tinzaparin (named patient use only and restricted use for patients transferred to SCH established on treatment)
2. Indications

Heparins are used as anticoagulants for the prophylaxis and treatment of venous and arterial thromboembolic events

   a) Thromboprophylaxis

   Thromboembolic events are rare in children but are underestimated and when they occur multiple risk factors can often be identified. The administration of anticoagulants is not without risk especially in patients with renal impairment or who may have additional risk factors for bleeding e.g. recent surgery or the need for invasive procedures. Patients can be risk stratified and thromboprophylaxis with heparin directed to those at highest risk.

   Relevant guidelines

   Thromboprophylaxis guidelines for perioperative and intensive care period at Sheffield Children’s NHS Foundation Trust CG844v4

   Acute venous thrombosis- CG1333

   The trust thromboprophylaxis guideline is applicable for:

   - Medical and surgical patients considered at high risk for a thromboembolic event and not already fully anticoagulated.

   The trust thromboprophylaxis guideline is not applicable for patients with artificial heart valves, congenital heart disease or cardiomyopathy who generally require full dose anticoagulation and not thromboprophylaxis doses (see below for doses of heparin and also see Warfarin and other outpatient anticoagulation: available on the intranet CG1010): These and other children who may be thought to be at increased risk of thromboembolic events should be discussed with a SpR or consultant in haematology. These may include

   - Medical patients not on PICU but considered as high risk for venous thromboembolism
   - children already on anticoagulant medications
   - Patients undergoing cardiac catheterisation
Heparin Guideline

b) Treatment (full dose or “therapeutic”)

The decision to anticoagulate a patient requires a balance of risks of bleeding versus potential consequences of a thromboembolic event (or extension/embolisation of an existing clot). In most circumstances it is best that this decision is made in conjunction with a consultant haematologist. Full dose anticoagulation at least initially with heparin may be appropriate in the following circumstances:

- Acute treatment of venous thrombosis e.g deep vein thrombosis, pulmonary embolus, central line thrombosis, renal vein thrombosis with extension
- Primary prophylaxis following congenital heart surgery e.g Norwood procedure, Fontan procedure or with dilated cardiomyopathy or following insertion of endovascular stents
- Mechanical and biological prosthetic heart valves
- Peripheral arterial thrombosis
- Aortic thrombosis (spontaneous event in neonate)
- Sinovenous thrombosis (controversial)
- Arterial ischaemic stroke (controversial)

3. Contraindications

Relative contraindications to heparin include

- Untreated haemophilia and other bleeding disorders
- Severe thrombocytopenia
- History of heparin induced thrombocytopenia (HIT)
- Recent cerebral haemorrhage
- Active peptic ulcer
- Severe hypertension
- Oesophageal varices
- Major trauma
- Recent neurosurgery or eye surgery
- Severe liver disease
- Hyperkalaemia (risk of exacerbation by heparin- caution if used in combination with ACE inhibitors or potassium sparing diuretics)
4. Types of Heparin

Both UFH and LMWH can be used for prophylaxis and treatment of thromboembolic disease in children. There are advantages and disadvantages of each which are summarised in the table below. The choice of heparin depends on patient factors, risk of thrombosis and risk of bleeding. In general, unless there is renal failure or a need for rapid reversal then LMWH is becoming the preferred option. Discuss with a haematologist if in any doubt.

