Northern Devon Healthcare NHS Trust

Document Control

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Reducing the risk of thrombosis and embolism during pregnancy and the puerperium Guidelines			
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2. Contents

3. Introduction

This document sets out Northern Devon Healthcare NHS Trust's best practice guidelines for reducing the risk of thrombosis and embolism during pregnancy and the puerperium.

4. Purpose

4.1. The purpose of this guideline is to set out the following principles, which should be applied in order to reduce the risk of thromboembolic disorders during pregnancy and puerperium.

- Thromboembolic risk assessment during pregnancy and puerperium.
- Thromboprophylaxis during pregnancy and puerperium.

4.2. These guiding principles are in accordance with best practice guidance from the Royal College of Obstetricians and Gynaecologists (2015). This clinical guideline applies to all staff employed within the Maternity Services and must be adhered to. Non-compliance with this guideline may be for valid clinical reasons only. The reason for non-compliance must be documented clearly in the patient's healthcare record.

5. Background

5.1. Absolute risk of venous thrombosis (VTE) in pregnancy and the puerperium is low with overall incidence of 1–2 per 1000. The relative risk of (VTE) in pregnancy is increased four- to six-fold and this is increased further postpartum.

5.2. Many fatal antenatal VTE events occur in the first trimester and therefore prophylaxis for women with previous VTE should begin early in pregnancy. The risk increases with gestational age, reaching a maximum just after delivery. C-section is a significant risk factor but women having vaginal deliveries are also at risk.

5.3. There was a significant fall in the maternal mortality rate from pulmonary embolism(PE) from 1.56 per 100,000 maternities in 2003 -2005 to 0.70 per 100,000 maternities in 2006–2008 due largely to reductions in deaths from antenatal VTE as well as deaths from VTE after vaginal delivery and it seemed likely as a result of adopting published recommendations of RCOG (2004) on "Thromboprophylaxis during pregnancy, labour and after normal vaginal delivery". However, 79% and 89% of the women who died from PE in the UK between 2003 and 2005 and between 2006 and 2008 respectively had identifiable risk factors.

5.4. According to "Saving Lives, Improving Mothers' Care" report by MBRRACE - UK in 2018, maternal deaths from direct causes are unchanged with no significant change in the rates between 2011–13 and 2014–16. Thrombosis and thromboembolism remain the leading cause of direct maternal death during or up to six weeks after the end of pregnancy in the UK

6. Abbreviations

6.1.	PE	Pulmonary embolism
6.2.	VTE	Venous thromboembolism
6.3.	LMWH	Low molecular weight heparin
6.4.	UFH	Unfractionated heparin
6.5.	AES	Anti-embolism stocking
6.6.	APS	Antiphospholipid syndrome
6.7.	OHHS	Ovarian hyperstimulation syndrome
6.8.	IVF	In vitro fertilisation

7. Responsibility

All midwives and doctors are responsible for thromboprophylactic risk assessment of pregnant women during any stage of pregnancy and puerperium in any setting. Immediately after delivery, risk assessment should be undertaken by the midwife from labour ward for normal vaginal deliveries and medical staff for operative deliveries. If the woman requires LMWH thromboprophylaxis following completion of the risk assessment, midwives should refer them to medical staff for further assessment and prescription of the LMWH. In any circumstances, if in any doubt, a Consultant Obstetrician must be consulted. If still in doubt, please seek an opinion from a Haematologist.

8. General principles of reducing the risk of thrombosis and embolism during pregnancy and the puerperium

8.1. Risk assessments

All women should undergo a documented assessment of risk factors for VTE pre-pregnancy or in early pregnancy. (Appendix A). Magnitude of risk should be classed as high, intermediate and low based on the type of risk factors identified.

Within NDDH, risk assessments should be completed and documented within the relevant Perinatal Institute notes of the women:

Pregnancy Notes (green): The Antenatal venous thromboembolism (VTE) assessment (page 13).

Postnatal Notes for Mother (dark purple): Postnatal venous thromboembolism (VTE) assessment (page 3).

Risk assessment should be repeated if the woman is admitted to hospital for any reason or develops other inter-current problems.

Risk assessment should be repeated intrapartum or immediately postpartum.

Reassessment of VTE risk and thromboprophylaxis after miscarriage and ectopic pregnancy are as important as reassessment of risk after giving birth

The risk of VTE should be discussed with women at risk and the reasons for individual recommendations explained.

