Management of Acute Thromboembolism in Pregnancy and the Puerperium

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<tr>
<th>Full Title of Guideline:</th>
<th>Guideline for the Management of Acute Venous Thromboembolism (DVT and PE) in Pregnancy and the Puerperium</th>
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<td>RCOG, NICE, BTS guidelines</td>
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*This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date or outside of the Trust.*
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1 Diagnosis of acute venous thromboembolism (VTE): Deep Vein Thrombosis (DVT) and Pulmonary Embolus (PE)

- Clinical diagnosis of VTE is unreliable and less than half of women with clinically suspected VTE have the diagnosis confirmed when objective testing is employed.

- The correct diagnosis however must be established in order to avoid either inadequate treatment of a potentially dangerous condition or unnecessary treatment of a mother (and hence her fetus). There are additional implications for the management of future pregnancies as a recurrence risk exists.

- VTE can occur at any stage in pregnancy but the puerperium is the time of highest risk.

- Acute VTE should be suspected at any time during pregnancy or the puerperium particularly in women with risk factors for VTE.

1.1 Risks factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
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<tbody>
<tr>
<td>Age &gt; 35</td>
<td>Sepsis</td>
</tr>
<tr>
<td>Parity ≥ 3</td>
<td>Dehydration/hyperemesis/OHSS</td>
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<tr>
<td>Obesity</td>
<td>Multiple pregnancy</td>
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<tr>
<td>Smoker</td>
<td>Pre-eclampsia</td>
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<tr>
<td>Gross varicose vein</td>
<td>Preterm delivery in current pregnancy</td>
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<tr>
<td>Thrombophilia</td>
<td>Stillbirth in current pregnancy</td>
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<tr>
<td>Personal history VTE</td>
<td>Prolonged labour (&gt;24 hours)</td>
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<tr>
<td>Family history VTE</td>
<td>Mid-cavity operative vaginal delivery</td>
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<tr>
<td>Medical co-morbidities</td>
<td>Caesarean Section</td>
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<tr>
<td>Immobility</td>
<td>PPH &gt; 1 litre or blood transfusion</td>
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<tr>
<td>Hospital admission</td>
<td>Surgical procedure in antenatal/puerperium</td>
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1.2 Signs and symptoms of acute DVT and PE

**Clinical diagnosis** of DVT/PE in pregnancy is often difficult and inaccurate:

Deep Vein Thrombosis

- Leg pain (or discomfort)
- Swelling – usually unilateral– especially the left leg
- Lower abdominal or groin pain may be a feature of an iliofemoral DVT
**Pulmonary Embolus**
- Pleuritic chest pain
- Breathlessness
- Haemoptysis
- Tachycardia
- Collapse
- Faintness
- Raised jugular venous pressure
- Symptoms and signs associated with DVT

In women with factors consistent with VTE, anticoagulant treatment should be started before an objective diagnosis is made (see below).

### 1.3 Principles of management (see flowchart in Appendix 1 and 2)

- Refer/admit any pregnant woman with suspected VTE to medical ward at QMC and obstetric/labour ward at CHN. If there are obstetrics or gynaecology concerns as well, a discussion need to happen between the referring, medical and obstetrics/gynaecological team at QMC regarding the best place of admission for that woman.

- Aim to establish an accurate diagnosis quickly (see imaging below).

- Consider other causes of chest symptoms (e.g. pneumonia, asthma, musculo-skeletal pain, pneumothorax, ischaemic heart disease) before pursuing investigation for PE.

- **WHEN THROMBOEMBOLISM IS SUSPECTED, TREATMENT SHOULD BE COMMENCED PENDING CONFIRMATION OF THE DIAGNOSIS** unless contraindication (e.g. active bleeding, labour imminent, renal failure) If a contraindication to anticoagulation exists, discuss with a haematologist (non-malignant haematology consultant on call). If >36 weeks’ gestation and is admitted to medical ward, please Inform obstetric team (consultant or registrar) before 1st dose.

- D-dimer is a useful screening test for VTE in the non-pregnant patient where it has a high negative predictive value i.e. it is useful for excluding thrombosis. A negative D-dimer (check normal values with laboratory as they differ between different laboratories) is useful as part of a treatment algorithm and suggests in a low risk patient that VTE is very unlikely.

There are many causes of a raised D-dimer including pregnancy and a raised D-dimer value is therefore not of diagnostic use during pregnancy.
D-dimer levels have been shown to be up to 10 times higher in late pregnancy than in healthy non-pregnant women (Cadroy et al, 1993). However, if D-dimer levels are found to be low, especially in late pregnancy, then VTE is unlikely. RCOG guideline does not recommend D-dimer testing in the investigation of acute VTE in pregnancy.

- Thrombophilia testing should not be performed in the acute setting as it has no impact on the immediate management of acute VTE. In addition, thrombophilia testing is rarely indicated when anticoagulation treatment is completed and should not be performed routinely.

- Refer all women with an ongoing pregnancy presenting with a pregnancy related event (including postnatal events) to the Haematology/Obstetric clinic - this is on a Tuesday morning at Queen’s Campus and Thursday afternoon at the City Campus. Request “VTEMĐT” on NoTIS to ensure follow up in haem/obstetric clinic on discharge or complete obstetric haematology referral form (Appendix 3, can also be found in ANC) and send it to feto-maternal medicine (FMM) at QMC/Antenatal (ANC) at CHN.

