The Prevention and Treatment of Thrombosis in pregnancy and the postpartum period Guideline

N.B. Staff should be discouraged from printing this document. This is to avoid the risk of out of date printed versions of the document. The Intranet should be referred to for the current version of the document.
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1. Executive Summary

This document aims to highlight women at risk of venous thromboembolism and give guidance during pregnancy as to which patients are at highest risk.

Venous thromboembolism (VTE) is an important direct cause of maternal death in the UK. In the latest CMACE review from 2011, there was a reduction in deaths from VTE with a maternal mortality of 0.79/100,000 maternities. The overall incidence of pregnancy related VTE is 1-2/1000. The risk is present throughout the pregnancy – with a bimodal distribution. Most cases occur in the first and third trimesters, with the majority of maternal deaths occurring in the first trimester. Postpartum, the incidence is 5 x higher than in pregnancy. DVT occurs in 85% of all VTE antenatally. Postnatally PE is more predominant.

Increased coagulation factors, stasis and vascular damage all heighten the thrombotic risk, and diagnosis of VTE in pregnancy is often difficult as the symptoms may mimic those of pregnancy.

DVT in pregnancy is more frequently proximal and 90% + cases affect the left leg. This is due to compression of the Left iliac vein the gravid uterus and the common iliac artery. There are often other risk factors –

<table>
<thead>
<tr>
<th>Non pregnancy related</th>
<th>Pregnancy related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous VTE</td>
<td>Multiple gestations</td>
</tr>
<tr>
<td>Heart disease</td>
<td>Assisted reproduction</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Hyperemesis</td>
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<tr>
<td>Smoking</td>
<td>Pre-Eclampsia</td>
</tr>
<tr>
<td>Obesity</td>
<td>Prolonged labour</td>
</tr>
<tr>
<td>Age &gt;35 years</td>
<td>Caesarean section, esp emergency</td>
</tr>
<tr>
<td>Sick cell disease</td>
<td></td>
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</tbody>
</table>

All women dying from VTE following vaginal delivery in the last Confidential Enquiry were either overweight or over the age of 35 years. Only one of the ten deaths involved operative vaginal delivery. This enquiry concluded that ‘there is a clear need for the development of national guidelines on thromboprophylaxis after normal delivery’.

This document has been formulated in response to this report to ensure pregnant women have a high standard of care and that all risk
factors for VTE have been considered at regular intervals throughout pregnancy and the puerperium, and appropriate action and treatment taken.

1.1 Scope of policy

This policy applies to all members of staff including midwives, Obstetric medical staff and nursing staff on the early pregnancy assessment unit and gynaecology ward.

1.2 Essential Implementation Criteria

Risk assessment of the pregnant women at all stages of pregnancy from

- Initial visit to midwife (may be community midwife)
- Booking visit
- Subsequent visits to antenatal clinic
- Any inpatient admission
- Presenting in labour
- Postpartum

This assessment can be carried out by a midwife, nurse or doctor using the Thromboprophylaxis risk assessment tool for pregnant women – see appendix 1.

2. Aims

This document aims to ensure every woman presenting in pregnancy has ongoing risk assessment for venous thromboembolism, and to treat risk factors appropriately with TED stockings and LMW heparin as needed at any stage of pregnancy and the postpartum period, giving the best possible treatment to these women to prevent VTE and hence serious complications.

3. Responsibilities

All health professionals involved in caring for women in pregnancy and the puerperium are responsible for implementing the policy including

- Midwives
- Doctors
- Nurses / midwives in EPA
- Nurses on gynaecology ward (caring for gestation < 20 weeks)
4. Training

The Directorate will cascade training to both medical and midwifery staff on the use of this guideline and the associated risk assessment tools.

5. Monitoring and Effectiveness

A commitment to audit this policy annually will be undertaken, and the results will be reported back to the Obstetrics and Gynaecology Directorate, and to the clinical governance committee who will act on them. The assessment tool (Appendix 1) will be audited as part of the departmental audit, as well as looking at outcome (review of women presenting with venous thrombosis in pregnancy and postnatally).