8.2. Antenatal prophylaxis (Appendix B)

8.2.1. Previous VTE (Appendix F)

Discuss with haematologist

Recommend thromboprophylaxis with LMWH for those with **previous VTE, unprovoked or idiopathic or related to oestrogen or transient risk factors other than major surgery,** throughout antenatal period, beginning from as early in pregnancy as practical. Those with a single **previous VTE related to major surgery** and no other risk factors can withhold until 28 weeks gestation provided no additional risk factors are present.

Offer higher dose LMWH (either 50%,75% or full treatment dose) to women with **previous VTE associated with antithrombin deficiency or antiphospholipid syndrome (APS), or with recurrent VTE (who will often be on long term oral anticoagulants)** antenatally (and for 6 weeks post-partum or until returned to oral anticoagulant therapy after delivery). Manage in collaboration with haematologist in antenatal anti-Xa monitoring.

Manage with standard doses of LMWH to **previous VTE with other heritable thrombophilic defects.**

8.2.2. Asymptomatic thrombophilia (Appendix G)

Discuss with haematologist.

Offer antenatal LMWH throughout pregnancy and (6 weeks postnatally) to those with **higher risk thrombophilic tendency**; Antithrombin, protein C or S deficiency, those with >one thrombophilic defects (including homozygous Factor V Leiden, compound heterozygous, homozygous prothrombin gene mutation).

Consider antenatal LMWH to **lower risk thrombophilic tendency;** heterozygosity for factor V Leiden or prothrombin gene mutation or antiphospholipid antibodies in the presence of three other risk factors throughout pregnancy and two other risk factors from 28 weeks.

8.2.3. Current risk factors

Consider antenatal prophylaxis with LMWH throughout pregnancy (and 6 weeks postnatally) for women with **four current risk factors** other than previous VTE, first trimester risk factors or admission to hospital.

Consider antenatal prophylaxis with LMWH from 28 weeks of gestation (and 6 weeks postnatally) for women with **three current risk factors** other than previous VTE, first trimester risk factors or admission to hospital.

8.2.4. First trimester risk factors

Consider thromboprophylaxis with LMWH in women with **first trimester risk factors** such as hyperemesis or ovarian hyperstimulation syndrome (OHSS) in the first trimester and discontinue when they resolve. IVF pregnancy with three other risk factors should be considered LMWH starting in the first trimester.

Consider **thrombophilia testing** to women with no personal or risk factors for VTE but who have a family history of an unprovoked or oestrogen-provoked VTE in first degree relative when aged under 50 years either antithrombin deficiency or where the specific thrombophilia has not been detected.

8.3. Labour and Delivery

Women receiving LMWH during the antenatal period should be advised to stop administering any further LMWH if they have vaginal bleeding or they think they are in labour. These women should be reassessed on admission and any further doses prescribed by medical staff. The timing of any epidural and last dose of LMWH should be discussed with the anaesthetist to minimize or avoid the risk of epidural haematoma.

Regional techniques should not be used until at least 12 hours after the previous prophylactic dose of LMWH or at least 24 hours after the last therapeutic dose of LMWH. For therapeutic doses or higher prophylactic doses (see Appendix D), no regional anaesthetic technique should be used unless previously discussed with Consultant Anaesthetist.

LMWH should not be given for four hours after use of spinal anaesthesia or after the epidural catheter has been removed; six hours if the procedure was traumatic (this should be discussed with anaesthetist).

The epidural catheter should not be removed within 12 hours of the most recent injection of prophylactic LMWH.

Women receiving antenatal LMWH having an elective caesarean section should receive a thromboprophylaxis dose of LMWH on the day prior to delivery and, on the day of delivery, any morning dose should be omitted, and the operation performed that morning or afternoon and give next dose at least 4 hours post spinal in most cases, on day of surgery.

If regional analgesia has not been used, the first thromboprophylaxis dose of LMWH should be given as soon as possible after delivery provided there is no postpartum haemorrhage.

Women at high risk of haemorrhage with risk factors including major antepartum haemorrhage, coagulopathy, progressive wound haematoma, suspected intra-abdominal bleeding and postpartum haemorrhage may be managed with anti-embolism stockings (AES), or intermittent pneumatic compression devices. Unfractionated heparin (UFT) may also be considered. Thromboprophylaxis should be started or reinstituted as soon as the immediate risk of haemorrhage is reduced.

