South Australian Perinatal Practice Guidelines

Thromboprophylaxis and Thromboembolic disease in pregnancy

Definitions

- **Superficial thrombophlebitis (ST)** refers to a pathological state characterised by an inflammatory-thrombotic process in a superficial vein (also known as superficial venous thrombosis) (Di Nisio et al. 2007)
- **Deep venous thrombosis (DVT)** is thrombus within the deep veins, usually of the lower extremity, and may involve much of the deep venous system
- **Pulmonary embolism (PE)** is movement of a peripheral clot to the pulmonary vasculature. It results from an asymptomatic DVT in 90 % of cases, and may present as sudden death, breathlessness, faintness, collapse or chest pain (SIGN 2002)
- **Venous thromboembolism (VTE)** refers to either the development of a blood clot in a deep vein (DVT) with associated leg pain and swelling or the development of a pulmonary embolus (Gates et al. 2003)
- **Thrombophilia** refers to an inherited or acquired condition which increases an individual's risk of VTE
    - Factor V Leiden (FVL), Prothrombin gene mutation (PGM), Antithrombin III deficiency, Protein C deficiency and Protein S deficiency
    - MTHFR variants and hyperhomocystinaemia are not considered thrombophilias for the purpose of calculating VTE risk

Venous thromboembolism prophylaxis

- Pregnancy increases a woman's risk of VTE 4 – 5 fold, but the overall risk is low, being estimated at 2 per 1,000 pregnancies. Approximately 25 % of events are PE's and of these, 1 in 40 is fatal; PE remains a leading cause of maternal death in developed nations. The risk of VTE is higher in the post-partum period, but up to 50 % of antepartum events occur during the first two trimesters; both antepartum and post-partum thromboembolism prophylaxis must be considered in high-risk women (McLintok et al. 2012)
- Data from the UK Confidential Enquiry into Maternal Deaths (2003 – 2005) suggests that up to 75 % of fatal PE's occurred in women with recognisable risk factors (CEMACH 2007)

NB: Some South Australian tertiary institutions may follow their pre-existing risk assessment and management VTE prophylaxis guidelines for obstetric and general populations

Women in whom antenatal thromboprophylaxis is advised:

- Previous proximal DVT / PE in pregnancy
- Previous unprovoked proximal DVT / PE.
- *Women on long-term anticoagulation for recurrent VTE (or other reason)
- Antithrombin III deficiency and previous VTE
- Nephrotic syndrome
- *Antiphospholipid antibody syndrome (APLS) including clinical features of APLS, and moderate to strong Cardiolipin IgG antibodies

Women in whom it should be strongly considered:

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- Previous distal DVT (in pregnancy or unprovoked)
- Lower limb fracture requiring cast
- Women with previous VTE where the combined oral contraceptive pill was the only risk factor, especially if previous event was a PE or a large / proximal DVT or occurred at age < 20
- FVL homozygous, PGM homozygous, FVL / PGM compound heterozygous
    - If previous proximal VTE
    - If family history of VTE or
    - If other risk factors are present (see below)
- Protein C or Protein S deficiency
    - If previous proximal VTE
    - If family history of VTE or
    - If other risk factors are present (see below)

While standard prophylaxis with low-molecular weight heparin (LMWH) should be sufficient for most women, those marked with an asterisk in the above list should be strongly considered for therapeutic LMWH regimens (i.e. enoxaparin 1mg / kg twice a day), as should any woman who has had an episode of VTE in pregnancy while on prophylactic anticoagulation

Women who should be considered for antepartum prophylaxis if admitted:

- After previous VTE, immobility carries the highest odds ratio of all acquired risk factors. Women who have 2 or more other risk factors should be considered for anticoagulation during antenatal admission

Major antepartum risk factors

- BMI > 30 kg/m^2
- Paraplegia
- Active medical co-morbidity (inflammatory, infective or malignant)
- Superficial thrombophlebitis or significant varicosities
- Family history of VTE (in first degree relatives)
- Pre-eclampsia
- Multiple pregnancy
- Assisted reproduction technology (ART)
- Ovarian hyperstimulation syndrome

Other antepartum risk factors (with lower odds ratios)

- Age > 35 years
- Multiparity > 2
- Smoking
- Hyperemesis

Post-partum anticoagulation:

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- Women on long-term anticoagulation should return to warfarin with appropriate LMWH until INR therapeutic
- Extended (6 weeks) post-partum anticoagulation
    - Any previous VTE (irrespective of circumstances)
    - Known 'high risk' thrombophilia in the absence of personal or family history of VTE: antithrombin III deficiency, Protein C or Protein S deficiency, FVL homozygous, PGM homozygous, FVL / PGM compound heterozygous
    - APLS (if not already on lifelong anticoagulation)
- Women with APLS, antithrombin III deficiency or who have had an episode of VTE on prophylactic anticoagulation should be considered for therapeutic anticoagulation post-partum; for all others prophylactic doses should be sufficient
- Consider post-partum prophylactic anticoagulation for 5 days (or until fully mobile):
    - Emergency caesarean section
    - 2 or more major risk factors
    - At least one major and 2 or more minor risk factors

Major postpartum risk factors:

- Elective caesarean section
- BMI > 30 kg/m^2
- Immobilisation, including paraplegia
- Medical co-morbidity (inflammatory, infective or malignant)
- Pre-eclampsia

Minor postpartum risk factors:

- Age > 35 years
- Prolonged labour (> 24 hrs)
- Smoker
- Post-partum haemorrhage > 1,000 mL
- Transfusion
- Extensive perineal trauma and prolonged repair
- Gross varicose veins / superficial thrombophlebitis
- Multiparous > 3

NB: Local guidelines regarding mandatory anticoagulation in at-risk post-partum women may be in place within your institution, and should be used where available

There is no evidence to support increased doses of LMWH (i.e. > 40 mg enoxaparin daily) in women with weight > 90 kg. There may be reason to believe higher doses are more effective with morbidly obese women (BMI > 40), and some institutions will have local guidelines regarding tailored weight-based dosing. If there are concerns about the adequacy of LMWH dosing in overweight or obese women on extended courses of LMWH, then monitoring with Factor Xa levels may be appropriate

Other antepartum care

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- Women with unknown thrombophilia status, but family history of VTE in first degree relative (especially if pregnancy-related) should be considered for thrombophilia testing + / - post-partum anticoagulation

Drug and dosing	Acceptable time after drug for performing a neuraxial regional block	Acceptable time post-insertion (and epidural catheter removal) for drug administration
LMWH - Standard prophylactic dosing (e.g. enoxaparin 40 mg daily SC)	- Delay until at least 10-12 hours after the last dose.	The first dose LMWH: - Post-caesarean section: 6-8 hours postoperatively *and*, if an epidural catheter has been inserted, at least four hours after the epidural catheter has been removed. - Post-vaginal birth: 6-8 hours after insertion *and*, if an epidural catheter has been inserted, at least two hours after the epidural catheter has been removed The epidural catheter is usually removed following vaginal birth or caesarean section. If, however, the epidural catheter remains in-situ post-delivery and prophylactic LMWH is to be administered: - The epidural catheter should be removed at least 10-12 hours after the last dose of LMWH AND - The next dose of LMWH should not be given until at least 2 hours after the removal of the epidural catheter

- Antepartum assessment by physician / clinical haematologist (early) and anaesthetist (between 34^{+0} weeks and 36^{+0} weeks gestation)
- Monitor for symptoms and signs of venous thromboembolism (see below) at routine antepartum clinic visits and educate high risk women regarding signs and symptoms of DVT / PE
- TEDS for women not on anticoagulation if:
  - Significant lower limb varicosities
  - Inpatient admission and risk factors