For women who had miscarriage or termination of pregnancy or ectopic pregnancy or pregnancy of unknown location and pregnancy related VTE, request “VTEMĐT” on NoTIS and the team will decide on appropriate place to follow up these women.

- If the woman is very close to delivery, the diagnosis and management should be discussed directly with a haematology consultant (non-malignant haematology consultant on call).

- All hospital associated thromboses (HAT) require a root cause analysis to be performed and presented to the specialty Clinical Governance Group. This will, in turn, be reviewed by the Thromboprophylaxis Committee/VTE Operational Group. Any woman who has a VTE following hospital admission (this includes delivery in hospital) should be reported to governance lead who will ensure the correct procedure is followed.

1.4 Appropriate diagnostic imaging

Imaging tests are vital to establish the diagnosis. Discuss with Radiologist, if necessary.

Any women with symptoms and/or signs of VTE should have objective testing performed and treatment with low molecular weight heparin given until the diagnosis is excluded. If there is a contraindication to
anticoagulation, the patient should be discussed with a haematologist (non-malignant haematology consultant on call).

For a **suspected DVT** tests include: -

- Doppler ultrasound of proximal (iliac, femoral and popliteal) veins. Although less reliable for distal leg veins, it is the investigation of first choice in experienced hands.
- If ultrasound is negative or equivocal and a high level of clinical suspicion exists, further investigation will be required. The woman’s care should be discussed with a haematologist before stopping anticoagulant treatment.

For a **suspected PE** tests include: -

- Initial investigation should include Chest X-ray (CXR) / Electro-cardiogram (ECG) / Arterial blood gas (ABG). This will also help to exclude other pathologies (fractured ribs, pneumothorax, chest infection, ischaemic heart disease).
  In PE ABG may show low pO2 (in contrast to low pCO2 but normal pO2 if hyperventilating). The commonest ECG change in PE is sinus tachycardia. Other changes include S-wave in lead 1, Q-waves and inverted T waves in lead 3 (S1Q3T3), right-axis deviation or ST-T changes in V1-V3. NOTE - blood gases and ECG may be completely normal.

- In women with suspected PE who also have symptoms and signs of DVT, compression duplex ultrasound should be performed. If compression ultrasonography confirms the presence of DVT, no further investigation is necessary and treatment for VTE should continue.

- In women with suspected PE without symptoms and signs of DVT, perform either
  - Ventilation Perfusion (V/Q) scan - Note that this is operator-dependent and not available every day (QMC campus: Tuesday to Friday; City Campus: there may be a delay by 24 hours following request as isotope is kept in QMC).
  - Computerised tomography pulmonary angiography (CTPA). Note that this may miss peripheral emboli. CTPA is particularly helpful in excluding PE in certain circumstances such as abnormal CXR, women presenting with threatened labour or needs delivery out of hours when other imaging are not available. Also consider CTPA when V/Q scan can’t be performed within a reasonable timeframe ~24 hours of initial review/suspected diagnosis.

- If V/Q scan or CTPA is normal or borderline but the clinical suspicion of PE remains, discuss with radiologist regarding alternative or repeat testing. Continue anticoagulant treatment until PE is definitely excluded.
The choice of technique for definitive diagnosis (V/Q scan or CTPA) will depend on availability and should be made after discussion with a radiologist. Women should be involved in the decision to undergo CTPA or V/Q scan. Women with suspected PE should be advised that, compared with CTPA, V/Q scanning may carry a slight increased risk of childhood cancer but is associated with a lower risk of maternal breast cancer. They should be advised that in both cases, the risk is very small and that the risks of undiagnosed PE are much higher.

The ventilation component of the V/Q lung scan can often be omitted during pregnancy, thereby minimising the radiation dose for the fetus (which is in any event small and not associated with a substantial increased risk of complications such as childhood cancer), especially if the X-ray is normal. After a V/Q scan, a lactating mother should be advised to express and discard her milk for 9 hours to avoid giving her child milk contaminated with radio isotopes. In contrast to CTPA, V/Q scanning may be delayed because of availability of isotope.

The British Thoracic Society recommends CTPA as first-line investigation for non-massive PTE in non-pregnant women. This technique has potential advantages over radionuclide (V/Q) imaging including better sensitivity and specificity (at least in non-pregnant women) and a lower radiation dose to the fetus. In addition, it can identify other pathology, such as pneumonia, pulmonary oedema, aortic dissection. The main disadvantage of CTPA is the high radiation dose to the maternal breasts, which is associated with an increased lifetime risk of developing breast cancer (lifetime risk increased by up to 13.6% with CTPA, background risk of 1/200 for study population). This is particularly relevant when it is known that only around 5% of such investigations will have a positive result. In addition, CTPA may not identify small peripheral PTE. Despite these potential advantages of CTPA, V/Q scanning may be the best investigation because of its high negative predictive value and its substantially lower radiation dose to pregnant breast tissue.