If a woman develops a haemorrhagic problem while on LMWH the treatment should be stopped and expert haematological advice sought.

8.4. Thromboprophylaxis after delivery (Appendix C)

Advise to continue LMWH for 6 weeks in high-risk women and for 10 days in intermediate-risk women.

Recommend prophylactic LMWH for 10 days postpartum to any woman with **two or more current or persisting risk factors** (other than previous VTE or thrombophilia).

Recommend six weeks' postnatal prophylaxis with LMWH to those with **asymptomatic thrombophilia; antithrombin, protein C or S deficiency or those with more than one thrombophilia defect** (including homozygous Factor V Leiden, homozygous prothrombin gene mutation and compound heterozygotes).

Consider postnatal LMWH for 10 days to other asymptomatic thrombophilic defects; **heterozygosity for factor V Leiden or prothrombin gene mutation or antiphospholipid antibodies in the presence of one other risk factor.**

All women with **BMI greater than or equal to 40 kg/m2** should be considered for prophylactic LMWH in doses appropriate for their weight for 10 days after delivery (Appendix D)

Risk assessment should be performed in each woman at least once following delivery and before discharge and arrangements made for LMWH prescription and administration (usually by the woman herself) in the community where necessary.

In women who have additional persistent (lasting more than 10 days postpartum) risk factors, such as prolonged admission, wound infection or surgery in the puerperium, thromboprophylaxis should be extended for up to 6 weeks or until the additional risk factor/s is/are no longer present.

8.5. Thromboprophylactic agents

Low molecular weight heparins (LMWH)

Low molecular weight heparins are the agents of choice for antenatal and postnatal thromboprophylaxis and safe in breast feeding. Doses of LMWH are based on the body weight (Appendix D), either booking or most recent weight.

LMWH is safe in pregnancy and breast feeding.

It is only necessary to monitor the platelet count if the woman has had prior exposure to unfractionated heparin (UFH).

Monitoring of anti-Xa levels is not required when LMWH is used for thromboprophylaxis.

Doses of LMWH should be reduced in women with renal impairment.

LMWH should be avoided, discontinued or postponed in women at risk of bleeding after careful consideration of the balance of risks of bleeding and thrombosis. (Appendix E)

Women with previous or current allergic reactions to LMWH should be offered an alternative preparation or alternative form of prophylaxis.

Further advice on the management of a woman with both VTE risk factors and bleeding risk factors or LMWH allergy may be sought from a haematologist with expertise in the management of thrombosis and bleeding disorders in pregnancy.

8.6. Unfractionated heparin (UFH)

In women at very high risk of thrombosis (previous VTE &/ thrombophilia), UFH may be used peripartum in preference to LMWH where there is an increased risk of haemorrhage or where regional anaesthetic techniques may be required.

If UFH is used after caesarean section (or other surgery), the platelet count should be monitored every 2–3 days from days 4–14 or until heparin is stopped.

8.7. Warfarin

Women on long-term warfarin or other oral anticoagulants should be counselled about the risks of these agents to the fetus and advised to stop their oral anticoagulant therapy and change to LMWH as soon as pregnancy is confirmed, ideally within 2 weeks of the missed period and before the sixth week of pregnancy.

Women receiving long-term anticoagulation with warfarin can be converted from LMWH to warfarin postpartum when the risk of haemorrhage is reduced, usually 5–7 days after delivery. Warfarin is safe in breastfeeding.

8.8. Aspirin

Aspirin is not recommended for thromboprophylaxis in obstetric patients.

8.9. Anti-embolism Stockings (AES)

The use of properly applied AES of appropriate size and providing graduated compression with a calf pressure of 14–15 mmHg is recommended in pregnancy and the puerperium for women who are hospitalised and have a contraindication to LMWH, those who are at high risk of VTE (in combination with LMWH) and women travelling long distance for more than 4 hours.

9. Education and Training

There is no formal training programme for VTE in pregnancy. However, all senior midwives and obstetricians are responsible to support the junior staff to learn the risk assessment and prevention of VTE during pregnancy and puerperium.

10. Consultation, Approval and Review Processes

The author consulted with all relevant stakeholders. Please refer to the Document Control Report.

Final approval was given by the maternity specialist governance forum.