6. References

2. Thrombosis in pregnancy : updates in diagnosis and management Ian Greer ASH guidelines 2012 p203-206
5. Royal College of Obstetricians and Gynaecologists Guideline No.37b Diagnosis and management of acute VTE in pregnancy 2009

*This policy has undergone an equality impact assessment screening process using the toolkit designed by the NHS Centre Equality & Human Rights. Details of the screening process for this policy are available from the policy owner.*

**Guideline for Prevention of Thrombosis in Pregnancy and Postpartum Period (thromboprophylaxis)**

**1. Antenatal assessment**

*All women should be assessed for risk of VTE at booking* and a decision made regarding the need for:

1) Post partum venous thromboprophylaxis  
2) Antenatal venous thromboprophylaxis throughout pregnancy  
3) Antenatal venous thromboprophylaxis at times of high risk  
4) Therapeutic anticoagulation throughout pregnancy

A personal and family history of VTE should be sought in all women. The Risk Assessment Tool for use through pregnancy and the postnatal period is enclosed in Appendix 1 and can be printed for use in all clinic/ward settings.

**2) Antenatal thromboprophylaxis**

- The need for thromboprophylaxis during pregnancy will depend on the woman’s medical history, personal and family history of venous thrombosis and inherited and acquired risk factors.

- Women who have an increased risk of VTE but do not require prophylactic LMWH throughout pregnancy will need VTE prophylaxis if immobilised, admitted to hospital or dehydrated.

- All women with an increased risk of venous thrombosis should wear graduated support stockings throughout pregnancy and for 6 weeks post partum.
Antenatal prophylactic doses dalteparin (Fragmin)

- Check **FBC, U+E** and **Coagulation screen** prior to commencing dalteparin
- Suggested prophylactic doses of dalteparin by body weight

<table>
<thead>
<tr>
<th>Booking Weight</th>
<th>Dose of Dalteparin</th>
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<tbody>
<tr>
<td>&lt; 50 kg</td>
<td>2500 units once daily</td>
</tr>
<tr>
<td>50-100 kg</td>
<td>5000 units once daily</td>
</tr>
<tr>
<td>&gt; 100 (BMI &gt; 40)</td>
<td>7500 units once daily</td>
</tr>
</tbody>
</table>

- Anti Xa monitoring should be carried out on all women on 7500 units of dalteparin:
  
  **If levels are normal monitor 6 weekly**
  **If levels outside of the prophylactic range please discuss with a consultant haematologist for advice regarding dose changing and repeat anti Xa in 2-3 weeks**

- Samples should be taken 4hrs post injection into a citrated (blue top) vacutainer

3. Delivery

- Women on any form of heparin should have an agreed delivery plan, involving obstetrician, obstetric anaesthetist and haematologist. For patients not attending the haematology clinic, a birth plan proforma is available

- Graduated support stockings should always be worn during this period.

- The pregnant woman should be advised that once she thinks she is in labour she must contact the labour ward for advice and should not inject any further heparin until she has been assessed.
4. Caesarean section

- All women should wear graduated support stockings.
- At Caesarean section consider the use of interrupted sutures and wound drains if on prophylactic LMW heparin
- Continue prophylactic heparin once haemostasis is secure.

5a. Thromboprophylaxis in the post-operative period for women not already on antenatal heparin

- Graduated support stockings should **always** be worn during this period
- **All** women should receive thromboprophylaxis after Caesarean section
- **At risk** women should be given dalteparin daily for at least 5 days or until fully mobile (which ever is longer) according to their weight. Early mobilisation and good hydration should be encouraged

**Suggested Prophylactic Doses of Dalteparin by Body Weight**

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</tr>
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5b. Duration of Post Partum Thromboprophylaxis

- Transient risk factors – **5 days** dalteparin or until fully mobile
- Previous DVT/PE, or family history of VTE, APLS – **6 weeks** prophylaxis with dalteparin
- Dalteparin is safe during breastfeeding
- The combined oral contraceptive pill should not be prescribed for the first three months post partum for women with risk factors for VTE
6. Epidural and spinal anaesthesia

- All women on heparin prophylaxis with complicating circumstances should be reviewed in the anaesthesia antenatal clinic.

- Always inform the on-call consultant anaesthetist when a pregnant woman on anticoagulation therapy is admitted in labour or with antenatal complications likely to result in imminent delivery.

