Greater Glasgow & Clyde Obstetric Guidelines

Thromboembolic Disease in Pregnancy and the Puerperium – Acute Management

Introduction and background

Venous thromboembolism (VTE) is a major cause of maternal death in the United Kingdom. Pregnant women presenting with a suspicion or symptoms of VTE, **regardless of gestation**, should be referred to an obstetrician. Women who are collapsed or shocked should be referred to Emergency Medicine and be reviewed there by an obstetrician. (for QEUH see Appendix 1) Clinical assessment and diagnosis of women presenting with suspected VTE in pregnancy is unreliable and therefore it is imperative that a clinical suspicion is always confirmed by appropriate objective testing. Acute VTE should be suspected during pregnancy in women with symptoms and signs consistent with possible VTE, particularly if there are other risk factors for VTE (see table 1). The symptoms and signs of VTE include leg pain and swelling (usually unilateral), lower abdominal pain, low grade pyrexia, dyspnoea, chest pain, haemoptysis and collapse.

Table 1. Risk factors for VTE in pregnancy and the puerperium (RCOG GTG 37a, 2015):

Pre- existing	Previous VTE	
	Thrombophilia	*Heritable* Antithrombin deficiency Protein C deficiency Protein S deficiency Factor V Leiden Prothrombin gene mutation
		Acquired Antiphospholipid antibodies Persistent lupus anticoagulant and/ or moderate/ high titre anticardiolipin antibodies and/ or $ß_2$ -glycoprotein 1 antibodies.
	Medical comorbidities e.g. cancer; heart failure; active SLE, inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type 1 diabetes mellitus with nephropathy; sickle cell disease.	
	Current intravenous drug user	
	Age > 35 years	
	Obesity (BMI > 30kg/m²) either pre pregnancy or in early pregnancy	
	Smoking	
	Gross varicose veins (symptomatic or above knee with assoc phlebitis, oedema/ skin changes)	
	Paraplegia	

Obstetric risk factors	Multiple pregnancy Current pre- eclampsia	
	Caesarean section Prolonged labour (> 24hrs) Mid- cavity or rotational operative delivery Stillbirth Preterm birth Post partum haemorrhage (>1 litre/ requiring blood transfusion)	
New onset/ transient *These risk factors are potentially reversible and may develop at later stages in gestation than the initial risk assessment or may resolve and therefore what is important is an ongoing individual risk assessment*	Any procedure in pregnancy or puerperium except immediate repair of the perineum, e.g. appendicectomy, post partum sterilization Bone fracture	
	Hyperemesis	
	Ovarian hyperstimulation syndrome (first trimester only)	Assisted reproductive technology (ART), in vitro fertilization (IVF)
	Admission or immobility (≥ 3 days bed rest)	e.g. pelvic girdle pain restricting mobility
	Current systemic infection (requiring intravenous antibiotics or admission to hospital)	e.g. pneumonia, pyelonephritis, post partum wound infection
	Long distance travel (>4hrs)	

Massive pulmonary embolism (PE)

Massive life-threatening PE is an obstetric emergency. Collapsed, shocked patients need to be assessed by a team of experienced clinicians, including the on-call obstetric team (including consultant obstetrician) and anaesthetic staff, and if appropriate the hospital cardiac arrest team (call 2222).

Factors to consider are:

- ABC – maternal resuscitation should commence. If cardiac arrest, CPR should be performed with the woman in a left lateral tilt. A perimortem Caesarean section should be performed by 5 minutes, if resuscitation is unsuccessful and the pregnancy is >20 weeks. This is primarily to assist resuscitation of the mother.
- Intravenous unfractionated heparin is the preferred treatment in massive PE with cardiovascular compromise (see section 11, below)
- The team should consider on an individual basis whether a woman receives intravenous unfractionated heparin, thrombolytic therapy or thoracotomy and surgical embolectomy
- The on-call medical team should be contacted immediately. An urgent portable echocardiogram or CTPA, ideally within 1 hour of presentation, should be arranged. If massive PE is confirmed or in extreme circumstances prior to confirmation, immediate thrombolysis should be considered.