High risk group

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LMWH - Therapeutic (e.g. enoxaparin 1mg / kg every 12 hours or enoxaprin 1.5 mg / kg daily)	> Delay until at least 24 hours after the last dose	> Post-delivery dosing should be individualised* as the risk of obstetric-related bleeding needs to be considered. > Following spinal / epidural puncture, or after removal of an epidural catheter, the next dose of LMWH should be delayed for at least 4 hours > The management plan should be developed following consultation between the obstetrician, anaesthetist and physician
Unfractionated heparin – prophylactic	> Delay until 4-6 hours	The epidural catheter is usually removed following vaginal birth or caesarean section. If, however, the epidural catheter remains in-situ post-delivery and prophylactic unfractionated heparin is to be administered: > The epidural catheter should be removed at least 4-6 hours after the last dose of unfractionated heparin AND > The next dose of prophylactic unfractionated heparin should not be given until at least one hour after insertion or removal of epidural catheter
Unfractionated heparin – therapeutic	> Cease heparin infusion 4-6 hours before insertion. Check APTT 3-4 hours after ceasing infusion and ensure within normal range before insertion	> *Post-delivery dosing should be individualised as the risk of obstetric-related bleeding needs to be considered > Following spinal / epidural puncture, or after removal of an epidural catheter, the commencement of therapeutic heparin should be delayed for at least 4 hours > The management plan should be developed following consultation between the obstetrician, anaesthetist and physician
Fondaparinux – prophylactic dosing e.g. 2.5 mg daily	Delay at least 36-42 hours	The first dose prophylactic fondaparinux should be delayed 12 hours after insertion or removal of epidural catheter
*If operative delivery or PPH, there may be additional obstetric reasons to delay commencing anticoagulant medication		

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- Commence subcutaneous low molecular weight heparin as early in pregnancy as practicable. Document plan for managing anticoagulation around delivery and duration of post-partum treatment

Dosage

- Prophylactic LMWH (for doses, see table 2 below)
- Educate women in self injection technique to enable out-patient management as appropriate

Management of anticoagulation around delivery and anaesthesia

- Withhold **prophylactic anticoagulation** for at least 12 hours before scheduled surgery or induction of labour (IOL) or if signs and symptoms of impending labour. In general, give last dose of LMWH by 2000 hours on day before IOL or planned LSCS
- Withhold **therapeutic anticoagulation** with LMWH for at least 24 hours before scheduled surgery, IOL or if spontaneous onset of labour. For women with high risk of VTE consideration to commencing intravenous (IV) unfractionated heparin (UFH) should be given (see chapter 106 Heparin infusion [unfractionated]). This can be ceased 4 – 6 hours before scheduled surgery or when it is estimated delivery is 4 – 6 hours away. Monitoring with APTT (in the absence of significant lupus anticoagulant) before procedures is recommended
- Mechanical prophylaxis, such as calf compression, should be considered in high risk women during operative delivery. Contraindications include severe peripheral vascular disease, severe peripheral neuropathy, severe lower limb oedema

Anaesthetic considerations:

- Abnormal coagulation at the time of insertion or removal of neuraxial catheter has been associated with spinal or epidural haematomas. For this reason, coagulation should be normalised at the time of neuraxial blockade and removal of catheter (see Table 1). If anticoagulation is unable to be ceased within a safe time frame, alternatives such as patient-controlled analgesia for labour or general anaesthetic for caesarean section will need to be considered

Both fresh frozen plasma (FFP) and protamine sulphate can be used to reverse the effects of anticoagulation with unfractionated heparin if required

Table 1: Anticoagulation and timing of insertion of neuraxial block or removal of neuraxial catheter [13, 14, 15]

- After taking Anaesthetic issues into consideration, anticoagulation with LMWH should be recommenced no earlier than 6 – 8 hours and within 16 hours post-delivery if there is no concern regarding excessive blood loss
  - Other contraindications to routine anticoagulation include:
    - Bleeding disorder or trauma
    - Thrombocytopenia (platelet count< 75)

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- Cerebrovascular accident within 4 weeks
- Severe hepatic disease
- Bacterial endocarditis
- Renal impairment (creatinine clearance < 30 mL / min)
- Uncontrolled hypertension (BP > 200 mmHg systolic or 120 mm Hg diastolic)

- Women who are at increased risk or have been assessed as definitely requiring post-partum anticoagulation, but who have contraindications must be discussed further with Obstetric Medicine or Haematology
- Warfarin can be started in the afternoon (1600 hours) of the day following delivery

Management of thromboembolic and other thrombotic conditions

Superficial thrombophlebitis (ST)

- In people diagnosed with ST
  - 6 % to 44 % are associated with or develop deep vein thrombosis
  - 20 % to 33 % are associated with asymptomatic pulmonary thromboembolism
  - 2 % to 13 % are associated with symptomatic pulmonary thromboembolism (Di Nisio et al. 2007)
- Refer care to Level IV or above health unit for multi disciplinary team management, which may include an obstetrician, obstetric physician, anaesthetist and haematologist