- **Full anticoagulation is a contra-indication to spinal or epidural anaesthesia.**

- There is a risk of spinal haematoma when an epidural is inserted or removed. Early diagnosis improves outcome. To minimise the risk, the following guideline should be followed:

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Low risk”/“intermediate risk” prophylactic LMWH (5000 units)</td>
<td>Ensure a delay of 12 hours from the last dose before inserting or removing an epidural.</td>
</tr>
<tr>
<td>Therapeutic dose LMWH (more than 5000 units daily)</td>
<td>Ensure a delay of 24 hours from the last dose before inserting or removing an epidural.</td>
</tr>
</tbody>
</table>

- **LMWH should not be given for 4 hours after use of spinal anaesthesia or after the epidural catheter has been removed.**

- The catheter should not be removed within 12 hours of the most recent injection

- These times are a guide and a risk benefit ratio assessment regarding regional or general anaesthesia should be made for
each individual patient dependent on the specific clinical circumstances.

- **Renal impairment:** LMWH is cleared more slowly and the above recommended times may not be sufficient. Discuss with haematologist and perform an urgent anti-Xa level prior to insertion or removal or an epidural.

- If an epidural has to be removed before these times have elapsed or falls out accidentally then documented regular assessment of changes in either motor or sensory function is recommended to ensure that a spinal haematoma is detected early. In addition it is noted that deep-seated back pain may be symptom of a spinal haematoma.

**Guideline for Investigation and Treatment of Thromboembolic Disease in Pregnancy and the Postpartum period**

**Acute Management**

**Background**

VTE continues to be a major cause of maternal death in the UK. VTE is 10 times more common in pregnant than no-pregnant women of the same age. VTE can occur at any stage in a pregnancy including the first trimester but is more common in the puerperium. If a women presents with any symptoms or signs suggestive of a VTE particularly if there is a personal or family history then she will require urgent investigation and treatment.

**Symptoms and Signs of VTE**

Leg pain and swelling (especially if unilateral)
Lower abdominal pain
Low grade pyrexia
Chest pain
Haemoptysis
Dyspnoea
Collapse

However, these symptoms and signs may be subtle.
**Diagnosis of Acute VTE**

Any woman presenting with signs and symptoms suggestive of a VTE should commence treatment with therapeutic doses of low molecular weight heparin (LMWH) until the diagnosis is excluded by objective testing, unless treatment is strongly contraindicated.

**Who Should Care for a Pregnant or Recently Pregnant woman with a VTE?**

Pregnant women should be investigated and managed by a specialist team of senior physicians, senior obstetricians and in a place appropriate to their gestation. This should ideally be in the medical admissions unit if early in pregnancy or on the obstetric unit if later in pregnancy.

The approach to the management of these women should be multidisciplinary and involve Senior Obstetricians, Physicians, Radiologists and Haematologists.

All antenatal women admitted through any other department or speciality within the Trust **must** be reviewed by an Obstetrician, and any care undertaken must then be in conjunction with the woman’s obstetric plan of care.

**Investigations for Diagnosis of an Acute DVT**

Compression duplex ultrasound should be undertaken. If the ultrasound is negative, anticoagulant treatment may be discontinued. If the clinical suspicion is high then anticoagulation should be continued and the scan repeated in 1 week.

When there is a suspicion of iliac vein thrombosis (whole limb swelling and back pain) magnetic resonance venography or conventional venography may be considered.

**Investigations for Diagnosis of an Acute Pulmonary Embolism**

A chest x ray should be performed and compression duplex Doppler if the x ray is normal. If both tests are negative, with persistent clinical suspicion, a perfusion scan or a computed tomography pulmonary angiogram (CTPA) should be considered. VQ scan is safest in the first trimester due to the radiation dosage although please discuss each case individually with a consultant radiologist.
Informed consent should be obtained and the patient made aware of the risk of an undiagnosed PE and subsequent morbidity and mortality is greater than that from the radiation.

If the perfusion scan or CTPA is normal and there is no evidence on ultrasound of a DVT and clinical suspicion of a PE remains high then anticoagulant therapy should be continued until a PE is definitely excluded. If the x ray is abnormal and there is a high clinical suspicion of a PE then a CTPA should be performed.

**D-DIMER TESTING SHOULD NOT BE PERFORMED TO DIAGNOSE ACUTE VTE IN PREGNANCY** unless it is specifically discussed with a consultant haematologist. Only a **negative** result is useful. It should be remembered that the d dimer may be raised in pregnancy due to the natural changes in haemostasis during pregnancy.