<table>
<thead>
<tr>
<th></th>
<th>UFH</th>
<th>LMWH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Administration</strong></td>
<td>Prophylaxis: subcut intermittent</td>
<td>Prophylaxis and treatment: subcut intermittent</td>
</tr>
<tr>
<td></td>
<td>Treatment: Continuous intravenous infusion (preferred) or subcut intermittent</td>
<td></td>
</tr>
<tr>
<td><strong>Clearance</strong></td>
<td>Both saturable and nonsaturable (renal) clearance</td>
<td>Predominantly renal so avoid if creat clearance &lt;30 mls/mins. Risk of accumulation and increased bleeding risk</td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td>Treatment doses all need monitoring by activated partial thromboplastin time (APTT) (non-linear relationship with heparinisation )</td>
<td>Limited indications for monitoring. anti-Xa assay used.</td>
</tr>
<tr>
<td><strong>Half life and reversal</strong></td>
<td>Rapid so can be interrupted for procedures. t½ 25 mins neonates, 45-60 mins adults. Reversal with protamine possible in acute bleeding.</td>
<td>Longer t ½= approx 4 hrs with sc use. Protamine reversal possible but incomplete</td>
</tr>
<tr>
<td><strong>Adverse effects</strong></td>
<td>Bleeding</td>
<td>Bleeding</td>
</tr>
<tr>
<td></td>
<td>Osteoporosis (rare)</td>
<td>Probable lower risk of osteoporosis</td>
</tr>
<tr>
<td></td>
<td>HIT (x10 risk of LMWH causing HIT in adults on prophylaxis)</td>
<td>Lower HIT risk</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Resistance of neonates as low antithrombin. Often need frequent dose changes to adequately anticoagulate. May need antithrombin replacement</td>
<td>More predictable dosing but wider range than in adults and less data available in children</td>
</tr>
</tbody>
</table>
Heparin Guideline

5. Investigations prior to starting heparin

Before commencing heparin samples should be taken for **FBC, clotting screen, renal function**

- Full anticoagulation should not be given with moderate/severe thrombocytopenia e.g. platelets <50 x 10^9/l
- If clotting screen is abnormal this should be discussed with a haematologist and the cause established. Correction may be required prior to starting heparin. If the APTT is prolonged due to lupus anticoagulant then the APTT will not be useful for monitoring UFH.
- Avoid LMWH in renal impairment. If creatinine clearance <30mls/min/1.73m^2 UFH is preferred and close monitoring is recommended.

The following formulae can be used to approximate creatinine clearance: (ml/minute/1.73m^2)

- Neonates: 30 x height (cm)/serum creatinine (micromol/l)
- Children >1yr: 40 x height (cm)/serum creatinine (micromol/l)

6. Low Molecular Weight Heparin (LMWH)

**Doses**

Recommended starting doses of LMWH are extrapolated from adult data and are based on anti-Xa levels. Doses are calculated to achieve a target anti Xa level in a sample taken 4 hours after a subcutaneous injection.

- For **treatment** an anti-Xa of **0.5-1.0 U/ml** is recommended for twice daily dosing
- For **prophylaxis** an anti-Xa level of **0.1-0.3 U/ml** is recommended (monitoring of prophylactic dosing very rarely required)

Several LMWHs are available and dosing varies between them. In SC(NHS)FT enoxaparin (clexane) is generally used, so to avoid confusion doses are only quoted for enoxaparin. If any other LMWH is used dosing should be discussed with a haematologist.

Dosing recommendations for **enoxaparin (clexane)**

<table>
<thead>
<tr>
<th></th>
<th>Age &lt;2months</th>
<th>Age &gt;2 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial treatment dose</strong></td>
<td>1.5mg/kg/dose 12hrly</td>
<td>1mg/kg/dose 12hrly</td>
</tr>
<tr>
<td><strong>Prophylactic dose</strong></td>
<td>0.75mg/kg/dose 12hrly</td>
<td>0.5mg/kg/dose 12hrly*</td>
</tr>
</tbody>
</table>

*maximum dose 20mg bd. Children over 40kg may be considered for adult dosing of 40mg od for prophylaxis
Heparin Guideline

Administration

- LMWH should be given subcutaneously either by rotating sites of injections or in patients over 3kg via an insuflon catheter.
- Insuflon catheters can be left insitu for up to a week before replacing at a different site.
- Other subcutaneous cannulas must NOT be used as the dead space is much larger and reliable dosing cannot be achieved.
- Local haematomas are common but can be reduced by applying firm pressure for 5mins following each injection.
- LMWH should be omitted within 12-24 hours before surgery and invasive procedures - see section 9 below.