The guideline will be reviewed every three years. The author will be responsible for ensuring the guidelines are reviewed and revisions approved in accordance with the Document Control Report.

11. Monitoring Compliance and Effectiveness

Incidents related to venous thromboembolism will be closely monitored and investigated by the Maternity Services Risk Co-ordinator. All maternity staff will learn from the incidents related to VTE.

12. References

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Baglin T et al. Guidelines on the use and monitoring of heparin. (British Society for Haematology) British Journal of Haematology, 133, 19-34

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Appendix A: Risk factors for venous thromboembolism in pregnancy and the puerperium

	Risk Factors
Pre-existing	Previous venous thromboembolism
	Thrombophilia **Heritable:** Antithrombin deficiency Protein C deficiency Protein S deficiency Factor V Leiden Prothrombin gene G 20210A mutation **Acquired:** Antiphospholipid antibodies Persistent lupus anticoagulant and/ Persistent moderate / high titre anticardiolipin antibodies and /or β_2-glycoprotein 1 antibodies
	Medical co-morbidities (cancer, heart failure, active SLE, inflammatory conditions - inflammatory bowel disease or inflammatory polyarthropathy, nephrotic syndrome , type 1 diabetes mellitus with nephropathy, sickle cell disease, intravenous drug user)
	Age > 35 years
	Obesity (BMI ≥ 30 kg/m^2) either pre-pregnancy or in early pregnancy
	Parity ≥ 3
	Smoking
	Gross varicose veins (symptomatic or above knee or with associated phlebitis, oedema/ skin changes)
	Paraplegia
Obstetric	Multiple pregnancy
	Current pre-eclampsia
	Caesarean section PPH (>1 litre /requiring blood transfusion) Prolonged labour > 24 hours Mid-cavity or rotational operative delivery Stillbirth Preterm birth
New onset/Transient / Potentially reversible (*)	Any surgical procedure in pregnancy or puerperium (e.g. ERPC, appendicectomy, postpartum sterilization) except immediate repair of the perineum Bone fracture

	Hyperemesis, dehydration OHSS (first trimester only) (ART, IVF) Admission or Immobility (≥ 3 days' bed rest, symphysis pubis dysfunction restricting mobility, paraplegia) Current systemic infection (requiring intravenous antibiotics or admission to hospital) e.g. pneumonia, pyelonephritis, postpartum wound infection Long-distance travel (> 4 hours)

Note: (*); potentially reversible risk factors which may develop at later stages in gestation than the initial risk assessment or may resolve. Therefore, continuing individual risk assessment is important.

Women with previous VTE should have a careful history documented. Where objective documentation is not available, the previous diagnosis of VTE can be assumed in cases where the woman gives a good history and received prolonged (greater than 6 weeks) therapeutic anticoagulation.

Appendix B: Antenatal risk assessment and management (to be assessed at booking and repeated if admitted)

- Any previous VTE except a single event related to major surgery

→ **High risk**

Requires antenatal prophylaxis with LMWH

Refer to haematologist

- Hospital admission
- Single previous VTE related to major surgery
- High risk thrombophilia + no VTE
- Medical co-morbidities e.g. cancer, heart failure, active SLE, IBD or inflammatory polyarthropathy, nephrotic syndrome, type 1 DM with nephropathy, sickle cell disease, current IVDU
- Any surgical procedures e.g. appendicectomy
- OHSS (1st trimester)

→ **Intermediate risk**

Consider antenatal prophylaxis with LMWH

- Obesity (BMI >30 kg/m^2)
- Age >35
- Parity≥3
- Smoker
- Gross varicose veins
- Current pre-eclampsia
- Immobility e.g. Paraplegia, PGP
- Family history of unprovoked or oestrogen-provoked VTE in 1st degree relative
- Low-risk thrombophilia
- Multiple pregnancy
- IVF/ART

Transient risk factors

- Dehydration/ hyperemesis, current systemic infection, long distance travel

→ **4 or more risk factors:**

Prophylaxis from 1st trimester

3 risk factors:

Prophylaxis from 28 weeks.