Guideline for management of DVT & sub-massive PE

1 Diagnostic testing:

Deep Vein Thrombosis
Compression Duplex ultrasound is the primary diagnostic test for DVT. If ultrasound confirms the diagnosis of DVT, anticoagulant treatment should be continued. If ultrasound is negative and a high level of clinical suspicion exists, anticoagulant treatment should be discontinued and the ultrasound repeated on days 3 and 7. If repeat testing is negative, no further treatment is required. If repeat testing confirms DVT, anticoagulant treatment should be recommenced and continued. When iliac vein thrombosis is suspected, (back pain and swelling of the entire limb), Doppler ultrasound of the vein, magnetic resonance venography or conventional contrast venography may be considered, and discussed with a radiologist.

Pulmonary Embolism
Perform chest X-ray. This may provide a reason for the chest symptoms. The woman's legs should be carefully assessed for symptoms and/or signs of DVT. An electrocardiograph should be performed and pulse oximetry is often more useful and safer than arterial blood gases.

If the chest x-ray is normal, PE is suspected, and there are symptoms and/or signs of DVT, leg Doppler scans should be performed. If these show a DVT, anticoagulant treatment should be continued and further radiological investigations are not required.

If the chest x-ray is normal, PE is suspected and there are NO symptoms and/or signs of DVT, a ventilation/perfusion scan (VQ scan) or CT-pulmonary angiography (CT-PA) should be performed. V/Q scanning is first line investigation for suspected PTE in all maternity units within NHS GG&C. If the patient has an abnormal chest X-ray or is unstable, a CT-PA is the investigation of choice.

2 Blood tests: that should be performed prior to starting heparin, include:

full blood count
coagulation screen
U&Es and LFTs

Testing for D-dimers and performing a thrombophilia screen in the acute situation, should **not** be performed.

3 Embolic Stockings: Organise for fitting of a graduated elastic compression stocking on the affected leg via an orthotics department (or an equivalent locally available service). Accurate fitting and careful instruction in the correct application of the hosiery is essential to avoid discomfort and assist rather than

prevent venous return.

4 Start treatment with a LMWH:

Refer to the RCOG guideline, '*Thromboembolic disease in pregnancy and the puerperium: acute management'* (April 2015).

https://www.rcog.org.uk/globalassets/documents/guidelines/gtg-37b.pdf

There is more experience of enoxaparin (Clexane) being used in pregnancy.

(i) Initial dose of **enoxaparin** (~1mg/kg SC 12 hourly, or 1.5mg/kg SC once daily) is determined as follows:

Early Pregnancy Weight	**Initial Dose of Enoxaparin**	
	1mg/kg SC 12 hourly	***1.5mg/kg SC once daily***
<50kg	40mg twice daily	Use a dose of 1.5 mg/kg, choosing a prefilled syringe dose *(syringes available include 60, 80, 100, 120 and 150 mg).* If the dose used is +/- 10% of correct dose, check anti-Xa level approximately 4 hours post dose after at least 3 doses have been given
50-69kg	60mg twice daily	
70-89kg	80mg twice daily	
90-109kg	100mg twice daily	
110-125kg	120mg twice daily	
› 125kg	Discuss with haematologist	

5 Monitoring LMWH therapy:

Anti-Xa activity - Routine measurement of peak anti-Xa activity for patients on LMWH for treatment of acute VTE in pregnancy or post-partum is not recommended except in women at extremes of body weight (<50kg and ≥90kg) or with other complicating factors (for example with renal impairment or recurrent VTE) putting them at high risk.

If once daily dosing is commenced, (1.5 mg/kg) and a prefilled syringe with the exact dose is not available, (see above), the anti-Xa level should be checked if the dose is +/- 10% of the calculated dose. Where monitoring of peak anti-Xa activity is indicated, a level of 0.5–1.2 units/ml, approximately 4 hours post-injection, after at least 3 doses have been given, is the aim.

Platelets - Routine platelet count monitoring is not required in obstetric patients who have received only LMWH. If the patient has received heparin (unfrationated or LMWH) in the last 100 days, then the platelet count should be checked after 24 hours

of initiating treatment. Further, obstetric patients who are postoperative and receiving unfractionated heparin, should have platelet count monitoring performed every 2-3 days from days 4-14 or until heparin is stopped.

6 LMWH:

Full dose LMWH should be continued throughout pregnancy (enoxaparin 1mg/kg 12 hourly or 1.5mg/kg daily).