Monitoring

a). Anticoagulant effect of LMWH

- APTTT is not usually prolonged and cannot be used for monitoring purposes.
- Some patients receiving LMWH for prophylaxis and treatment do not require routine monitoring since fixed dosing has been shown to be safe and efficacious.
- Monitoring may be particularly indicated in the following situations.
  - Infants <3months (pharmacokinetics differ)
  - Renal failure (risk of accumulation)
  - Obese patients
  - Unexpected bleeding (discuss with haematologist as a trough level may be more informative)
- Anti-Xa activity can give useful pharmacokinetic information in an individual but the assay has limitations.
  - The anticoagulant effect of LMWH is not restricted to anti-Xa activity.
  - Comparability between commercial assays is poor.
  - Anti-Xa activity is poorly predictive of bleeding in patients receiving LMWH.
  - Anti-Xa activity is poorly predictive of antithrombotic efficacy.
- Anti-Xa assays (chromogenic method recommended)
  - Take from day 2 onwards of heparin treatment.
  - Discuss with haematology laboratory biomedical scientist and perform within working hours wherever possible.
  - Peak level measured by a citrated sample (purple top filled to line) taken 4 hours after a subcutaneous dose.
  - Venous sample not taken from a line contaminated with heparin. Do not take samples form arterial lines as they are heparinised.
  - Capillary sampling is permitted if a venous sample is not possible. A 0.5ml citrated (purple top) sample tube should be obtained from the haematology laboratory for this purpose.
Local laboratories should validate the anti-Xa assay for the particular LMWH in use. If the patient is on a LMWH other than enoxaparin the lab must be made aware of any requirement for monitoring and the particular LMWH used e.g tinzaparin or dalteparin clearly stated on the request form.

A guide to dose adjustment for enoxaparin is given below:

<table>
<thead>
<tr>
<th>Anti-Xa level (U/ml)</th>
<th>Hold next dose?</th>
<th>Dose change</th>
<th>Next anti-Xa level</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.35</td>
<td>No</td>
<td>↑25%</td>
<td>Next day 4hrs after morning dose</td>
</tr>
<tr>
<td>0.35-0.49</td>
<td>No</td>
<td>↑10%</td>
<td>1-2 days 4 hrs after morning dose</td>
</tr>
<tr>
<td>0.5-1.0</td>
<td>No</td>
<td>0</td>
<td>Not usually required*</td>
</tr>
<tr>
<td>1.1-1.5</td>
<td>No</td>
<td>↓20%</td>
<td>Next day 4hrs after morning dose</td>
</tr>
<tr>
<td>1.6-2.0</td>
<td>3hours</td>
<td>↓30%</td>
<td>Consider trough level before next dose and check peak level after adjusted dose</td>
</tr>
<tr>
<td>&gt;2.0</td>
<td>Until anti-Xa &lt;0.5</td>
<td>↓40%</td>
<td>Before next dose until anti-Xa&lt;0.5 U/ml</td>
</tr>
</tbody>
</table>

*Once the anti Xa is in the therapeutic range further monitoring is not usually required. However further anti Xa levels may be needed in some circumstances e.g if the child develops acute kidney injury or if there are large body weight changes whilst on anticoagulation.

b) FBC/platelet monitoring for LMWH

Heparin Induced Thrombocytopenia (HIT) is a rare but serious adverse effect of heparin. Monitoring is required to detect the occurrence of HIT. The greatest risk period is between days 4 and 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.

a) If exposed to heparin within the previous 100 days check FBC within 24 hours of starting heparin

b) If not exposed within last 100 days Routine monitoring not required
Outpatients on LMWH

Children who need short term anticoagulation e.g for a venous thrombotic event may require outpatient anticoagulation. Guidance on the choice between converting to oral anticoagulation i.e warfarin or continuing with LMWH can be obtained by discussion with a consultant haematologist. The trust guideline on oral anticoagulation contains additional information.