Symptoms

- Pain and inflammation over superficial vein(s) with areas of intravascular thrombus palpable
- May also have erythema and oedema in surrounding area
- Chills, high fever, and leucocytosis indicate septic superficial thrombophlebitis (staphylococcus aureus is the most frequent cause)
- Increasing swelling may indicate association with DVT

Investigations

- Compression duplex ultrasound of both limbs to exclude DVT (detects the extension of thrombi and their characteristics)
- Occasionally venography may be used

Bloods

- Complete blood picture
- C-reactive protein
- Serum urea and electrolytes

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- Coagulation studies
- Liver function tests (to confirm normal hepatic and renal function before commencing anticoagulant therapy)

Treatment

- ST is generally a self limiting condition that can be managed with simple analgesics (if < 2 cm in extension) without hospital admission
- Treatment aims to relieve painful local symptoms and prevent extension or the development of thromboembolic events
    - Aspirin 100 mg daily for 5 – 7 days
    - Prophylactic LMWH if failure of resolution on aspirin or extensive area of thrombus on initial examination or if ascending long saphenous thrombosis
    - Analgesia - topical with nonsteroidal, anti-inflammatory creams e.g. Hirudoid cream
    - Graduated elastic compression stockings (reduces venous pooling)
    - Exercise and ambulation (reduces possibility of DVT)
    - Antibiotics are usually not indicated unless documented infection
    - Investigations should be repeated if worsening symptoms or failure of resolution after 1 week on LMWH

Venous thromboembolism

- Refer to Level IV or above health unit for multi disciplinary team management, which may include an obstetrician, obstetric physician, anaesthetist, haematologist and intensivist
- Following confirmed diagnosis of deep venous thrombosis or pulmonary thromboembolism, inform woman of:
    - The diagnosis
    - Potential complications
    - Treatment

Deep venous thrombosis

- Up to 90 % of deep venous thromboses in pregnant women occur in the left leg and over 70 % are **iliofemoral** in their location (Nelson-Piercy & Greer in Powrie et al. 2010; RCOG 2010)
- Distal deep venous thromboses are sited distal to the popliteal vein

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- Proximal deep venous thromboses are in or above the popliteal vein, including pelvic vein thromboses
- An iliofemoral DVT is more likely to embolise than a calf vein thrombosis. Pulmonary thromboembolism has a maternal mortality of 1:100,000 (Nelson-Piercy & Greer in Powrie et al. 2010)

Symptoms and signs

- Recommend early presentation for assessment / investigation if any symptoms and / or signs of deep venous thrombosis
- Clinicians should be aware of the potential for deep venous thrombosis to present in pregnancy with lower abdominal or groin pain only
    - Leg pain or discomfort in the absence of trauma (especially left leg)
    - Swelling
    - Tenderness
    - Increased temperature and oedema
    - Lower abdominal pain
    - Dyspnoea, chest pain, haemoptysis and collapse
    - Elevated white cell count
- Dorsiflexion of the calf causes pain (Homan's sign). Homan's sign is unreliable as it is present in only 8 % to 30 % of symptomatic women with deep venous thrombosis and can be elicited in up to 50 % of symptomatic women who do not have a deep venous thrombosis (Hamper et al. 2007)

Investigations

- Compression duplex ultrasound
- When iliac vein thrombosis is suspected, (backpain and swelling of the entire limb) magnetic resonance venography or contrast venography (abdominal shielding) may be considered (RCOG 2010) if ultrasound fails to visualise thrombus adequately
- D dimer measurements are UNRELIABLE in pregnancy/post partum: a negative D-dimer does not exclude VTE in a high risk woman

Treatment

Commence therapeutic low molecular weight heparin until deep venous thrombosis is excluded by objective testing (see table 2 below). Analgesia - topical with nonsteroidal, anti-inflammatory creams e.g. Voltaren gel or an antithrombotic cream (e.g. Hirudoid) – evidence base is low

- Encourage the woman to avoid prolonged immobilisation (i.e. stretch legs every two hours during the day) and elevate the leg to avoid unnecessary pressure on the legs
- Graduated elastic compression stockings – Below knee compression socks (class I) are acceptable for women without thigh or knee swelling. Class II compression

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stockings (Firm compression 20-30 mm Hg) are more effective than class I compression stockings **if there is persisting leg oedema**