Pregnant women who develop heparin-induced thrombocytopenia or have heparin allergy and require continuing anticoagulant therapy should be managed with the heparinoid, danaparoid sodium or fondaparinux, under specialist advice.

7 Labour:

Advise a woman to withhold enoxaparin once she thinks she is in labour - further doses will be prescribed by hospital staff following assessment.

Patients undergoing induction of labour or elective Caesarean section should discontinue their heparin treatment temporarily 24 hours before IOL or section (see section 9). Where delays occur leading to a prolonged period off anticoagulation, discuss management with a consultant obstetrician.

Where the thromboembolism has occurred ≥36+0 weeks gestation or the onset of labour occurs within 4 weeks of the acute episode of thrombosis, the advice of a senior haematologist should be sought – this may involve the use of unfractionated heparin or an IVC filter.

8 Regional anaesthesia:

Regional anaesthesia/analgesia may not be an option for women on anticoagulant therapy and the anaesthetists should be aware of such patients when in labour ward and preferably earlier if delivery has been planned.

Epidural anaesthesia can be sited only after discussion with a senior anaesthetist, in keeping with local anaesthetic protocols. When a woman presents whilst on a therapeutic regimen of LMWH, regional techniques should not be employed for at least 24 hours after the last dose of LMWH. LMWH should not be given for at least four hours after the epidural catheter has been removed and the cannula should not be removed within 12 hours of the most recent injection.

9 Elective Caesarean section:

Enoxaparin - omit the previous evening's dose and the morning dose of enoxaparin and give a thromboprophylactic dose (enoxaparin 40mg) 4 hours post caesarean section (or more than 4 hours post removal of epidural catheter). Re-commence full treatment dose LMWH 24 hours following the prophylactic enoxaparin dose.

Because of the increased risk of wound haematoma in patients receiving therapeutic doses of LMWH, consideration should be given to the use of drains (abdominal and rectus sheath) and closing the skin incision with staples or interrupted sutures to allow drainage of any haematoma.

10 Haemorrhage:

Any woman considered to be at high risk of haemorrhage, in whom continued heparin treatment is considered essential, should be managed with IV unfractionated heparin until the risk factors for haemorrhage have resolved eg major ante-partum haemorrhage, coagulopathy, progressive wound haematoma, suspected intra-abdominal bleeding, post partum haemorrhage. Unfractionated heparin has a shorter half life than LMWH and its activity is more completely reversed with protamine sulphate.

11 Administration of intravenous unfractionated heparin:

Note: prolonged use of unfractionated heparin in pregnancy is associated with osteoporosis and fractures.

- loading dose of 80 units/kg, followed by a continuous intravenous infusion of 18 units/kg/hour
- if a patient has received thrombolysis (see below), the loading dose of heparin should be omitted and an infusion started at 18 units/kg/hour
- it is mandatory to measure APTT level 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 usually 1.5-2.5 times the average laboratory control value.
- using this weight-adjusted regimen, the infusion rate should be adjusted according to the APTT ratio as below:

APTT ratio	dose change (units/kg/hr)	additional action	next APTT (hr)
< 1.2	+ 4	Re-bolus 80 u/kg	6
1.2 - 1.5	+ 2	Re-bolus 40 u/kg	6
1.5 - 2.5	no change		24
2.5 - 3.0	- 2		6
> 3.0	- 3	stop infusion 1 hr	6

12 Postnatal anticoagulation:

Anticoagulant therapy 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. Women should be offered a choice of LMWH or oral anticoagulant for

postnatal therapy 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 postpartum haemorrhage.

Warfarin therapy should be administered at 1800 hours. A loading regimen of 7mg day 1, 7mg day 2 should be commenced. Check INR on morning of day 3 and daily thereafter to determine dose from chart below. LMWH should be continued until the INR is satisfactory (2 - 3) on two successive days. Once the INR has been 2-3 for 2 consecutive days a repeat INR should be performed within one week. The patient must always be referred to an appropriate outpatient monitoring service.

The direct oral anticoagulants (DOACs) can be considered in the post partum period if a woman has decided not to breastfeed. The DOAC of choice in GG&C is apixaban. This should be commenced at a dose of 5mg bd as long as the woman has already received at least 1 week of therapeutic dose LMWH. This should be commenced once the woman is considered to no longer to be at increased bleeding risk. The first dose should be 12 hours (bd LMWH regimen) or 24 hours (od LMWH regimen) after the last dose of LMWH.