If discharged on heparin it is essential that parents are given detailed information including the practicalities of administration before discharge. Information should include the reason for anticoagulation, risk of bleeding, planned length of anticoagulation.

Arrangements must be made for 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.

Note that LMWH is only available in pre-filled syringes in a limited number of dose sizes. The pharmacy at SCH can prepare other doses but not for more than a week at a time. Other hospitals are often unwilling to supply doses other than those provided by the manufacturer. The potential for travelling back to SCH each week to collect further supplies should be considered when prescribing.

Please note: Since most children on LMWH do not need regular monitoring they are NOT ROUTINELY FOLLOWED UP in the haematology clinic. Unless a specific written referral has been made, the responsibility for follow-up, organisation of monitoring and any booking/reviewing of imaging tests remains with the supervising medical or surgical team. The haematology team are available to advise on dosing and length of anticoagulation if required.
7. Unfractionated Heparin (UFH)

Administration

UFH for therapeutic anticoagulation in children is best administered by continuous intravenous infusion via a dedicated venous line. Anticoagulation is achieved more quickly if a loading dose of heparin is given immediately prior to starting the continuous infusion but the bleeding risk may be increased and so the loading dose may be omitted in certain circumstances – see below.

In cases of MASSIVE pulmonary embolism where there is cardiovascular compromise with hypotension and/or if cardiac arrest is imminent an immediate bolus dose of heparin should be given as detailed below. This should be followed by consideration of thrombolysis e.g with alteplase (dosed as per SPC).
Thrombolysis should be followed by an intravenous infusion of heparin at detailed below. If a decision to give thrombolysis is made after starting the intravenous infusion then the heparin infusion should be stopped whilst giving thrombolysis.

Treatment doses
Use Heparin 1000 units in 1ml preparation (available as 1ml or 5ml ampoules)

a) Loading dose
- OMIT loading dose if increased bleeding risk e.g arterial ischaemic stroke, cerebral sinovenous thrombosis, CNS pathology

75 units/kg over 10 minutes (maximum 5000 units) (50 units/kg if premature neonate <35/40 corrected age). Heparin can be given neat or diluted

Followed by
b) Continuous infusion
- <1yr age 25 units/kg/hr
- >1yr age 20 units/kg/hr
Infusion can be made by adding heparin to Glucose 5%, Sodium chloride 0.9% or Glucose/Sodium chloride. Any suitable volume of diluent can be used. The worked example below shows how the solution for maintenance UFH therapy can be prepared using a 50mls syringe for the infusion.

Obtain the patient’s weight

Weight (kg) x 10units/kg/hr x volume of solution (50mls) = units of heparin in solution

e.g. a child weighing 15kg
15 x 10 x 50 = 7500 units of heparin in 50mls= 150units/ml
Therefore, 1ml/hr=10units/kg/hr and 2mls/hr = 20units/kg/hr

Monitoring

a) Anticoagulation effect of unfractionated heparin

Heparin infusions must be monitored and doses adjusted to ensure that the patient is in the therapeutic range to minimise the risks associated with over or under coagulation. UFH is monitored by the APTT ratio

The target APTT ratio is that which reflects a anti-Xa activity of 0.35-0.7U/ml

Currently in SCH this corresponds to an APTT ratio of 1.9-2.6

An APTT ratio should be checked (venous blood not taken from same line or limb as heparin infusion in x1 purple top citrated bottle filled to line) 4 hours after commencement of the infusion and 4 hours after any changes in heparin dose. Capillary sampling will give inaccurate results so should be avoided.

Once anticoagulation is stable and in the therapeutic range the APTT ratio should be checked once daily.