- Class II compression stockings should be taken off at night and do not need to be worn on the unaffected leg

Pulmonary thromboembolism

- Occurs in approximately 1:7,000 pregnancies
- Deep venous thrombosis usually precedes pulmonary thromboembolism and the thrombosis may be asymptomatic until embolisation occurs

Symptoms and signs

- Dyspnoea with or without reduced oxygen saturation on pulse oximetry
- Collapse with hypotension
- Chest pain (pleuritic)
- Haemoptysis
- Faintness
- Tachycardia or arrhythmia
- Raised jugular venous pressure
- Focal signs in chest as well as symptoms and signs associated with deep venous thromboses in peripheries

Investigations

- Bloods
  - Arterial blood gas on air
  - Complete blood count
  - Coagulation screen (a prolonged APTT should raise the suspicion of a lupus anticoagulant being present, consult the physician / haematologist)
  - Troponin (not diagnostic of PE: consider other causes such as myocardial infarction or pre-eclampsia)
  - Urea and electrolytes
  - Liver function tests (if not already on anticoagulant therapy)
- Electrocardiogram
- Chest X-ray
- A consultant physician opinion should be sought before proceeding to further imaging

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- If persistent clinical suspicion of acute pulmonary thromboembolism, a ventilation-perfusion (V / Q) lung scan or a computed tomography pulmonary angiogram (CTPA) should be performed
- Informed consent should be obtained from the woman before making the decision to undergo CTPA or V / Q scanning
    - Advise that V / Q scanning carries a slightly increased risk of childhood cancer compared with CTPA (1 / 280,000 versus < 1 / 1,000,000) but carries a lower risk of maternal breast cancer (lifetime risk increased by up to 13.6 % with CTPA, background risk of 1 / 200 for study population) (RCOG 2007)

Treatment

- **NB**: Where a provisional diagnosis of deep venous thrombosis or pulmonary thromboembolism has been made, low molecular weight heparin anticoagulant treatment should be given until the diagnosis is clarified. Treatment for other differential diagnoses such as bronchopneumonia should be given concurrently whilst awaiting definitive diagnosis

Massive, life threatening pulmonary thromboembolism

- Intravenous unfractionated heparin is the preferred treatment in massive pulmonary thromboembolism with cardiovascular compromise
- Collapsed, shocked patients need to be assessed by a team of experienced clinicians, including the on-call consultant obstetrician, physician, consultant anaesthetist, and cardiologist / intensivist who should decide on an individual basis whether the woman receives intravenous unfractionated heparin or thrombolytic treatment and referral to an Adult intensive care service

Methods of Anticoagulation

Low molecular weight heparin

- Low molecular weight heparin is the Australasian medical consensus recommendation for standard initial therapeutic and prophylactic treatment of VTE in the absence of contraindications.
- In DVT or PTE, treatment with LMWH should be given until the diagnosis is excluded by objective testing, unless treatment is strongly contraindicated
- Women over 100 kg should only receive 100 mg bd (maybe up to 120 mg bd). In high-risk women e.g. APLS, consider monitoring with Factor Xa levels to ensure adequacy of dosing
- Duration of therapy is three months for an uncomplicated distal DVT, and six months for women with either PE or significant proximal DVT. If therapy is due to finish before the end of the pregnancy, prophylactic anticoagulation should be continued for the remainder of the pregnancy and for a further six weeks post-partum
- In selected women with distal DVT's, give consideration to reducing LMWH to a single daily dose of 1.5 mg / kg after at least six weeks on 1mg / kg twice daily

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Table 2: Low molecular weight heparin dosage

Low molecular weight heparin	Therapeutic dose	Prophylactic dose
Enoxaparin (Clexane)	1 mg / kg every 12 hours	40 mg daily
Dalteparin (Fragmin)	100 IU / kg every 12 hours	5,000 IU daily

- Enoxaparin is available in preloaded syringes of 20 mg, 40 mg, 60 mg, 80 mg and 100 mg
- Dalteparin is available in preloaded syringes of 2,500 IU, 5,000 IU, 7,500 IU and 10,000 IU
- Administer via subcutaneous injection (rotate sites)
- Duration of treatment is individualised according to indication

Side Effects

- Bruising and pain at injection site
- Thrombocytopenia
- Osteoporosis (reversible)
- Rise in serum transaminases (ALT)

