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NHS Foundation Trust

Title of Guideline	**Prevention of Venous Thromboembolic Events (VTE) during pregnancy and the puerperium**
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Explicit definition of patient group to which it applies	Maternity patients
Abstract	
Statement of evidence base of the guideline Evidence Base (1-5)	

1a	Meta analysis of RCT
1b	At least 1 RCT
2a	At least 1 well designed controlled study without randomisation
2b	At least 1 other well designed quasi experimental study
3	Well –designed non-experimental descriptive studies (ie comparative / correlation and case studies)
4	Expert committee reports or opinions and / or clinical experiences of respected authorities
5	Recommended best practise based on the clinical experience of the guideline developer

Consultation Process	O&G Guideline Group
Target Audience	Staff caring for pregnant women
This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date.	

Prevention of Venous Thromboembolic Events (VTE) during pregnancy and the puerperium

Written by Chris Gregory, Consultant Haematologist, July 2018 Appendix 4 updated April 2021 (v1.1)
(Replacing the previous guideline Administration of prophylactic heparin during pregnancy and puerperium to prevent venous thromboembolism (VTE) last updated July 2015)
Reviewed November 2021 (v2)

Introduction

The risk of a blood clot (thrombosis) is 10 times higher for women during pregnancy and the post-natal period. To reduce this risk national guidelines have been produced which all Trusts are expected to follow. This guideline is based on the national recommendations to reduce the risk of a blood clot during pregnancy.

Thrombosis Risk Assessment

All women should undergo a documented assessment of risk factors for VTE in early pregnancy or pre-pregnancy (see Appendix I and III).

The risk assessment should be completed on the standard antenatal risk assessment proforma which should be filed in the main orange hospital notes

This risk assessment should be repeated at 28 weeks and if the woman is admitted to hospital for any reason or develops other intercurrent problems.

The risk assessment should be repeated again intrapartum or immediately postpartum.

Who should be considered for prophylaxis

Any woman with four or more current risk factors (other than previous VTE or thrombophilia) should be considered for prophylactic Low Molecular Weight Heparin (LMWH) throughout the antenatal period and will usually require it for 6 weeks postnatally.

Any woman with three current risk factors (other than previous VTE or thrombophilia) should be considered for prophylactic LMWH from 28 weeks and will usually require it for 6 weeks postnatally.

Any woman with two current risk factors (other than previous VTE or thrombophilia) should be considered for prophylactic LMWH for 10 days postpartum.

Any woman admitted to hospital when pregnant (including to a gynaecology ward with hyperemesis gravidarum or ovarian hyperstimulation syndrome) should usually be offered thromboprophylaxis with LMWH, within 14 hours of admission and risk assessment, unless there is a specific contraindication such as risk of labour or active bleeding.

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

Women with previous VTE should be offered pre-pregnancy counselling and a prospective management plan for thromboprophylaxis in pregnancy made. Those who become pregnant before receiving such counselling should be referred at the

earliest opportunity in pregnancy to a clinician with expertise in thrombosis in pregnancy.

Women with previous VTE should be offered thromboprophylaxis with LMWH throughout the antenatal period (except those with a single previous VTE related to major surgery and no other risk factors who should be offered it from 28 weeks).

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.

Women with previous VTE associated with antithrombin deficiency (who will often be on long-term oral anticoagulation) should be offered thromboprophylaxis with higher dose LMWH (either 50%, 75% or full treatment dose) (see Appendix II) antenatally and for 6 weeks postpartum or until returned to oral anticoagulant therapy after delivery. Management should be undertaken in collaboration with a haematologist with expertise in thrombosis in pregnancy and consideration given to antenatal anti-Xa monitoring and the potential for antithrombin replacement at initiation of labour or prior to caesarean section. This would normally involve the consultants at Manchester University Hospital NHS Foundation Trust.

If anti-Xa levels are measured, a test that does not use exogenous antithrombin should be used and 4-hour peak levels of 0.5–1.0 iu/ml aimed for.

Other heritable thrombophilic defects are lower risk and can be managed with standard doses of thromboprophylaxis.

Women with VTE associated with the antiphospholipid syndrome (APS) (who will often be on long-term oral anticoagulation) should be offered thromboprophylaxis with higher dose LMWH (either 50%, 75% or full treatment dose) (see Appendix II) antenatally and for 6 weeks postpartum or until returned to oral anticoagulant therapy after delivery.