Isotope scans using fibrinogen labelled with I\textsuperscript{131} are contraindicated during pregnancy and the puerperium due to damage to the fetal / neonatal thyroid.

2. Initial treatment of VTE

2.1 Low molecular weight heparins (LMWH)

2.1.1 Enoxaparin

This is the low molecular weight heparin used across Nottingham. The initial treatment dose of enoxaparin is \textbf{1mg/kg TWICE daily} based on early pregnancy
weight. The rationale for twice daily dosing relates to increased renal clearance in pregnancy and therefore ensuring adequate anticoagulation throughout the 24-hour period. The dose can be changed to 1.5mg/kg ONCE daily in the postnatal period, after discussion with consultant haematologist. Individualised delivery plans should be reviewed where specific dosing advice will be documented.

Enoxaparin is available in syringes of 20mg, 40mg, 60mg, 80mg, and 100mg. The closest to the woman’s weight should be used and continued 12 hourly until objective testing has been performed.

Initial dosing of enoxaparin is determined as follows:

<table>
<thead>
<tr>
<th>Early pregnancy weight*</th>
<th>Initial Dose of enoxaparin</th>
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<tbody>
<tr>
<td>Less than 50 kg</td>
<td>40mg twice daily</td>
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<tr>
<td>50 - 69kg</td>
<td>60mg twice daily</td>
</tr>
<tr>
<td>70 - 89kg</td>
<td>80mg twice daily</td>
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<tr>
<td>90 - 109kg</td>
<td>100mg twice daily</td>
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<tr>
<td>110 – 125kg</td>
<td>120mg twice daily</td>
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<tr>
<td>More than 125 kg</td>
<td>Discuss with haematologist</td>
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*At extremes of weight, doses should be discussed with a pharmacist and/or haematologist

The dose of enoxaparin may be reduced to 75% (i.e. 1.5 mg/kg/day) in selected cases after the initial treatment period, usually after 10-12 weeks. However, expert opinion is divided on this and the decision must be made by an experienced haematologist /maternal medicine consultant.

2.1.2 Monitoring (anti Xa levels)

This is not routinely necessary. However, the RCOG recommends monitoring at extremes of weight range (<50kg or >90kg), in the event of renal impairment or if symptoms are not improving despite treatment. A blood sample for anti-Xa level should be taken into a blue, citrate tube 3 – 4 hours after the injection. Warn the coagulation laboratory that the sample is coming. Discuss dosage adjustment with haematologist or maternal medicine consultant if not in therapeutic range (0.6 - 1.2 iu/ml).

2.1.3 Platelet count

There is no need to routinely monitor platelet counts in women on LMWH but it is necessary if woman receive unfractionated heparin, or in a woman receiving LMWH who has previously received unfractionated heparin. Pregnant women
who are receiving unfractionated heparin should have platelet count monitoring performed every 2–3 days from days 4 to 14 or until heparin is stopped in the postoperative period.

2.1.4 Risks of LMWH

As contrasted with unfractionated heparin, long-term use of LMWHs is associated with a lower risk of osteoporosis and bone fractures. Occasionally, women may develop haemorrhage, hyperkalaemia or an allergic rash. Heparin-induced thrombocytopenia (HIT) is extremely rare in pregnancy. Care should be taken with women with long term diabetes, chronic renal failure and metabolic disorders.

2.2 Intravenous unfractionated heparin (UFH)

This is the preferred treatment in massive pulmonary emboli or if imminent labour because of its rapid effect and extensive experience of its use in this situation. It is also sometimes used in women who are diagnosed with a thrombosis very close to the end of pregnancy. Such women will be seen in the obstetric haematology clinic and formal delivery plans made. The decision to use this should always be made by a consultant haematologist or maternal medicine consultant.

2.3 Other measures in the initial management of DVT include:

2.3.1 Compression stockings / TEDs

In the initial management of DVT and/or with ongoing symptoms, mobilisation with graduated elastic compression stockings should be encouraged as it reduces oedema, pain and swelling. The role of compression stockings in the prevention of post-thrombotic syndrome is unclear. Graduated elastic compression stockings should be worn on the affected leg. Thigh-length compression elastic stockings do not offer better protection against post-thrombotic syndrome than below-knee hosiery and are less well tolerated.

2.3.2 Vena Caval Filters

A temporary inferior vena caval filter may be required in women with recurrent PE despite satisfactory anticoagulation or in situations where anti coagulation is contra-indicated. It is also important to consider a filter if a large, proximal clot is diagnosed close to delivery or if there is a recurrent clot.

Consult the maternal medicine team and interventional radiology prior to organising this. It should be remembered that IVC filters have their own risks,
and liaison with a senior radiologist, haematologist and obstetrician is needed with clear counselling of these risks to the woman. Current opinion is that they are rarely necessary.

2.4 Life threatening massive PE

See also NUH policy for Massive Pulmonary Embolism at http://nuhnet/nuh_documents/Guidelines/Acute Medical/Acute Medicine/2786.pdf (flowchart 4 and 5)

Management should involve a multidisciplinary team including senior physicians, obstetricians and radiologists. The first port of call in this situation is the on-call medical team who can arrange urgent portable echocardiogram or CTPA as well as and can perform immediate thrombolysis, if indicated.