The following table is a guide to adjustment of heparin dose according to the APTT ratio. If in any doubt, or if APTT ratio is fluctuating widely dose adjustments should be discussed with an SpR or consultant in haematology

<table>
<thead>
<tr>
<th>APTT ratio</th>
<th>Bolus, (units/kg)</th>
<th>Stop for...</th>
<th>Rate Change of</th>
<th>Repeat APTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.5</td>
<td>50</td>
<td>0</td>
<td>+ 10-20%</td>
<td>4 h</td>
</tr>
<tr>
<td>1.6-1.8</td>
<td>0</td>
<td>0</td>
<td>+ 10%</td>
<td>4 h</td>
</tr>
<tr>
<td>1.9-2.6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Next day</td>
</tr>
<tr>
<td>2.7-3.0</td>
<td>0</td>
<td>0</td>
<td>− 10%</td>
<td>4 h</td>
</tr>
<tr>
<td>3.1-3.7</td>
<td>0</td>
<td>30</td>
<td>− 10%</td>
<td>4 h</td>
</tr>
<tr>
<td>&gt;3.8</td>
<td>0</td>
<td>60</td>
<td>− 15%</td>
<td>4 h</td>
</tr>
</tbody>
</table>

Adapted from table in reference 2.
FBC/platelet monitoring on unfractionated heparin

a) If exposed to heparin within the previous 100 days
   Check FBC within 24 hours of starting heparin, then on alternate days until day 14.

b) If not exposed within last 100 days
   Check FBC on alternate days from day 4-14 of starting heparin

8. Adverse effects

Bleeding

Bleeding is the main serious adverse effect of heparin.

In addition to the other recommendations for dosing and administration of heparin in this guideline the risk of bleeding can be minimised by the following:

- Careful selection of patients for anticoagulation (see contraindications above)
- Avoiding antiplatelet medications where possible e.g aspirin, NSAIDs. Antiplatelet agents may be rarely used in addition to heparin for anti-thrombotic effect in arterial thrombosis. This should only be undertaken after careful consideration on advice from a consultant neurologist/cardiologist/haematologist depending on the clinical situation.
- Avoidance of intramuscular injections and arterial stabs whilst on heparin
- Beware of patients with renal dysfunction (or deterioration in renal function whilst on heparin). Heparin clearance is mostly renal and doses may need to be reduced to avoid accumulation of heparin
- Appropriate actions taken in the event of need for an invasive procedure/surgery (see 11. Procedural interventions for a patient on heparin)

Osteoporosis

Osteoporosis is a well described risk in adults on long-term heparin. The risk is thought in general to be greatest with UFH. Although there are only a few case reports of heparin induced osteoporosis in children long term treatment with unfractionated heparin should be avoided when alternative anticoagulation is possible.

Heparin induced thrombocytopenia

Case reports describe cases of heparin induce thrombocytopenia (HIT) in children from 3 months upwards. HIT can occur with low dose exposure such as heparin flushes for central lines as well as full dose heparin anticoagulation. Cardinal features are thrombocytopenia (or a 50 % drop in platelet count) +/- thrombosis 6-10 days after heparin started. Onset may be more rapid if previously exposed to heparin. Laboratory tests aid the diagnosis but action should be taken on the basis of clinical suspicion. A high index of suspicion is required to diagnose HIT in children, as many patients in the neonatal ICU/PICU who are exposed to heparin have multiple potential reasons for thrombocytopenia and/or thrombosis. Primary treatment is to stop all heparin including flushes and alternative anticoagulation is usually required. See Heparin induced thrombocytopenia CG1552 for more detailed guidance. Discuss any suspected cases with a consultant haematologist,
9. Reversal of heparinisation

In the event of major bleeding or if urgent surgical procedure is required the anticoagulant effect of heparin may need to be reversed.

Unfractionated heparin

Since the half-life of UFH is short, termination of an intravenous infusion of heparin is usually sufficient to achieve reversal of anticoagulation within a few hours. In the event of overdose however, it may take significantly longer for clearance of the excess heparin.

If immediate reversal is required or if a large overdose has been given protamine sulfate can be given as a neutralising agent. Neutralisation of heparin occurs within 5 minutes of intravenous injection. The dose of protamine sulphate is based on the amount of heparin received and is shown in the table below.