Pregnant women with APS and prior VTE or arterial thromboses should be managed in collaboration with a haematologist and/or rheumatologist with expertise in this area. This would normally involve the consultants at Manchester University Hospital NHS Foundation Trust.

Medical Prophylaxis

This Trust uses the LMWH Dalteparin for VTE prophylaxis. For patients who want to avoid a porcine based treatment or if they have had a reaction to heparin products they can receive Fondaparinux instead. This should be prescribe on advice from a Consultant Haematologist with expertise in haemostasis and pregnancy.

In the event of Dalteparin being unavailable Enoxaparin should be used instead.

The doses recommended by the Royal College of Obstetricians and Gynaecologists are based on booking body weight (see Boxes 1 and 2).

Box 1. Prophylactic doses of Dalteparin

Booking Weight (kg)	Daily Dalteparin Dose (units)	Dose if Creatinine Clearance is <30mls/min
<50	2 500	2 500
50-90	5 000	2 500
91-130	7 500	5 000
131-170	10 000	7 500
>170	75 units per kg/day	7 500

Box 2. Prophylactic doses of Enoxaparin

Booking Weight (kg)	Daily Enoxaparin Dose (mg)	Dose if Creatinine Clearance is <30mls/min
<50	20	20
50-90	40	20
91-130	60	40
131-170	80	60
>170	0.6mg/kg/day	60

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 prophylaxis.

Doses of LMWH should be reduced in women with renal impairment where the creatinine clearance is below 30mls/min.

LMWH is safe in breastfeeding.

The use of LMWH in those under 18 is off label as it is not licensed for those under 18. This should be explained to the patient.

LMWH is a "red drug" and must be prescribed in secondary care so do not ask a GP to start or continue the prescription

Stopping Anticoagulation

Women receiving antenatal LMWH should be advised that if they have any vaginal bleeding or once labour begins they should not inject any further LMWH. They should be reassessed on admission to hospital and further doses should be prescribed by medical staff.

Regional techniques should be avoided if possible until at least 12 hours after the previous prophylactic dose of LMWH.

LMWH should not be given for 4 hours after use of spinal anaesthesia or after the epidural catheter has been removed and the catheter should not be removed within 12 hours of the most recent injection.

When a woman presents while on a therapeutic regimen of LMWH, regional techniques should be avoided if possible for at least 24 hours after the last dose of LMWH.

Women receiving antenatal LMWH having an elective caesarean section should receive a thromboprophylactic dose of LMWH on the day prior to delivery. On the day of delivery, any morning dose should be omitted and the operation performed that morning.

The first thromboprophylactic dose of LMWH should be given as soon as possible after delivery provided there is no postpartum haemorrhage and regional analgesia has not been used.

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), foot impulse devices or intermittent pneumatic compression devices. Unfractionated heparin (UFT) may also be considered.

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

Thromboprophylaxis should be started or reinstituted as soon as the immediate risk of haemorrhage is reduced.

Thromboprophylaxis after Delivery

All women with class 3 obesity (BMI greater than or equal to 40 kg/m^2) should be considered for prophylactic LMWH in doses appropriate for their weight for 10 days after delivery.

Women with two or more persisting risk factors (see antenatal risk factor assessment) should be considered for LMWH in prophylactic doses appropriate for their weight for 10 days after delivery.

All women with a previous history of confirmed VTE should be offered thromboprophylaxis with LMWH or warfarin for at least 6 weeks postpartum regardless of the mode of delivery.

Women with thrombophilia without previous VTE should be stratified according to both the level of risk associated with their thrombophilia and the presence or absence of a family history or other risk factors.

Women with a family history of VTE and an identified thrombophilia should be considered for 6 weeks' postnatal thromboprophylaxis.

All women who have had caesarean sections should be considered for thromboprophylaxis with LMWH for 10 days after delivery apart from those having an elective caesarean section who should be considered for thromboprophylaxis with LMWH for 10 days after delivery if they have any additional risk factors (see Appendix I).

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.

Thromboprophylaxis should be continued for 6 weeks in high-risk women and for 10 days in intermediate-risk women (see Appendix I).

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.

Anticoagulation other than LMWH

Unfractionated Heparin

In women at very high risk of thrombosis (scoring 4 or more on assessment), where there is an increased risk of haemorrhage or where regional anaesthetic techniques may be required, UFH may be used peripartum in preference to LMWH.

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.

