Trust Guidelines on Therapeutic Anticoagulation in Pregnancy Including Management of Venous Thromboembolism

A clinical guideline recommended for use

In:	Maternity Services
By:	Medical and Midwifery Staff
For:	Therapeutic Anticoagulation
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Background

Thromboembolism is the most common direct cause of maternal death in the UK. The CEMACH report for 2003-2005 attributed the deaths of 41 women to thromboembolism. Of these, the majority of the deaths (33) were attributed to pulmonary thromboembolism (PTE). The proportion of postpartum deaths following caesarean section have fallen, however no impact has been made on reducing the deaths from antenatal PTE or from PTE following vaginal delivery. Care was judged to be substandard in two-thirds (22 of the 33) cases of PTE. The main causes of failure identified in CEMACH report were inadequate risk assessment in early pregnancy, failure to recognise or act on risk factors and a failure to appreciate the significance of signs and symptoms in the light of known risk factors. There were also failures to initiate treatment promptly or in adequate dosages.

This guideline deals with pregnant women who develop venous thromboembolism (VTE) requiring therapeutic anticoagulation during pregnancy and with pregnant women who are already on therapeutic anticoagulation prior to pregnancy (also refer to guideline on prophylactic anticoagulation in pregnancy).

Management of acute VTE

An individual management plan should be documented in the health records of women who require therapeutic anticoagulation.

Suspicion of VTE

Acute VTE should be suspected during pregnancy in any women with symptoms and signs consistent with possible VTE, particularly if there are other risk factors for VTE (for list of risk factors refer to departmental guideline on prophylactic anticoagulation). The symptoms and signs of VTE include leg pain and swelling (usually unilateral), lower abdominal pain, low-grade pyrexia, dyspnoea, tachypnoea, tachycardia, chest pain, haemoptysis and collapse.

The subjective, clinical assessment of deep vein thrombosis (DVT) and PTE is particularly unreliable in pregnancy. Any woman with signs and symptoms suggestive of VTE should have objective testing performed expeditiously and treatment with low molecular weight heparin (LMWH) should be considered until diagnosis is excluded (especially in the light of known risk factors in the woman), and after discussion with the on-call obstetric consultant.

D-dimer testing should not be performed to diagnose acute VTE in pregnancy. D-dimer can be elevated in pregnancy because of the physiological changes in the coagulation system and also if there is a concomitant problem such as pre-eclampsia. Thus a ‘positive’ D-dimer test in pregnancy is not necessarily consistent with VTE and objective testing is required.

The following baseline blood investigations should be performed

- Full blood count
- Coagulation screen
- Urea and electrolytes
- Liver function tests

Initial anticoagulant treatment of VTE is with therapeutic dose of the low molecular weight heparin, Tinzaparin.

Dosage chart

Therapeutic dose	175 units/kg once daily in 1st and 2nd trimester 90 units/kg 12-hourly in 3rd trimester 175 units/kg once daily postpartum

Tinzaparin comes in fixed dose syringes and multi-dose vials. Only fixed dose syringes should be used for pregnant women. The concentration to use for therapeutic tinzaparin is 20,000 IU/ml.

Diagnosis of an acute DVT

Compression duplex ultrasound should be undertaken where there is clinical suspicion of DVT. If ultrasound is negative and there is a low level of clinical suspicion, anticoagulant treatment should be discontinued. If ultrasound is negative and a high level of clinical suspicion exists, the woman should be anticoagulated and ultrasound repeated in 1 week. If repeat testing is negative, anticoagulant treatment should be discontinued.

When iliac vein thrombosis is suspected (back pain and swelling of the entire limb), magnetic resonance venography or conventional contrast venography may be considered.

Diagnosis of an acute PTE **(see Trust Guideline CA 2084)**

A chest X-ray should be performed. It may identify other pulmonary disease such as pneumonia, pneumothorax or lobar collapse. Abnormal features caused by PTE include atelectasis, effusion, focal opacities or pulmonary oedema. In most cases an ECG and arterial blood gases should be performed.

A half dose perfusion lung scan should be performed. If nuclear medicine is out of action (e.g. out of hours), a Computed Tomography Pulmonary Angiogram (CTPA) should be performed. CTPA should also be carried out where perfusion scan is normal but the clinical suspicion of PTE is high. Where it has already been

commenced, anticoagulant treatment should be continued until PTE is definitely excluded.

Perfusion scanning carries a slightly increased risk of childhood cancer compared with CTPA (1/280,000 versus less than 1/1,000,000) due to higher fetal radiation dose. 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).

Additional therapies

Initial management of DVT should include leg elevation and a graduated elastic compression stocking to reduce oedema. Mobilisation with stockings should be encouraged.

Consider temporary inferior vena caval filter in the perinatal period for women with iliac vein VTE, to reduce the risk of PTE or in women with proven DVT and who have continuing PTE despite anticoagulation.

The management of massive life-threatening PTE in pregnancy

Collapsed shocked patients need to assessed by a team of experienced clinicians, including the on-call consultant obstetrician.

Intravenous unfractionated heparin is the preferred treatment in massive PTE with cardiovascular compromise because of its rapid effect and the extensive experience.

The on-call medical team should be contacted immediately. An urgent CTPA within 1 hour of presentation should be arranged. If massive PTE is confirmed, immediate thrombolysis should be considered.

Management should involve a multidisciplinary resuscitation team including senior physicians, obstetricians, haematologists and radiologists.