<table>
<thead>
<tr>
<th>Time since last heparin dose/mins</th>
<th>Protamine dose per 100 units of heparin received</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>1mg</td>
</tr>
<tr>
<td>30-60</td>
<td>0.5-0.75mg</td>
</tr>
<tr>
<td>60-120</td>
<td>0.375-0.5mg</td>
</tr>
<tr>
<td>&gt;120</td>
<td>0.25-0.375mg</td>
</tr>
</tbody>
</table>

If used in excess, protamine sulphate can have an anticoagulant effect. The maximum dose of protamine given is usually 50mg. It is usually given in a concentration of 10mg/ml at a rate not to exceed 5mg/minute, but can be diluted in 0.9% sodium chloride. If administered too quickly protamine sulphate can lead to circulatory collapse. Patients with hypersensitivity reactions to fish and those who have previously received protamine or protamine insulin may be at particular risk of hypersensitivity reactions to protamine sulphate.

A clotting screen should be taken 15 minutes after protamine sulphate to monitor efficacy of reversal.

LMWH

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

The dose required depends on amount of LMWH administered and time elapsed since last dose. Suggested doses for enoxaparin (clexane) are given below.

<table>
<thead>
<tr>
<th>Time since enoxaparin dose</th>
<th>Protamine dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 8 hours</td>
<td>1mg protamine to 1mg enoxaparin</td>
</tr>
<tr>
<td>8 to 12 hours</td>
<td>0.5mg protamine to 1mg enoxaparin</td>
</tr>
<tr>
<td>&gt; 12 hours</td>
<td>May not be required</td>
</tr>
</tbody>
</table>

Maximum recommended protamine dose 50mg as above.
Repeated doses are best given on the basis of clinical response. Anti-Xa activity is never completely neutralised whereas anti IIa neutralisation is more rapid and may correlate better with bleeding risk. Therefore normalisation of a prolonged APTT may be more important than reversal of anti Xa activity. If the APTT remains prolonged 2 to 4 hours after the first infusion of protamine a second infusion of 0.5mg protamine to 1mg enoxaparin should be considered.

Recombinant VIIa has been used in life threatening bleeding associated with LMWH but experience in the use of VIIa for this purpose is very limited. There is no role for fresh frozen plasma (FFP) in reversal of heparinisation.

10. Switching between anticoagulants

1. The factors leading to the decision to use UFH or LMWH for a given patient may change with time and it may become desirable to convert from UFH to LMWH or vice versa. The following points should be noted to achieve uninterrupted therapeutic anticoagulation

   a) conversion of UFH to LMWH
      Give the first dose of LMWH at the same time as the intravenous infusion of UFH is stopped

   b) conversion of LMWH to UFH
      Wait for at least 8 hours after the last dose of LMWH before commencing an UFH infusion. If started between 8 and 12 hours a loading dose is not required and the infusion should be started at a rate as suggested above in section 7 UFH.

2. If long term anticoagulation is planned it is usually decided to convert from heparin to oral anticoagulation with warfarin. If treating an acute thrombotic event heparin should always be continued for at least 5 days. Warfarin induction should overlap with heparin therapy and the latter only discontinued when the international normalised ratio (INR) has been in the therapeutic range for at 2 days ( see also warfarin and other outpatient anticoagulation CG1010

11. Procedural interventions for a patient on heparin

The benefits of the procedure should outweigh the risks of interruption of anticoagulation.

When to stop heparin prior to a procedure?

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

LMWH
All therapeutic doses should be omitted in the 24 hours prior to surgery or lumbar punctures. For children on twice daily dosing having a procedure in the morning this means omission of the dose the night before and the morning of surgery.