Cardiorespiratory resuscitation will usually be required and intravenous unfractionated heparin should be given. Thrombolytic therapy, percutaneous catheter thrombus fragmentation or surgical embolectomy may be required. This will vary with local expertise. Where a DVT threatens leg viability through venous gangrene, the leg should be elevated, anticoagulation given and consideration given to surgical embolectomy or thrombolytic therapy. In this situation, advice should be sought from the vascular surgical on call team.

3. Maintenance treatment of DVT/PE

3.1 Warfarin

Oral anticoagulants (warfarin) should not be used in pregnancy except in exceptional circumstances. They cross the placenta readily and are associated with a characteristic embryopathy in the first trimester, central nervous system abnormalities and fetal haemorrhage. This treatment should only be considered for post-natal anticoagulation and good contraception is mandatory to avoid the risk of warfarin embryopathy in an unplanned pregnancy. Occasionally warfarin is used during pregnancy for women with high risk metallic heart valves. Such decisions should always be made with a haematologist and cardiologist.

3.2 Heparins

Low molecular weight heparin (Enoxaparin at NUH) is the treatment of choice for anticoagulation of venous thrombosis in pregnancy and in the early postnatal period. See section 2.1 for further details.
3.2.1 Self injecting

Women should be taught to self-inject and can be managed as outpatients until delivery. Women should be given the information leaflet ‘Enoxaparin in pregnancy’ (Appendix 4, can also be found in ANC).

3.2.2 Needles

Arrangements should be made to allow safe disposal of sharps and syringes. Women should be provided with a sharps bin on discharge from hospital.

3.3 Therapeutic ranges

LMWH administered subcutaneously 12 hourly to achieve a peak anti Xa activity; three hours post injection of 0.6-1.2units/ml.

Unfractionated heparin to achieve a target APTT ratio of 1.5-2.5 times the control value.

3.4 Heparin–induced thrombocytopenia (HIT)

This is rare and usually only occurs with unfractionated heparin (or when a patient is on LMWH, having previously received UFH). Pregnant women who develop heparin-induced thrombocytopenia and require continuing anticoagulant therapy should be discussed with a consultant haematologist who has expertise in haemostasis and thrombosis, as there are some alternative heparinoids available.

3.5 Duration of therapy

Following VTE in pregnancy, therapeutic anticoagulation should continue for at least 3 months and this must include anticoagulation for at least 6 weeks postpartum. If the VTE has occurred early in pregnancy, consideration can be given to reducing the LMWH dose to 75% of the initial dose after a period of 10-12 weeks, but individualised plans will be made by the expert Obstetric Haematology team. Normally no adjustment is made for the weight gain in pregnancy. Following delivery, treatment should continue for at least 6 weeks, dependent on risk factors and discussion with the haematologists. Warfarin can be used post partum and is safe during breast-feeding, although many women prefer to continue LMWH for ease of use and because blood tests are not needed for monitoring.
4. Women on anticoagulant therapy at high risk of haemorrhage

Any woman who is considered to be at high risk of haemorrhage, and in whom continued heparin treatment is considered essential, should be managed with intravenous, unfractionated heparin until the risk factors for haemorrhage have resolved. These risk factors include major antepartum haemorrhage, coagulopathy, progressive wound haematoma, suspected intra-abdominal bleeding and postpartum haemorrhage. Unfractionated heparin has a shorter half-life than LMWH and its activity is more completely reversed with protamine sulphate. It is important to carefully monitor APTT ratios in all women on intravenous UFH to ensure that levels of anticoagulation are neither excessive nor inadequate. **If a woman is receiving IV UFH, protamine should be available on the ward for immediate use if required.** Use should always be discussed with a senior obstetrician. If a woman develops a haemorrhagic problem while on LMWH the treatment should be stopped and expert haematological advice sought.

5. Management of miscarriage, termination of pregnancy, ectopic pregnancy and pregnancy of unknown location (PUL) for women who have a recent diagnosis of venous thrombosis

- All women with recent VTE who require management of miscarriage, termination of pregnancy, ectopic pregnancy or PUL should be managed by a named Consultant Gynaecologist/Obstetrician and Consultant Haematologist (non-malignant haematology consultant on call). This will also include those women who are being managed expectantly.

- Women with recent VTE who require management of miscarriage or termination of pregnancy should be offered surgical management rather than expectant or medical management unless a significant contraindication exists. In this case the risks and benefits of each approach should be clearly discussed with the woman at Consultant level, she should be involved in the decision making process and the safest approach adopted on an individual care basis. She must be counselled that as anticoagulation has to be stopped to allow management of the pregnancy, there is a risk of recurrent thrombosis. Although we try and reduce this risk as much as possible with an anticoagulation plan, recurrence does rarely still occur and can be life threatening.

- The risk of recurrent VTE when anticoagulation is stopped is highest within the first 4 weeks after an acute event. Therefore, consideration should be given to delaying the procedure if this is clinically appropriate; this is only likely to be possible for elective termination of pregnancy.
• These women should be considered as high risk. Therefore, for elective procedures these should be performed within normal working hours.