**Investigations to Perform before Initiating Heparin Therapy**

- Full Blood Count
- Coagulation Screen including fibrinogen
- U&E’s
- LFT’s

**Additional Therapies in the Management of VTE in Pregnancy**

Full length, correctly fitted, graduated elastic compression stockings should be encouraged. If the woman is particularly obese, early consideration should be given to ordering appropriate sized compression hosiery.

Under the guidance of a Haematologist & Vascular Surgeon, in the presence of an iliac thrombosis consideration should be given to the use of an inferior vena caval filter.

**Maintenance Treatment of VTE**

Therapeutic doses of subcutaneous LMWH should be prescribed for the remainder of the pregnancy (100 units/kg twice daily dalteparin)
Recommended treatment doses of dalteparin based on early pregnancy weight for PE and DVT

<table>
<thead>
<tr>
<th>Initial dose (kg)</th>
<th>Early pregnancy weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>50-69</td>
</tr>
<tr>
<td>Dalteparin</td>
<td>5000 units bd</td>
</tr>
<tr>
<td>50-69</td>
<td>6000 units bd</td>
</tr>
<tr>
<td>70-89</td>
<td>8000 units bd</td>
</tr>
<tr>
<td>&gt;90</td>
<td>10,000 units bd</td>
</tr>
<tr>
<td>bd = twice daily</td>
<td></td>
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</tbody>
</table>

Platelet counts and anti-Xa levels should be monitored monthly under the guidance of a Consultant Haematologist. This assay should be performed 4 hours post dose of morning dalteparin.

Arrangements should be made to allow safe disposal of needles and syringes and out-patient specialist follow-up should be arranged in the haematology obstetric clinic at either NHH or RGH.

**Oral anticoagulants should not be used in the management of VTE in the antenatal period except in certain circumstances for example extension of a venous thrombosis on therapeutic twice daily dalteparin. This should only be initiated after the teratogenic period of 6 - 12 weeks gestation has passed. This should always be done under the close guidance of a consultant haematologist with a specialist interest in obstetrics.**

**LABOUR and DELIVERY**

Where Induction of labour or delivery is planned, LMWH should be discontinued 24 hours before. The aim should be as far as possible to maintain normality through labour and birth and reduce interventional procedures that will increase the risk of VTE. Women taking therapeutic doses of dalteparin should be managed on a case by case basis after careful discussion with the multi-disciplinary team. A plan should be clearly made in the Obstetric notes by 36 weeks gestation. The risks of haemorrhage from continued anti-coagulation should be balanced against the risks of a further thrombo-embolic episode. All these women must have correctly fitted, graduated elastic compression stockings on admission.

The woman taking LMWH maintenance dose who goes into spontaneous labour should be advised to discontinue immediately until post delivery.
If delivery is by elective caesarean section, the treatment doses of LMWH should be omitted for 24 hours before surgery. A thromboprophylactic dose of LMWH (dalteparin 5000 units) should be given in the evening post operative delivery.

**Anaesthesia**

Involvement of a senior anaesthetist during the antenatal period is imperative. All eventualities should be discussed early in with reference to analgesia and anaesthesia with an antenatal documented plan of care. A senior anaesthetist should be contacted when the woman is admitted in labour or delivery planned.

Regional anaesthetic should not be undertaken for at least 24 hours after the last dose of therapeutic LMWH.

The epidural catheter should not be removed within 12 hours of prophylactic LMWH injection and 24 hours after therapeutic LMWH injection.

**Surgery**

A senior obstetrician should be in attendance at time of caesarean section for all women receiving therapeutic LMWH. Attention should be given to haemostasis before closure and a sheath drain as well as an intraperitoneal drain given consideration. Interrupted sutures for skin closure should be used.

The use of a Syntocinon infusion 10 units/hour should be considered following placental delivery.

**Post Partum Management**

Once haemostasis is secure, give prophylactic dalteparin within 12 hrs of delivery. After 24 hrs restart therapeutic dose according to the patients’ weight – see below

**Recommended dosage of dalteparin for adults**

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;45</td>
<td>7 500 units</td>
</tr>
<tr>
<td>46-56</td>
<td>10 000 units</td>
</tr>
<tr>
<td>57-68</td>
<td>12 500 units</td>
</tr>
<tr>
<td>69-82</td>
<td>15 000 units</td>
</tr>
<tr>
<td>83 and over</td>
<td>18 000 units</td>
</tr>
</tbody>
</table>
Once daily administration 200 units/kg body weight according to weight ranges. The single daily dose should not exceed 18,000 units. Single dose syringes are available.