Anticoagulant service providers

Within GG&C all community INR monitoring services are provided by the Glasgow and Clyde Anticoagulant Service (GCAS), rather than individual GPs.

The GCAS Anticoagulant Monitoring and Clinic referral form contains all necessary information and other contact details – see StaffNet

Breast feeding is not contra-indicated with either heparin or warfarin.

Suggested protocol for commencing warfarin treatment in the puerperium (RCOG, 2015)

Day of warfarin treatment	INR	Warfarin dose (mg)
First		7.0
Second		7.0
Third	<2.0	7.0
	2.0-2.1	5.0
	2.2-2.3	4.5
	2.4-2.5	4.0
	2.6-2.7	3.5
	2.8-2.9	3.0
	3.0-3.1	2.5
	3.2-3.3	2.0
	3.4	1.5
	3.5	1.0

Fourth	<1.4	>8.0
	1.4	8.0
	1.5	7.5
	1.6-1.7	7.0
	1.8	6.5
	1.9	6.0
	2.0-2.1	5.5
	2.2-2.3	5.0
	2.4-2.6	4.5
	2.7-3.0	4.0
	3.1-3.5	3.5
	3.6-4.0	3.0
	4.1-4.5	omit next day's dose then give 2 mg
	>4.5	omit two days' doses then give 1 mg

13 Discharge Planning

Following DVT, a graduated elastic compression stocking should be worn on the affected leg to reduce pain and swelling. This should be appropriately fitted by an orthotics department (or an equivalent locally available service). The role of stockings in the prevention of post-thrombotic syndrome is unclear.

Patients developing VTE in pregnancy should be referred to anticoagulant clinic: Please refer to current version of “Therapeutics: A Handbook for Prescribers”.

Sources of information:

Greer IA, Thomson AJ. RCOG Green-Top Guideline 37b. Thromboembolic disease in pregnancy and the puerperium: acute management. RCOG Press (2001, revised 2007 and 2015)

Bates SM, Greer IA, Middeldorp S, Veenstra DL, Prabulos AM, Vandvik PO. Venous thromboembolism, thrombophilia, antithrombotic therapy, and pregnancy: the 9th ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2012; 141: e691s-e736s

Scottish Intercollegiate Guidelines Network (SIGN). Prevention and management of venous thromboembolism (Clinical Guideline 122). SIGN, Edinburgh, 2010

NHS Greater Glasgow and Clyde Acute Services Division Therapeutics A Handbook for Prescribers

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Other Professionals Consulted:

Obstetric Clinical Governance Group: 12th October 2017

GGC Thrombosis Committee

Title: Thromboembolic Disease in Pregnancy and the Puerperium – Acute Management Obstetrics

Implementation / Review Dates

Implementation date: 18th October 2017
Review date 1st October 2020

APPENDIX 1

QEUH Guideline for pregnant women presenting with non-obstetric symptoms, with specific reference to VTE

For non-obstetric symptoms:

1. All pregnant women referred to the Maternity Assessment Unit (MAU) will be seen in MAU by the obstetric team.

2. All pregnant women referred to IAU (Immediate Assessment Unit, QEUH) will be seen there by a physician.

3. Pregnant women assessed in IAU, and who are fit for discharge, will be transferred to MAU for a routine antenatal check before going home. This applies to women from 12 weeks gestation onwards, and is organised by phoning MAU – 24 hour service.

4. Pregnant women who are admitted to a medical ward should be notified to the labour ward outliers board so that the on-call obstetric team are aware of the admission. This is done by phoning the labour ward.

5. Pregnant women admitted to the antenatal ward requiring medical review – contact the relevant specialty registrar (9-5pm) or medical registrar out of hours (24 hour service). Specialty consultants provide a 24 hour on-call service.

With specific reference to Pulmonary embolism / DVT:

1. All pregnant women with ?DVT will be seen in MAU for assessment. Pregnant women with ?DVT who are referred to the physicians will automatically be diverted to MAU. This is irrespective of gestational age, booking status and includes women up to 6 weeks post partum. The nurse in charge of IAU will advise the GP to refer the patient to MAU.