• All women undergoing management of miscarriage, termination of pregnancy, ectopic pregnancy or PUL should have a formal written plan for anticoagulation made and this should be available on her NOTIS, DHR or Medway maternity record, if appropriate.

• If complications arise during the procedure which means that the anticoagulation plan cannot be followed, the woman’s care should be discussed again with the named consultant Gynaecologist/Obstetrician and consultant Haematologist.

• If a woman presents with miscarriage or suspected ectopic pregnancy out of hours, she should be discussed with the senior gynaecology/obstetric team and the on call haematologist. In both cases the consultant gynaecologist/obstetrician and consultant haematologist should be informed of the woman and be involved in the management plan.

• Women who require evacuation of uterus due to incomplete miscarriage should be considered ‘high risk’ and surgery should not be delayed.

• In the event that the surgical plan has been changed (e.g. theatre cancellation) then the consultant gynaecologist and consultant haematologist should be re-contacted.

6. Anticoagulant therapy during labour and delivery, including the use of regional anaesthesia

The timing of the thrombosis and the woman’s thrombotic risk will determine the peripartum management plan. An individualised delivery plan will be made when the woman attends the obstetric haematology clinic; this will be available on NOTIS and Medway maternity record. If no delivery plan is available, contact consultant haematologist and obstetrician and general principles for management of women taking therapeutic enoxaparin during pregnancy is outlined under Section 6.2.

6.1 Regional Anaesthesia

Refer women on therapeutic dose of enoxaparin to the Obstetric anaesthetists antenatally to discuss analgesic options during labour.
Regional anaesthesia can be sited only after discussion with a senior anaesthetist.

Confirm platelet count before any regional anaesthetic technique. The platelet count should be $80 \times 10^9/l$ or above.

To minimise the risk of epidural/spinal haematoma in women on treatment doses of LMWH (i.e. twice daily regimen of LMWH OR on a reduced 75% dosing regimen)

- Should not have regional anaesthetic techniques performed for at least 24 hours after the last dose of LMWH.
- LMWH should not be given for 4 hours after the use of spinal anaesthesia or after the epidural catheter has been removed, and the epidural catheter should not be removed within 24 hours of the most recent injection.

(regional anaesthesia in women taking prophylactic enoxaparin is outside of the scope of this guideline)

6.2 Spontaneous labour and Induction of labour

An individualised plan for the woman will be made in the obstetric haematology clinic and uploaded to NOTIS/Medway maternity record (under Document Section), in advance of labour. If a woman presents unexpectedly in labour and no plan is available, she should be discussed with a haematologist; contact switchboard and ask to speak to the haematologist on call for non malignant conditions.

General principles for management of women taking therapeutic enoxaparin during pregnancy include;

- Omit enoxaparin and contact the hospital at the first signs of spontaneous labour
- Planned omission of enoxaparin if labour is to be induced or for elective caesarean section (as advised by the obstetric haematology clinic plan)
- Check FBC, clotting screen and group and save on admission and ensure IV access
- Inform the obstetric anaesthetist when the woman is admitted
- Monitor carefully for excessive bleeding.
- Hydration and use of graduated compression stockings are recommended throughout labour.
- Active management of 3rd stage of labour.
- Any perineal tear/ trauma should be repaired as soon as possible with close attention to haemostasis.
- Monitor carefully for postpartum haemorrhage.
• Anticoagulation should only be recommenced postnatally when haemostasis is secure; this decision should be made by a doctor (O&G registrar or consultant).

6.3 Elective Caesarean Section (CS)

An individualised plan will be made in the obstetric haematology clinic and uploaded to NOTIS/ Medway maternity record (under Document Section), in advance of elective CS. If a woman needs emergency CS and no plan is available, she should be discussed with a haematologist.

6.4 Drains and skin closure

Women who are receiving therapeutic doses of LMWH, are at increased risk of ongoing bleeding and wound haematoma. Meticulous haemostasis is important and peritoneal closure should be considered, as it aids earlier recognition of intra-abdominal bleeding. Wound drains should be considered at Caesarean section as it will help to identify the ongoing blood loss in these cases. Skin incision should be closed with staples or interrupted sutures to allow drainage of any haematoma. Consider pressure dressings.

7. Postnatal anticoagulation

7.1 Duration

Anticoagulant treatment should be continued postnatally to complete the 3 month course of anticoagulation and should incorporate a minimum of 6 weeks in the postpartum period (even if this extends the total duration of anticoagulation beyond 3 months). The woman should be followed up in the Haematology/Obstetric clinic in 2 – 3 weeks post delivery to discuss duration of anticoagulation, future investigation, contraception and circumstances where future prophylaxis would be advised. All women should be reviewed by haematologists to assess the risk of thrombosis before discontinuing treatment.

7.2 Warfarin Initiation

Postpartum warfarin should be avoided until at least the fifth day and for longer in women at increased risk of postpartum haemorrhage. If the woman wishes to commence warfarin postpartum, this can usually be initiated around a week post-delivery as, practically, it is difficult to establish on warfarin before then. This will depend on the individual needs and haemostasis peri-delivery. The woman should be discharged home on LMWH and brought back to the Obstetric Haematology clinic within 7-10 days. All women who are commenced on
warfarin need to be referred to the anticoagulation clinic for ongoing International normalized ratio (INR) monitoring via the following link: http://nuhnet/diagnostics_clinical_support/Haemostasis_and_Thrombosis/Pages/InformationforClinicians.aspx

Many women choose to stay just on LMWH for 6 weeks of the puerperium, due to the difficulties in stabilising warfarin doses and the need for frequent blood tests.