→ **Fewer than 3 risk factors:**

(Lower risk)

Mobilisation and avoidance of dehydration

Appendix C: Postnatal risk assessment and management (to be assessed on delivery suite)

- Any previous VTE
- Anyone requiring antenatal LMWH
- High risk thrombophilia
- Low risk thrombophilia+ family history

→ **High risk**
At least 6 wks. postnatal prophylactic LMWH

- Caesarean section in labour
- BMI≥40 kg/m^2
- Readmission or prolonged admission in the puerperium(≥3 days)
- Any surgical, procedure in puerperium except immediate repair of perineum
- Medical co-morbidities e.g. cancer, heart failure, active SLE, IBD or inflammatory polyarthropathy, nephrotic syndrome, type 1 DM with nephropathy, sickle cell disease, current IVDU

→ **Intermediate risk**

At least 10 days postnatal prophylactic LMWH

If persisting or >3 risk factors, consider extending thromboprophylaxis with LMWH

- Obesity (BMI >30 kg/m^2)
- Age >35
- Parity≥3
- Smoker
- Elective caesarean section
- Gross varicose veins
- Current pre-eclampsia
- Current systemic infection
- Immobility e.g. Paraplegia, PGP, Long distance travel
- Family history of VTE
- Low-risk thrombophilia
- Multiple pregnancy
- Preterm delivery in this pregnancy<37+0 weeks
- Still birth in this pregnancy
- Mid-cavity operative delivery
- Prolonged labour>24 hrs.
- PPH>1 L or blood transfusion

2 or more risk factors

Fewer than 2 risk factors →

Lower risk

Early mobilisation and avoidance of dehydration

Appendix D: Suggested thromboprophylaxis doses for antenatal and postnatal LMWH

Weight	Enoxaparin	Dalteparin
<50 kg	**20mg daily**	**2500units daily**
50-90 kg	**40mg daily**	**5000units daily**
91-130 kg	**60mg daily**	**7500units daily**
131-170 kg	**80mg daily**	**10000units daily**
>170 kg	**0.6mg/kg/day**	**75units/kg/day**
High prophylactic dose for women weighing 50-90 kg	**40mg 12hrly**	**5000units 12 hourly**

Appendix E: Contraindications/ Cautions to LMWH

Contraindications/ Cautions
Known bleeding disorder (e.g. haemophilia, von Willebrand disease, acquired coagulopathy)
Active antenatal or postpartum bleeding
Women considered at increased risk of major haemorrhage (e.g. placenta praevia)
Thrombocytopenia (platelet count < 75 × 10^9/l)
Acute stroke in previous 4 weeks (haemorrhagic or ischaemic)
Severe renal disease(g**lomerular filtration rate [GFR]**< 30 ml/minute/1.73m^2**)**
Severe liver disease (prothrombin time above normal range or known varices)
Uncontrolled hypertension (blood pressure > 200 mmHg systolic or > 120 mmHg diastolic)

Appendix F: Previous VTE and Thromboprophylaxis

Previous VTE		Prophylaxis (Manage in collaboration with haematologist)
Single previous VTE (unprovoked or idiopathic or related to oestrogen or risk factors other than major surgery)		LMWH throughout antenatal period
Single previous VTE related to major surgery+no other risk factors		LMWH from 28 weeks gestation
Previous VTE associated with thrombophilia	Heritable (Antithrombin deficiency)	Higher dose LMWH antenatal and 6 weeks post-partum
	Heritable (other thrombophilic defects)	Standard dose LMWH
	Acquired (Antiphospholipid syndrome)	Higher dose LMWH antenatal and 6 weeks post-partum
Previous recurrent VTE		Higher dose LMWH antenatal and 6 weeks post-partum

Appendix G: Asymptomatic Thrombophilia and Thromboprophylaxis

Thrombophilia	Level of risk of VTE	Prophylaxis
Antithrombin, protein C or S deficiency, those with >one thrombophilic defects (including homozygous Factor V Leiden, compound heterozygous, homozygous prothrombin gene mutation) + no other risk factors (family or other risk factors)	Higher risk thrombophilic tendency	Consider LMWH antenatal and 6 weeks postpartum
Heterozygous Factor V Leiden, heterozygous prothrombin gene mutation, antiphospholipid antibodies (Lupus anticoagulant&/anticardiolipin &/beta 2 glycoprotein 1) +3 other risk factors	Lower risk thrombophilic tendency	Consider antenatal LMWH prophylaxis from early pregnancy
Same +2 other risk factors		Consider antenatal LMWH prophylaxis from 28 weeks gestation
Same +1 other risk factor		Consider postnatal LMWH for 10 days