Danaparoid

Potential use of danaparoid should be in conjunction with a consultant haematologist with expertise in haemostasis and pregnancy.

Low Dose Aspirin

Aspirin is not recommended for thromboprophylaxis in obstetric patients

Warfarin

Warfarin use in pregnancy is restricted to the few situations where heparin is considered unsuitable, e.g. some women with mechanical heart valves.

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.

Dextran

Dextran should be avoided antenatally and intrapartum because of the risk of anaphylactoid reactions.

Oral Thrombin and Xa Inhibitors

Non-Vitamin K antagonist oral anticoagulants (NOACs) should be avoided in pregnant women. The use of NOACS is not currently recommended in women who are breastfeeding.

Anti-embolism Stockings

The use of properly applied anti-embolism stockings (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. These include women who are hospitalised post-caesarean section (combined with LMWH) and considered to be at particularly high risk of VTE (e.g. previous VTE, more than four risk factors antenatally or more than two risk factors postnatally) and women travelling long distance for more than 4 hours.

Contraindications to LMWH

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.

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.

References

RCOG Green-top Guideline No. 37a April 2015

https://www.rcog.org.uk/en/guidelines-research-services/guidelines/

Appendix I: Obstetric thromboprophylaxis risk assessment and management

Antenatal 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 trust-nominated thrombosis in pregnancy expert/team

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

→ **INTERMEDIATE RISK**
Consider antenatal prophylaxis with LMWH

Obesity (BMI > 30 kg/m²)
Age > 35
Parity ≥ 3
Smoker
Gross varicose veins
Current pre-eclampsia
Immobility, e.g. paraplegia, PGP
Family history of unprovoked or estrogen-provoked VTE in first-degree relative
Low-risk thrombophilia
Multiple pregnancy
IVF/ART

→ **Four or more risk factors: prophylaxis from first trimester**

Three risk factors: prophylaxis from ≥28 weeks

Fewer than three risk factors →

Transient risk factors: Dehydration/hyperemesis; current systemic infection; long-distance travel

→ **LOWER RISK**
Mobilisation and avoidance of dehydration

APL = antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, β_2-glycoprotein 1 antibodies); ART = assisted reproductive technology; BMI based on booking weight; DM = diabetes mellitus; FHx = family history; gross varicose veins = symptomatic, above knee or associated with phlebitis/oedema/skin changes; high-risk thrombophilia = antithrombin deficiency, protein C or S deficiency, compound or homozygous for low-risk thrombophilias; IBD = inflammatory bowel disease; immobility = ≥ 3 days; IVDU = intravenous drug user; IVF = in vitro fertilisation; LMWH = low-molecular-weight heparin; long-distance travel = > 4 hours; low-risk thrombophilia = heterozygous for factor V Leiden or prothrombin G20210A mutations; OHSS = ovarian hyperstimulation syndrome; PGP = pelvic girdle pain with reduced mobility; PPH = postpartum haemorrhage; thrombophilia = inherited or acquired; VTE = venous thromboembolism.

Postnatal assessment and management (to be assessed on delivery suite)

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

→ **HIGH RISK**
At least 6 weeks' postnatal prophylactic LMWH

Caesarean section in labour
BMI ≥ 40 kg/m²
Readmission or prolonged admission (≥ 3 days) in the puerperium
Any surgical procedure in the puerperium except immediate repair of the perineum
Medical comorbidities e.g. cancer, heart failure, active SLE, IBD or inflammatory polyarthropathy; nephrotic syndrome, type I DM with nephropathy, sickle cell disease, current IVDU

→ **INTERMEDIATE RISK**
At least 10 days' postnatal prophylactic LMWH

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

Age > 35 years
Obesity (BMI ≥ 30 kg/m²)
Parity ≥ 3
Smoker
Elective caesarean section
Family history of VTE
Low-risk thrombophilia
Gross varicose veins
Current systemic infection
Immobility, e.g. paraplegia, PGP, long-distance travel
Current pre-eclampsia
Multiple pregnancy
Preterm delivery in this pregnancy (< 37+0 weeks)
Stillbirth in this pregnancy
Mid-cavity rotational or operative delivery
Prolonged labour (> 24 hours)
PPH > 1 litre or blood transfusion