The direct oral anticoagulants (DOACS) Rivaroxaban, Apixaban, Dabigatran and Edoxaban are now licenced for the treatment of venous thrombosis and are an option for treatment in the postnatal period. They are contraindicated during pregnancy and whilst breast feeding.

7.3 Breastfeeding

Warfarin is safe for women and babies who are breastfeeding, as it is not excreted into breast milk. There is little information about LMWH and breastfeeding, but is considered to be safe as it is unlikely that LMWH are secreted in breast milk due to their high molecular weight. If heparin was present in milk, then it would be inactivated in the baby’s gastrointestinal tract. DOACS are contraindicated.

Useful phone numbers

Maternal medicine QMC 61924
Haematology/Obstetric clinic NCH 55244

Coagulation laboratory QMC 61183
Coagulation laboratory NCH 57568

Queen’s Campus:
  Doppler ultrasound 61159 (Ultrasound)
  V/Q scans 64052 (Medical Physics)

City Campus:
  Doppler ultrasound 56703 (Ultrasound)
  V/Q scans 55794 (Medical Physics)
References


Appendix 1. PREGNANT OR IN THE PUERPERIUM WITH SUSPECTED DEEP VEIN THROMBOSIS?

YES

Early pregnancy weight | Initial Dose of enoxaparin
--- | ---
Less than 50 kg | 40mg twice daily
50 - 69kg | 60mg twice daily
70 - 89kg | 80mg twice daily
90 - 109kg | 100mg twice daily
110 – 125kg | 120mg twice daily
More than 125 kg | Discuss with haematologist

Compression Duplex USS leg

ABNORMAL - DVT CONFIRMED

Continue treatment with enoxaparin
Teach woman to self inject, give leaflet and inform of arrangements for safe disposal of sharps
Inform maternal medicine teams prior to discharge and arrange follow up - request “VTEMDT” on NoTIS or complete obstetric haematology referral proforma and send it to FMM at QMC/ANC at CHN

NORMAL – NO DVT or EQUITVOCAL TEST RESULTS

High clinical suspicion
Consider isolated iliac DVT Further investigation is required
Discuss with haematologist before stopping anticoagulant treatment

Low clinical suspicion
Stop LMWH

ABNORMAL - DVT CONFIRMED

CHECK FBC and anti Xa level* if body weight <50kg or > 90kg or symptoms persisting despite treatment

(*needs to be taken into blue citrate bottle 3 - 4 hours after the third enoxaparin injection The therapeutic level to aim for is 0.6-1.2iu/ml. Further anti Xa testing will be guided by the obstetric haematology clinic

General Rules:
1) 3 months’ full anticoagulation required and this must include anticoagulation for at least 6 weeks postpartum. If VTE occurs early in pregnancy, consider reducing the LMWH dose to 0.75% of the initial dose after a period of 10-12 weeks.
2) Individualised labour plan required – aim to reduce heparin to doses for labour provided sufficient time has elapsed since DVT. NOTE – may require admission and conversion to unfractionated heparin pump
3) Advise women regarding injections: do not give if labour suspected – contact labour suite.
Early pregnancy weight | Initial Dose of enoxaparin
--- | ---
Less than 50 kg | 40mg twice daily
50 - 69kg | 60mg twice daily
70 - 89kg | 80mg twice daily
90 - 109kg | 100mg twice daily
110 – 125kg | 120mg twice daily
More than 125 kg | Discuss with haematologist

**General Rules:**
1) 3 months’ full anticoagulation required and this must include anticoagulation for at least 6 weeks postpartum. If VTE occurs early in pregnancy, consider reducing the LMWH dose to 0.75% of the initial dose after a period of 10-12 weeks.
2) Individualised labour plan required – aim to reduce heparin to doses for labour provided sufficient time has elapsed since PE. NOTE – may require admission and conversion to unfractionated heparin pump
3) Advise women regarding injections: do not give if labour suspected – contact labour suite
4) Warn re epidural rules – see guideline.

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**Appendix 2. PREGNANT OR IN THE PUERPERIUM WITH SUSPECTED PULMONARY EMBOLUS?**

- Urgent involvement of critical care team, senior anaesthetist, obstetrician, haematologist, cardiothoracic surgeon
- Give unfractionated heparin and organise confirmatory ECHO +/- CTPA in <1 hour
- Consider thrombolysis, percutaneous thrombus fragmentation or surgical embolectomy