Intravenous unfractionated heparin

- Intravenous (IV) unfractionated heparin (UH) infusion is the preferred mode of treatment in acute venous thromboembolism and pulmonary embolism when there is haemodynamic instability (RCOG 2010)
- Used as a substitute for therapeutic low molecular weight heparin during the 24 - 36 hour period before elective induction of labour or caesarean section

Table 3 Intravenous unfractionated heparin

Heparin sodium: 5,000 IU per 1 mL
Before commencing infusion: Take blood for group and save, Activated Partial Thromboplastin Time (APTT), complete blood picture and any thrombophilia studies that may be recommended

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Dosage and administration

NB: Omit the loading dose and commence infusion at 1,000 IU per hour in the following:

- **If the woman has received thrombolysis**
- **If the last dose of therapeutic LMWH (e.g. Clexane®) has been given < 12 hours before commencing IV UH infusion**

Set up

- Draw up x 5 ampoules of heparin sodium 5,000 units (IU) (a total of 25,000 IU) and make up to 50 mL in sodium chloride 0.9 %
- Administer through syringe pump

Loading dose

- Give intravenous bolus loading dose of 5,000 IU heparin sodium

Maintenance dose

- Commence IV UH infusion at 1,000 IU per hour

Ongoing maintenance dose according to APTT

- Check APTT 4-6 hours after bolus dose, and 6 hours after any dose change
- In consultation with physician / obstetrician, adjust the rate of administration of UH to prolong the APTT to a range 1.5 to 2.5 times the laboratory baseline value
- If APTT is within the therapeutic range, maintain infusion rate and check APTT daily
- Contact haematologist for advice if a therapeutic APTT is not established within the first 24 hours

Precautions

- If bleeding occurs, cease UH and notify medical officer
- Cease intravenous UH when in labour or 6 hours before
- Elective operative delivery: check APTT after 4 hours to assess return to normal before considering regional anaesthesia

Last reviewed 23/07/2012

Side effects

- Thrombocytopenia
- Osteoporosis (reversible)
- Rise in serum transaminases

Investigations

- Women on regular therapeutic heparin should have daily APTT and alternate daily complete blood picture for thrombocytopenia
- If there is a significant fall in the platelet count, an opinion should be sought from a consultant haematologist / physician

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Complications

- If a complication occurs during treatment (e.g. haemorrhage), the appropriate consultant opinion as to whether to continue, vary or discontinue the unfractionated heparin treatment, should be sought
- In acute pulmonary embolism, oxygen and intravenous fluids may be required to maintain PO_2 and cardiac output

Clinical considerations

- Do not draw blood from the same line or arm as the unfractionated heparin infusion
- Fill coagulation tubes to the specified mark and send to the lab urgently to avoid erroneous results or clotting and the need for a further sample to be taken
- Avoid intramuscular injections and arterial stabs during anticoagulant treatment
- Place a copy of this guideline in the clinical chart for ready reference by clinical staff

Heparin antidote

- If anticoagulation with heparin needs to be discontinued for clinical reasons, termination of the heparin infusion will usually suffice
- Discuss management with consultant Physician and / or Haematologist
- If an immediate effect is required, the heparin antidote protamine sulphate may be considered (see PPG 'Heparin infusion [unfractionated]' for further information)

Thrombolytic treatment

- Thrombolytic treatment (e.g. Tenecteplase, Actilyse) may be considered in massive life-threatening pulmonary thromboembolism with haemodynamic compromise as anticoagulant therapy will not reduce the obstruction of the pulmonary circulation (RCOG 2010)
- Thrombolytic treatment converts plasminogen to plasmin, which then catalyses the breakdown of the fibrin matrix of the thrombus
- After thrombolytic treatment has been given, an infusion of unfractionated heparin can be given, but the loading dose should be omitted

Table 4 Thrombolytic treatment

Tenecteplase (Metalyse®)
Tenecteplase (TNK / Metalyse®) ADEC category C is the international standard drug of choice for thrombolytic treatment in PTE
Precautions
Ensure resuscitation equipment is at the bedside Cardiac monitoring