2. Pregnant women referred by their GP to the physicians with breathlessness / chest pain, symptoms for which one of the differential diagnoses is PE, will be seen in IAU by a physician. Following assessment, a stable patient in whom other pathology has been excluded but who requires to wait (eg. overnight) for a VQ scan may be more appropriately admitted to the antenatal ward pending this investigation. The VQ request will be generated in IAU/ARU prior

to transfer. Page the labour ward registrar (17111) to organise a bed. Subsequent inpatient care will be taken over by the obstetric team.

3. Postnatal women referred by their GP to the physicians with breathlessness / chest pain, symptoms for which one of the differential diagnoses is PE, who have been assessed in IAU and are stable, will be admitted to the postnatal ward pending investigations for PE. This will be accommodated up to six weeks postpartum. The VQ request will be generated in IAU/ARU prior to transfer. Page the labour ward registrar (17111) to organise a bed. Subsequent inpatient care will be taken over by the obstetric team.

4. The ongoing management of all pregnant women with VTE, and initial follow up of postnatal women with VTE, is via the obstetric haematology clinic. For an appointment phone 62252 (9-5pm)

5. There is no role for outpatient management of pregnant women with VTE in the anticoagulation service that is run by advanced nurse practitioners – outpatient management comes under the umbrella of obstetrics once the diagnosis has been made.

Contact Numbers:

Maternity Assessment Unit – 64363 (24/7)

Labour ward – 62292 or 64317 (24/7)

IAU Consultant – 82360

IAU Charge Nurse – 82468

Medical Registrar – page 14666, for general medical advice (24/7)

Specialty Registrars (for example cardiology, respiratory, renal, endocrine, ID) – contact via switchboard

Specialty Consultants – contact via switchboard (24/7)

Maternity Medical Records 62252 – Obstetric Haematology Clinic (Dr Brennand), for appointment for pregnant / postnatal women with confirmed VTE

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Implementation Date: 18th October 2017

Review Date: 1st October 2020

MANAGEMENT OF THERAPEUTIC ANTICOAGULATION IN PREGNANCY, DELIVERY AND POSTPARTUM

Patient Information

Thrombosis History:

☐ DVT in current pregnancy
Date of event:……..

☐ PE in current pregnancy
Gestation at time of event:……

Or/

☐ Long term anticoagulation pre pregnancy
Anticoagulant:……

Indication:……

Anticoagulation during pregnancy

Agent:

Dose:

Planned Duration of Treatment:

Delivery Plan

☐ Spontaneous labour (ensure patient knows not to take LMWH if suspects/in labour)

Or/

☐ Planned delivery: Induction of labour caesarean section

Date of planned delivery:

Last dose of LMWH: Date…….Dose……..Time…….
(*Therapeutic LWMH should be discontinued 24 hours prior to IOL or caesarean section)*

Authorized by Dr…….Date…….

Post Delivery

1. **Delivery with no bleeding complications:**

   a. Prophylactic dose LWMH dosage…….. 4 hours post delivery or 4 hours post epidural catheter removal

   b. Treatment dose LMWH 24 hours post prophylactic dose e.g. Clexane 1.5mg/kg single daily dose (use postpartum weight) Weight……..Dose……..

Authorized by Dr……Date…….

2. **Delivery with bleeding complications:**

Options are to delay dose of LMWH, or in rare situations consider the use of UF Heparin. These cases should be discussed with the on-call haematology consultant

Plan:

Duration of postnatal anticoagulation

All women treated for a VTE in the current pregnancy require a minimum of 6 weeks postnatal anticoagulation at treatment dose and a total duration of therapy of 3 months (therefore for some women treatment dose anticoagulation will be extended beyond 6 weeks postpartum depending on when the VTE occurred). Women should not convert from LMWH to Warfarin or a DOAC until Day 5 postpartum. DOACs are contraindicated in breast feeding women

Planned duration of PN anticoagulation

Options: ☐ **Continue LWMH** ☐ **LMWH/Warfarin** ☐ **DOAC**

(*Refer to GG&C Guideline Thromboembolic Disease in Pregnancy and the Puerperium – Acute Management for dosing regimens)*

Postnatal Follow-up Arrangements:

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Approved by Obstetric Guideline Group:……Approved by Obstetric Governance Group:……..

Implementation Date:……04/12/18…….Review Date:……01/12/23……...