Two or more risk factors →

Fewer than two risk factors →

→ **LOWER RISK**
Early mobilisation and avoidance of dehydration

Antenatal and postnatal prophylactic dose of LMWH

Weight < 50 kg = 20 mg enoxaparin/2500 units dalteparin/3500 units tinzaparin daily
Weight 50–90 kg = 40 mg enoxaparin/5000 units dalteparin/4500 units tinzaparin daily
Weight 91–130 kg = 60 mg enoxaparin/7500 units dalteparin/7000 units tinzaparin daily
Weight 131–170 kg = 80 mg enoxaparin/10000 units dalteparin/9000 units tinzaparin daily
Weight > 170 kg = 0.6 mg/kg/day enoxaparin/ 75 u/kg/day dalteparin/ 75 u/kg/day tinzaparin

Appendix II: Summary of guideline for thromboprophylaxis in women with previous VTE and/or thrombophilia

Very High Risk	Previous VTE on long-term oral anticoagulant therapy Antithrombin deficiency Antiphospholipid syndrome with previous VTE	Recommend antenatal high-dose LMWH and at least 6 weeks' postnatal LMWH or until switched back to oral anticoagulant therapy *These women require specialist management by experts in haemostasis and pregnancy*
High Risk	Any previous VTE (except a single VTE related to major surgery)	Recommend antenatal and 6 weeks' postnatal prophylactic LMWH.
Intermediate Risk	Asymptomatic high-risk thrombophilia homozygous factor V Leiden/compound heterozygote Protein C or S deficiency. Single previous VTE associated with major surgery without thrombophilia, family history or other risk factors.	Refer to local expert Consider antenatal LMWH Recommend postnatal prophylactic LMWH for 6 weeks. Consider antenatal LMWH (but not routinely recommended) Recommend LMWH from 28 weeks of gestation and 6 weeks' postnatal prophylactic LMWH.
Low Risk	Asymptomatic low-risk thrombophilia (prothrombin gene mutation or factor V Leiden)	Consider as a risk factor and score appropriately (see Appendix III) Recommend 10 days' if other risk factor postpartum (or 6 weeks' if significant family history) postnatal prophylactic LMWH

Appendix III: Risk assessment for venous thromboembolism (VTE)

- If total score ≥ 4 antenatally, consider thromboprophylaxis from the first trimester.
- If total score 3 antenatally, consider thromboprophylaxis from 28 weeks.
- If total score ≥ 2 postnatally, consider thromboprophylaxis for at least 10 days.
- If admitted to hospital antenatally consider thromboprophylaxis.
- If prolonged admission (≥ 3 days) or readmission to hospital within the puerperium consider thromboprophylaxis.

For patients with an identified bleeding risk, the balance of risks of bleeding and thrombosis should be discussed in consultation with a haematologist with expertise in thrombosis and bleeding in pregnancy.

Risk factors for VTE

Pre-existing risk factors	Tick	Score
Previous VTE (except a single event related to major surgery)		4
Previous VTE provoked by major surgery		3
Known high-risk thrombophilia		3
Medical comorbidities e.g. cancer, heart failure; active systemic lupus erythematosus, inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease; current intravenous drug user		3
Family history of unprovoked or estrogen-related VTE in first-degree relative		1
Known low-risk thrombophilia (no VTE)		1[a]
Age (> 35 years)		1
Obesity		1 or 2[b]
Parity ≥ 3		1
Smoker		1
Gross varicose veins		1
Obstetric risk factors		
Pre-eclampsia in current pregnancy		1
ART/IVF (antenatal only)		1
Multiple pregnancy		1
Caesarean section in labour		2
Elective caesarean section		1
Mid-cavity or rotational operative delivery		1
Prolonged labour (> 24 hours)		1
PPH (> 1 litre or transfusion)		1
Preterm birth < 37+0 weeks in current pregnancy		1
Stillbirth in current pregnancy		1
Transient risk factors		
Any surgical procedure in pregnancy or puerperium except immediate repair of the perineum, e.g. appendicectomy, postpartum sterilisation		3
Hyperemesis		3
OHSS (first trimester only)		4
Current systemic infection		1
Immobility, dehydration		1
TOTAL		

Abbreviations: ART assisted reproductive technology; IVF in vitro fertilisation; OHSS ovarian hyperstimulation syndrome; VTE venous thromboembolism.

[a] If the known low-risk thrombophilia is in a woman with a family history of VTE in a first-degree relative postpartum thromboprophylaxis should be continued for 6 weeks.

[b] BMI ≥ 30 = 1; BMI ≥ 40 = 2