Standard duration of treatment of DVT or PE in pregnancy is for the duration of the pregnancy and for at least 6 weeks postnatally. Some patients may require three months of treatment post delivery if they present close to term. These patients should all be referred to the haematology clinic for counselling and further investigation post delivery.

**The Woman who is at a High Risk of Bleeding but requires Anticoagulation**

- When continued heparin treatment is considered essential, unfractionated IV heparin should be used.
- Protamine sulphate can be used to reverse the effects in discussion with the Haematologist.
- Involvement of a senior haematologist is essential and consideration given to referral to a tertiary unit.

**Post Natal Anticoagulation**

- Post delivery restart IV heparin until the risk of bleeding is reduced. Once haemostasis is secure, convert to therapeutic dalteparin once daily for at least 6 weeks. Follow up in a specialist Haematology Clinic should be arranged on completion of treatment. Warfarin can be considered and both LMWH and Warfarin are safe in breastfeeding mothers. Warfarin should be commenced on the recommendation of the Haematologist and dalteparin continued until therapeutic doses are reached.
Management of Life-Threatening Pulmonary Embolism

CONTACT CONSULTANT ANAESTHETIST, CHEST PHYSICIAN AND HAEMATOLOGIST IMMEDIATELY FOR ADVICE

Massive PE?
If suspect massive PE (definition: one so severe as to cause circulatory collapse (BP<90 systolic, HR >120) or signs of shock: Airway, Breathing, Circulation

Arrange EMERGENCY CTPA with radiologists (contact duty radiologist within normal working hours, or out-of-hours contact the radiology consultant on call via switchboard).
Imaging should be performed as soon as possible, ideally within an hour.
If collapsed patient/ too unwell for CTPA: consider emergency referral to cardiologists for urgent echocardiogram/ consider thrombolysis on clinical grounds.

- All patients should have FBC, coagulation screen, urea and electrolytes, liver function tests, ECG, CXR and arterial blood gases performed.
- Patients on oral anticoagulants or LMWH (prophylactic or therapeutic doses) should proceed directly to imaging investigations.

Patients in whom investigations show an alternative cause for the symptoms ie pneumothorax, heart failure, rib fracture do not need further investigations to exclude a PE.

Massive PE:
- Bolus UFH (5000IU) followed by maintenance infusion when diagnosis considered pending results of investigations.
- Appropriate resuscitation if shocked.
- IF CARDIAC ARREST IS IMMINENT: CONSIDER THROMBOLYSIS ON CLINICAL GROUNDS
- Diagnosis confirmed and BP <90 mmHg: THROMBOLYSE
- If cardiac arrest seems imminent and thrombolysis is either failing or contraindicated, consider mechanical thrombectomy - contact UHW
- If uncertainty regarding thrombolysis contact physician on call
- Patients should be managed on a Level 2 Unit
- High flow oxygen to maintain O₂ saturations >94%; 28% O₂ if patient known to have COPD- monitor arterial blood gases
Submassive PE (PE with evidence of right heart strain but without hypotension):

- Current evidence does not support the use of thrombolysis in these patients. Thrombolysis has been shown to improve haemodynamic parameters more rapidly than heparin, but does not reduce mortality or morbidity.
- Recurrent PE is the principle cause of death in haemodynamically stable patients with PE: thrombolysis does not reduce the rate of recurrent PE when compared with heparin.
- Consideration should be given to managing patients with submassive PE in a closely monitored environment (at least level 1) so that emergency thrombolysis can be given if clinical condition deteriorates.
- Anticoagulate as below for ‘Haemodynamically stable patients with PE’.

Thrombolysis in pregnancy is likely to induce termination: discuss with obstetricians and consider caesarean section.

- Patients at high risk of bleeding, (or if anticoagulation may have to be rapidly reversed) should be given a bolus of unfractionated heparin (5000IU) followed by maintenance UFH infusion (monitor APTT ratio 4 hourly until stable).

- Consider IVC filter if episode of VTE close to due date (discuss with interventional vascular radiologists).

- All patients should have obstetric review. Consider discussing with respiratory physician and/or haematologists if concern.

- All women with negative investigations should be reviewed in the antenatal clinic a week after the investigations, by their own team. This is regardless of whether clinical suspicion is high or low.