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Adjunctive treatment	> **Pre-Tenecteplase:** Give intravenous bolus loading dose of 5,000 IU heparin sodium > **Post-Tenecteplase:** Commence IV unfractionated heparin infusion at 1,000 IU per hour (as above)
Dosage	> 0.5 mg / kg – Maximum dose = 50 mg (=10,000 units)
Administration	> Use a dedicated intravenous access and administer via a **non-glucose containing line** > Do not add any other medication to tenecteplase solution > Immediately before use, reconstitute the 50 mg vial by adding 10 mL sterile water for injections from the pre-filled syringe into the vial containing the tenecteplase (5 mg / mL) > Withdraw the correct volume of reconstituted solution according to the medical order > Give as an IV bolus dose over 10 seconds
Last reviewed 23/07/12	

Adopted with permission from RAH ICU Drug dosing and administration guidelines – March 2006

Labour and birth management

- An elective birth is preferred for women who are receiving therapeutic or prophylactic anticoagulant treatment
- Use anti-embolic stockings and encourage mobilisation
- In women with need for therapeutic anticoagulation (i.e. management of thrombosis or prosthetic valve), cease LMWH and commence intravenous unfractionated heparin 24 – 48 hours before elective procedure
- Aim to maintain APTT at 1.5 – 2 times laboratory baseline

Induction of labour

- Cease intravenous unfractionated heparin once established in labour. This allows 4 – 6 hours for the APTT to return to normal before birth
- Ensure active management of third stage

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Caesarean section

- Cease intravenous unfractionated heparin 6 hours before elective operative delivery and send urgent APTT prior to regional anaesthesia
- Ensure anti embolic stockings are in place before caesarean section
- Consider use of compression devices (e.g. electrical calf stimulators) in the postpartum period

Regional anaesthesia / analgesia considerations

- See Table 1: Anticoagulation and timing of insertion of neuraxial block or removal of neuraxial catheter for management of therapeutic anticoagulation

Non elective deliveries

- Monitor for signs or symptoms of spinal haematoma (e.g. lower limb numbness or weakness, severe back pain, urinary or faecal incontinence)

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Postpartum management

- Duration of post-partum anticoagulation should be decided before discharge. Women should continue LMWH initially, with plan to cease after agreed treatment time or until stabilised on therapeutic warfarin
- Warfarin can be commenced before discharge, or women may elect to remain on clexane until they are able to easily access regular blood testing for INR as an outpatient
    - If the woman has previously been on warfarin it can either be recommenced at the usual dose or a higher dose can be given for the first two days. For other women, commencing at 10 mg daily for two days before taking an INR is reasonable
- For women on warfarin, adjust dose according to the INR range of 2 to 3; in some women, the target INR may be higher. INR should be done before starting warfarin and after 2 days. Thereafter it can be done every 1 – 2 days until stable
- Once stabilised, measure INR weekly for first month, then monthly thereafter
- Neither warfarin nor heparin (LMWH or unfractionated heparin) appears in breast milk to any significant degree and breastfeeding is not contraindicated
- Before discharge the woman should be fully informed about the potential complications and possible drug interactions from warfarin treatment where used
- The combined oral contraceptive is contra-indicated in women with a history of thrombosis. Non-hormonal contraceptive measures must be discussed and arranged before discharge

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Abbreviations

APLS	Antiphospholipid antibody syndrome
APTT	Activated partial thromboplastin time
ART	Assisted reproduction technology
bd	Twice a day
BMI	Body mass index
cm	Centimetre(s)
DVT	Deep venous thrombosis
e.g.	For example
et al.	And others
FVL	Factor V Leiden
g	Gram(s)
IOL	induction of labour
INR	International normalised ratio
IU	International units
IV	Intravenous
kg	Kilogram(s)
LMWH	Low-molecular weight heparin
LSCS	Lower segment caesarean section
mg	Milligram(s)
mL	Millilitre(s)
min	Minute(s)
mmHg	Millimetres of mercury
MTHFR	Methylene tetrahydrofolate reductase
PGM	Prothrombin gene mutation
PE	Pulmonary embolism
PTE	Pulmonary thromboembolism
ST	Superficial thrombophlebitis
TEDS	Thrombo embolic deterrent stockings
%	Percentage
U	Units
UK	United Kingdom
UFH	Unfractionated heparin
VTE	Venous thromboembolism

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1.0	28 July 04	23 July 12	Original version
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