**Early pregnancy weight**

Less than 5
0kg

40mg twice daily

50 – 69kg

60mg twice daily

70 – 89kg

80mg twice daily

90 – 109kg

100mg twice daily

110 – 125kg

120mg twice daily

More than 125 kg

Discuss with haematologist

---

**Features of massive pulmonary embolus:** collapse, hypotension, hypoventilation, peri-arrest

- YES
- NO

**Assess for clinical signs of DVT**

**Compression Duplex USS leg**

Positive

Negative

**PE confirmed or high probability of PE**

- Perform V/Q scan (consider CTPA if unable to perform V/Q scan within 24 hours)
- Continue treatment with enoxaparin
- Teach woman to self inject, give leaflet and inform of arrangements for safe disposal of sharps
- Inform maternal medicine teams prior to discharge and arrange follow up - request ”VTEMDT” on NotIS or complete obstetric haematology referral proforma and send it to FMM at QMC/ANC at CHN.
- Request Troponin
- Review CTPA for right heart strain
- Consider ECHO, if PE diagnosed on USS Doppler leg/V/Q scan
- Further management from respiratory point depends on presence or absence of right heart strain and/or elevated Troponin – see NUH guideline on PE pathways (chart 5): http://nuhnet.nuh_documents/Guidelines/Acute_Medicine/Acute_Medicine/2786.pdf
- Positive
- Negative
- Normal
- Abnormal

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**CTPA**

**Discussions with radiologist regarding alternative or repeat testing.**

- Negative or borderline results but clinical suspicion of PE persists
- Discuss with radiologist regarding alternative or repeat testing.
- Continue LMWH until PE definitely excluded

---

**CHECK FBC and anti Xa level* if body weight <50kg or > 90kg or symptoms persisting despite treatment**

* needs to be taken into blue citrate bottle 3 - 4 hours after the third enoxaparin injection The therapeutic level to aim for is 0.6-1.21ui/ml. Further anti Xa testing will be guided by the obstetric haematology clinic

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**Presentation**

- Normal
- Positive
- Negative
Appendix 3.

Referral form for Obstetric Haematology clinic

<table>
<thead>
<tr>
<th>Patient's name, DOB, Hospital Number</th>
<th>Campus: City/QMC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Date of referral:</td>
</tr>
<tr>
<td></td>
<td>Referring person: SHO/SpR/SR/Consultant</td>
</tr>
<tr>
<td></td>
<td>Lead Consultant:</td>
</tr>
</tbody>
</table>

Gravida........................................ Parity............................EDD................................

Reason for referral:

Other Medical or Surgical history: Any relevant family history:

Current Medications: Allergies:

Plan for delivery:

Vaginal delivery Y/N
Planned Caesarean Section Y/N

Any other specialities involved? If yes, Name of the speciality, Consultant and the reason:
Feedback
We appreciate and encourage feedback. If you need advice or are concerned about any aspect of care or treatment please speak to a member of staff or contact the Patient Advice and Liaison Service (PALS):

Freephone: 0800 183 0204
From a mobile or abroad: 0115 924 9924 ext 65412 or 62301
E-mail: pals@nuh.nhs.uk
Letter: NUH NHS Trust, c/o PALS, Freepost NEA 14614, Nottingham NG7 1BR

www.nuh.nhs.uk

Treatment with Enoxaparin during pregnancy and after delivery
Information for patients

Family Health

If you require a full list of references for this leaflet please email patientinformation@nuh.nhs.uk or phone 0115 924 9924 ext. 67184.

The Trust endeavours to ensure that the information given here is accurate and impartial.
This leaflet is for women who have been advised to have treatment with Enoxaparin during their pregnancy and/or after delivery.

**What is Enoxaparin?**

Enoxaparin is a type of heparin. This is a medicine called an anticoagulant which is used to treat blood clots or reduce the risk of them occurring. In some situations it can be used to try to reduce the risk of miscarriage. Enoxaparin has to be prescribed by a doctor and is given by injection into the fatty layer under the skin (subcutaneous layer). It is usually given once or sometimes twice a day. There are 2 main types of Enoxaparin used in Nottingham; Clexane and Inhixa. These are brand names and the active drug is the same.

**Why do we give Enoxaparin during pregnancy and after delivery?**

During pregnancy the risk of blood clots is increased because of the normal changes happening in the body, to prepare for childbirth. Even following the birth of the baby, the risk of blood clots remain high as the mother’s body adapts to not being pregnant.

Enoxaparin is given to women who are thought to have a higher chance of clots during this time. Some women will be advised to start Enoxaparin whilst they are pregnant because of a blood clot occurring during pregnancy, previous miscarriages or certain pregnancy complications. Some women will only need Enoxaparin for a short time after the birth of their baby.

At the beginning of pregnancy, all women will be assessed by their community midwife to see if they are at increased risk of blood clots. If there is sufficient risk during pregnancy, they will be referred to the hospital clinic to discuss Enoxaparin treatment.

All women will be assessed again at 28 weeks and at the time of delivery and Enoxaparin will be prescribed if this is required.
When is Enoxaparin given?
Enoxaparin treatment may be given during pregnancy and / or for between 10 days and six weeks after the birth of the baby, when the risk of clots is highest.

Although we may start Enoxaparin treatment very early in pregnancy, it is not recommended to start when planning a pregnancy because of the uncertainty about the length of time it may take to conceive. It is preferable to give medication for the least time possible, to reduce the risk of side effects.

Are there any risks with Enoxaparin treatment?
Enoxaparin is considered to be safe to use in pregnancy as it does not cross the placenta and does not affect the baby. The most common side effect for the mother is a small amount of bruising at the injection site.