Regimen for administration of IV unfractionated heparin (as per RCOG green top guideline):

- Loading dose of 80 units/kg, followed by a continuous intravenous infusion of 18 units/kg/hour
- If a woman has received thrombolysis, the loading dose of heparin should be omitted and an infusion started at 18 units/kg/hour
- Measure APTT 4-6 hours after the loading dose, 6 hours after any dose change and then at least daily when in the therapeutic range. The therapeutic target APTT ratio is 1.5-2.5 times the average laboratory control value.
- The infusion rate should be adjusted according to the APTT as shown in the table

APTT ratio	Dose change (units/kg/hour)	Additional action	Next APTT (hours)
<1.2	+4	Re-bolus 80 units/kg	6
1.2-1.5	+2	Re-bolus 40 Units/kg	6
1.5-2.5	No change	none	24
2.5-3.0	-2	none	6
>3.0	-3	Stop infusion 1 hour	6

In massive life-threatening PTE with haemodynamic compromise thrombolytic therapy should be considered as anticoagulant therapy will not reduce the obstruction of the pulmonary circulation. Problems associated with treatment include maternal bleeding (1-6%) and fetal deaths (1.7%). The decision to offer thrombolytic therapy should be made by a respiratory medicine consultant.

If the woman is not suitable for thrombolysis or is moribund, a discussion with the thoracic surgeons with a view to urgent thoracotomy and surgical embolectomy should be undertaken.

Women receiving therapeutic-dose unfractionated heparin should have their platelet count monitored at least every other day until day 14 or until the heparin is stopped, whichever occurs first.

Maintenance treatment of VTE during antenatal period
Treatment with therapeutic doses of subcutaneous LMWH should be employed during the remainder of pregnancy with the advice of the haematologist (see dosage chart).

Anticoagulant therapy during labour and delivery and regional anaesthesia
The woman taking therapeutic doses of LMWH should be advised that once she is established in labour or thinks that she is labour, she should not inject any further heparin. She should be reassessed on admission to hospital and further doses should be prescribed by medical staff.

Consider induction of labour at term to allow elective changes in dosing. Where delivery is planned (elective caesarean section or induction of labour), therapeutic dose of LMWH should be discontinued 24 hours before planned delivery.

LMWH should be continued in the prophylactic dose during labour.

Regional anaesthetic or analgesic techniques should not be undertaken until at least 24 hours after the last dose of therapeutic LMWH **(see Trust Guideline CA 2031)**. Regional anaesthesia is contraindicated in women receiving IV heparin unless it is safe to temporarily stop the infusion and the APTT becomes normal (check 3 hours after stopping IV heparin).

For delivery by elective caesarean section, a thromboprophylactic dose of LMWH should be given within 3 hours post-operatively (or more than 4 hours after removal of the epidural catheter, if appropriate) and the treatment dose recommenced that evening.

In women receiving therapeutic doses of LMWH, wound drains (abdominal and rectus sheath) should be considered at caesarean section and the skin incision should be closed with staples or interrupted sutures to allow drainage of any haematoma.

Role of warfarin

Warfarin should be avoided during pregnancy unless absolutely necessary e.g. women with metal heart valves. In women with **mechanical heart valves**, an individualised care plan should be drawn after consulting the cardiologists and the haematologists. Warfarin is associated with up to 5% risk of teratogenesis if used between 6 and 12 weeks of gestation. It also increases the risk of miscarriage, fetal and maternal haemorrhage, neurological problems in the baby and stillbirth. It is safe after delivery and during breast feeding. However it requires close monitoring, frequent visits to an anticoagulant clinic and carries an increased risk of PPH and perineal haematoma as compared with LMWH.

Postnatal anticoagulation

Postnatal anticoagulation should begin as soon as possible after delivery provided that there is no postpartum haemorrhage. Therapeutic anticoagulation should be continued for the duration of the pregnancy and for at least 6 weeks postnatally and until at least 3 months of treatment has been given in total.

Both LMWH and warfarin can be used. The woman should be offered a choice after discussion about the need for regular blood tests for monitoring of warfarin, particularly during the first 10 days of treatment.

Postpartum warfarin should be avoided until at least the fifth day and for longer in women at increased risk of PPH. The INR should be checked on day 2 of warfarin treatment and subsequent warfarin doses titrated to maintain the INR between 2-3. Heparin treatment should be continued until the INR is greater than 2 on two successive days. Anticoagulant nurse can help to monitor warfarin dosage and INR measurements (Bleep – 0799 in office hours).

Postnatal clinic review

All women who develop VTE during pregnancy or puerperium should be offered an appointment with an appropriate clinician at 6 to 8 weeks postpartum.

Review should include

- Assessment of post-thrombotic venous damage by a duplex ultrasound of the veins. If any abnormality is noted the woman should be referred to a vascular surgeon. This is because late leg ulceration has been noted in patients who have had deep vein thrombosis.
- Review of Thrombophilia tests and arrangements to repeat them if necessary
- Advice on thromboprophylaxis in future pregnancies and other times of increased risk
- Discussion on hormonal contraception

Auditable standards

The maternity services are committed to the philosophy of clinical audit, as part of its Clinical Governance programme. The standards contained in this clinical guideline will be subject to continuous audit, with multidisciplinary review of the audit results at one of the monthly departmental Clinical Governance meetings. The results will also be summarised and a list of recommendations formed into an action plan, with a commitment to re-audit within three years, resource permitting.

1. Correct therapeutic dose of LMWH.
2. Appropriate interval for administration of postpartum anticoagulant therapy.
3. Documentation of postpartum management plan.
4. Attendance for postnatal review and appropriate thrombophilia testing.

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References

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