For children on prophylactic LMWH, doses should be avoided for 12 hours prior to surgery and invasive procedures including lumbar punctures and epidurals.
**Heparin Guideline**

**When to restart heparin after surgery?**
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.

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

**12. References**


**SC(NHS)FT Guidelines**

Thromboprophylaxis guidelines for perioperative and intensive care period at Sheffield Children’s NHS Foundation Trust CG844v4

Acute venous thrombosis- CG1333

Warfarin and other outpatient anti-coagulation CG1010

Heparin induced thrombocytopenia CG1552
Appendix A.
Quick reference guide to heparin dosing
(detailed guidance given in accompanying guideline)

1. Low Molecular Weight Heparin - Enoxaparin (clexane)

Table 1. Starting doses for enoxaparin for treatment and prophylaxis

<table>
<thead>
<tr>
<th></th>
<th>Age &lt;2 months</th>
<th>Age &gt;2 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial treatment dose</strong></td>
<td>1.5mg/kg/dose 12hrly</td>
<td>1mg/kg/dose 12hrly</td>
</tr>
<tr>
<td><strong>Prophylactic dose</strong></td>
<td>0.75mg/kg/dose 12hrly</td>
<td>0.5mg/kg/dose 12hrly*</td>
</tr>
</tbody>
</table>

*maximum dose 20mg bd. Children over 40kg may be considered for adult dosing of 40mg od for prophylaxis

Table 2. Guide to adjustment of treatment dose enoxaparin to achieve anti-Xa level of 0.5-1.0 U/ml

<table>
<thead>
<tr>
<th>Anti-Xa level (U/ml)</th>
<th>Hold next dose?</th>
<th>Dose change</th>
<th>Next anti-Xa level</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.35</td>
<td>No</td>
<td>↑25%</td>
<td>Next day 4 hrs after morning dose</td>
</tr>
<tr>
<td>0.35-0.49</td>
<td>No</td>
<td>↑10%</td>
<td>1-2 days., 4hrs after morning dose</td>
</tr>
<tr>
<td>0.5-1.0</td>
<td>No</td>
<td>0</td>
<td>Not usually required</td>
</tr>
<tr>
<td>1.1-1.5</td>
<td>No</td>
<td>↓20%</td>
<td>Next day 4 hrs after morning dose</td>
</tr>
<tr>
<td>1.6-2.0</td>
<td>3hours</td>
<td>↓30%</td>
<td>Consider trough level before next dose and check peak level after adjusted dose</td>
</tr>
<tr>
<td>&gt;2.0</td>
<td>Until anti-Xa &lt;0.5</td>
<td>↓40%</td>
<td>Before next dose until anti-Xa&lt;0.5 U/ml</td>
</tr>
</tbody>
</table>

2. Unfractionated Heparin (UFH) - treatment dose

*Loading dose of 75units/kg over 10 minutes* (maximum 5000 units) *(50 units/kg if premature neonate <35/40 corrected age)*

Followed by *continuous infusion of 25units/kg/hr if <1yr age or 20units/kg/hr if >1yr age*

**APTT ratio** checked 4 hrs after start of infusion then 4-6 hrly

**Target APTT ratio 1.9-2.6**

Table 3. Guide to adjustment of UFH infusion rate according to APTT ratio

<table>
<thead>
<tr>
<th>APTT ratio</th>
<th>Bolus, (units/kg)</th>
<th>Stop for… mins</th>
<th>Rate Change of infusion, (%)</th>
<th>Repeat APTT ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.5</td>
<td>50</td>
<td>0</td>
<td>+ 10-20%</td>
<td>4h</td>
</tr>
<tr>
<td>1.6-1.8</td>
<td>0</td>
<td>0</td>
<td>+ 10%</td>
<td>4h</td>
</tr>
<tr>
<td>1.9-2.6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Next day</td>
</tr>
<tr>
<td>2.7-3.0</td>
<td>0</td>
<td>0</td>
<td>– 10%</td>
<td>4h</td>
</tr>
<tr>
<td>3.1-3.7</td>
<td>0</td>
<td>30</td>
<td>– 10%</td>
<td>4h</td>
</tr>
<tr>
<td>&gt;3.8</td>
<td>0</td>
<td>60</td>
<td>– 15%</td>
<td>4h</td>
</tr>
</tbody>
</table>