The risk of bleeding with low dose Enoxaparin is small. Enoxaparin doesn’t usually cause bleeding by itself, but bleeding for other reasons, for example from a threatened miscarriage, may be heavier than normal.

It is important that if you have any bleeding in pregnancy that you do not take any more Enoxaparin and contact the hospital immediately.

Older types of heparin (unfractionated) could rarely cause osteoporosis (thinning of the bones). This is much less likely with modern heparin such as Enoxaparin but it is advisable to have plenty of calcium in your diet (for example from milk, cheese and yoghurt).

Around 5% of women experience a skin rash at the site of the injection. If this happens, please contact the hospital on the numbers on the inside of your hand held notes. If a woman has an allergy to Enoxaparin there are other types of injection which can be used instead.
How is Enoxaparin given?
The syringes come ready prepared with the correct dose for you to give. You will be shown how to give your own injections, and most women, or their partners, manage this very easily.

The needle on the syringe is very fine, and although the injection may sting slightly, it is not usually too painful. You will be given a sharps box (a strong plastic box just for syringes) so that you can dispose of the syringes safely.

Instructions
- Make sure you have a sharps box ready for after the injection
- Wash your hands before giving the injection
- Sit in a comfortable position so that you are relaxed
- Select the site for injection

Suitable injection sites include the sides of your tummy (avoiding the area near your belly button) and the front of your thighs. Avoid bruised, scarred, reddened or hard areas. Rotate the sites of injection to avoid skin irritation.

The needle is very small and does not reach anywhere near your baby, even in the later stages of pregnancy.

Where can I get further information or advice?
If you have any questions or concerns about your Enoxaparin treatment you should discuss these with your community midwife or Doctor.

Useful contact numbers
Labour suite
- City hospital site (0115) 9627710
- Queens Medical Centre (0115) 8754672
What happens during labour and delivery?

It is important that Enoxaparin is stopped at the time of labour and delivery. If you think you are going into labour, do not inject any further Enoxaparin. You should telephone the number for labour suite which can be found on the inside of your hand held notes and also on the back of this leaflet. You will be advised on any further dosing by the hospital team.

If you are having a planed delivery, you should not take any Enoxaparin on the day of delivery.

An epidural or spinal anaesthetic cannot be given within 12 hours of a standard preventative dose of Enoxaparin. When you are admitted to hospital for delivery, the Doctors will ask you when you last took your injection of Enoxaparin.

If you are prescribed a treatment dose of Enoxaparin (for example if you have had a clot during pregnancy, have a condition called antiphospholipid syndrome or a metallic heart valve) an individual plan for delivery will be made when you attend the clinic. An epidural or spinal anaesthetic cannot be given within 24 hours of the last dose of Enoxaparin if you are taking the higher treatment dose of the medication.

What happens after delivery?

Enoxaparin will usually be started again approximately four to six hours after delivery. Some women will need to take Enoxaparin for 10 days but in some cases a 6 week course will be required. You will be given information about this when you are in the hospital and provided with a supply of medication on discharge.

It is important that if you need to see any other Doctors or Dentists whilst you are taking Enoxaparin that you inform them of this treatment.

How is Enoxaparin given? (continued)

Take the syringe and with your thumb and forefinger and carefully remove the cap covering the needle. Take care not to touch the sterile needle. The syringe pre filled and ready to use.

Do not remove the air bubble in the pre-filled syringe. Hold the syringe halfway down the barrel in one hand.

Use your other hand to gently grasp a fold of skin for your injection. Hold the skin between your thumb and index finger.
How is Enoxaparin given? (continued)

Hold the syringe at right angle to the skin and insert the needle all the way into the skin fold.

Push the syringe plunger down steadily until all of the fluid is injected into the skin.

Make sure you hold the skin fold throughout the injection.

Keep your finger pressed on the plunger, release the skin fold and then pull the needle straight out at the same angle that it was inserted.

If you are using Clexane then simply discard the needle into your sharps container.

If you are using Inhixa, press the plunger firmly after removal from the skin. This will cause the needle guard to activate and cover the needle. Then discard into your sharps container.

What do I do if I miss a dose of Enoxaparin?

If you forget to take a dose and are close to your next scheduled dose, skip the missed dose and inject the next dose at the regularly scheduled time. Do not take a double dose. It is important to try and remember to take your Enoxaparin as prescribed.

How do I get a further supply of Enoxaparin?

You will be prescribed 4 weeks of medication at your hospital visit. Further supplies of Enoxaparin should be obtained from your own doctor. You will need to request a repeat prescription from your GP, allowing enough time so that you do not run out of medication. If you have problems getting Enoxaparin from your GP, please contact the hospital for advice.

How is Enoxaparin stored?

Enoxaparin does not need to be kept refrigerated. Store the syringes at room temperature (between 15 and 30°C). It is important to keep the stock of injections and sharps box in a safe place, out of reach of children.

How do I dispose of my needles?

Discard the needle in the sharps container and store out of reach of children. You should ask for a new sharps box before the old one is completely full.

When the container is full to the line, close and lock it and give to your GP, nurse, midwife or the hospital for disposal. Do not put it in the household rubbish.