Royal College of Obstetricians and Gynaecologists

Setting standards to improve women's health

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THROMBOPROPHYLAXIS DURING PREGNANCY, LABOUR AND AFTER VAGINAL DELIVERY

1. Aim

This guideline summarises the available evidence on the prevention of venous thromboembolism (VTE) during pregnancy and following vaginal delivery. It does not address thromboprophylaxis following caesarean section[1] or the acute management of VTE in pregnancy, which was the subject of a previous guideline.[2]

2. Introduction and background

Pulmonary thromboembolism (PTE) is the most common direct cause of maternal death in the UK.[3] Successive reports on Confidential Enquiries into Maternal Deaths have highlighted failures in recognising risk factors for VTE and employing adequate prophylaxis. Although PTE remains the leading cause of maternal death, in the latest Confidential Enquiry,[3] the proportion of postpartum deaths following caesarean section had fallen, suggesting that adoption of published recommendations[1] may have had a beneficial effect. However, no impact has been made over the last decade on reducing the four to five deaths annually from antenatal PTE or the three deaths annually from PTE following vaginal delivery.[3] In the most recent Confidential Enquiries into Maternal Deaths, 8/13 (62%) of women with fatal antenatal PTE died in the first trimester and 10/14 (71%) of postpartum deaths followed vaginal delivery.[3] Although most VTE occurs antenatally, the risk per day is greatest in the weeks immediately after delivery.[4] All women dying from VTE following vaginal delivery in the last Confidential Enquiry were either overweight or over the age of 35 years.[3] Only one of the ten deaths involved operative vaginal delivery.[3] This enquiry concluded that 'there is a clear need for the development of national guidelines on thromboprophylaxis after normal delivery'.[3]

3. Identification and assessment of evidence

A search of Medline from 1966 to 2002 was performed to identify all relevant randomised controlled trials (RCTs), systematic reviews and meta-analyses. The databases were searched using the relevant MeSH terms including all subheadings. The principal terms used were: 'venous thromboembolism', 'thrombosis', 'pregnancy', 'postpartum', 'puerperium', 'antenatal' and 'prenatal'.

In addition, current guidelines for the prevention of VTE in pregnancy and the puerperium were reviewed.[5–7] A Cochrane review has highlighted the lack of evidence from randomised trials evaluating strategies for the prevention of VTE during pregnancy[8] and, in general, guideline recommendations for the prevention of VTE during pregnancy are extrapolated from studies in nonpregnant women.

The definitions of types of evidence used in this guideline originate from the US Agency for Health Care Research and Quality. Where possible, recommendations are based on, and explicitly linked to, the evidence

that supports them. Areas lacking evidence are highlighted and annotated as 'good practice points'.

4. Preconceptual antenatal risk assessment

4.1 Risk factors

Pregnancy is a risk factor for VTE and is associated with a ten-fold increase compared with the risk for nonpregnant women. Some women are at even higher risk during pregnancy because they have one or more additional risk factors (Table 1).[9,10] The level of risk associated with many of these factors is unclear, however. An individual assessment of thrombotic risk should be undertaken, ideally before pregnancy or in early pregnancy. Women at high risk of VTE, including those with previous confirmed VTE, should be offered prepregnancy counselling with a prospective management plan. This is important because thrombotic risk exists from the beginning of the first trimester and often the antenatal booking visit is at the end of the first trimester.

All women should undergo an assessment of risk factors for VTE in early pregnancy or before pregnancy. This assessment should be repeated if the woman is admitted to hospital or develops other intercurrent problems. **C**

Table 1. Risk factors for venous thromboembolism in pregnancy and the puerperium[a]

Pre-existing	New onset or transient[b]
Previous VTE	Surgical procedure in pregnancy or puerperium, e.g. evacuation of retained products of conception, postpartum sterilisation
Thrombophilia	Hyperemesis
congenital	Dehydration
antithrombin deficiency	Ovarian hyperstimulation syndrome
protein C deficiency	Severe infection, e.g. pyelonephritis
protein S deficiency	Immobility (> 4 days bed rest)
Factor V Leiden	Pre-eclampsia
prothrombin gene variant	Excessive blood loss
acquired (antiphospholipid syndrome)	Long-haul travel
lupus anticoagulant	Prolonged labour [c]
anticardiolipin antibodies	Midcavity instrumental delivery [c]
Age over 35 years	Immobility after delivery [c]
Obesity (BMI > 30 kg/m2) either pre-pregnancy or in early pregnancy	
Parity > 4	
Gross varicose veins	
Paraplegia	
Sickle cell disease	
Inflammatory disorders e.g. inflammatory bowel disease	
Some medical disorders, e.g. nephrotic syndrome, certain cardiac diseases	
Myeloproliferative disorders, e.g. essential thrombocythaemia, polycythaemia vera	

[a] Although these are all accepted as thromboembolic risk factors, there are few data to support the degree of increased risk associated with many of them; [b] these risk factors are potentially reversible and may develop at later stages in gestation than the initial risk assessment or may resolve; an ongoing individual risk assessment is important; [c] risk factors specific to postpartum VTE only

4.2 Investigation of women with previous VTE

Women with previous VTE have an increased risk of recurrence in pregnancy.[11] A retrospective comparison of the overall risk of recurrence of VTE during pregnancy and the nonpregnant period revealed risks of 10.9% during and 3.7% outside pregnancy. Using regression analysis gave a relative risk during pregnancy of 3.5 (95% CI 1.6–7.8).[11]

Evidence level III

For women with a single previous thrombosis and no known thrombophilia, the risk of recurrence in pregnancy was increased to 2.0–3.0%[12] from about 0.1%.[13] However, the risk was higher if the woman had thrombophilia or if the previous VTE was in an unusual site or was unprovoked.[11]

Evidence level III

Women with a previous VTE should have a careful history documented and undergo screening for both inherited and acquired thrombophilia, ideally before pregnancy. The relevant inherited and acquired thrombophilias are listed in Table 1. It is important to be aware of the effects of pregnancy on the results of a thrombophilia screen.[2] The diagnosis of a past VTE can be assumed if the woman gives a good history and received prolonged (6–12 weeks) therapeutic anticoagulation.

Women with previous VTE should be screened for inherited and acquired thrombophilia ideally before pregnancy. **B**

5. Thromboprophylaxis during pregnancy and the puerperium

Expert haematological advice or referral to a joint obstetric and haematology clinic should be sought in cases when the antenatal team are uncertain about thromboprophylaxis.

Regardless of their risk of VTE, immobilisation of women during pregnancy, labour and the puerperium should be minimised and dehydration should be avoided. ✓

5.1 Women with a previous VTE and no thrombophilia

Women with previous VTE and no thrombophilia should be offered prophylaxis with low molecular weight heparin (LMWH) for six weeks after delivery. Whether they also require antenatal thromboprophylaxis is controversial. There is some evidence that if the previous VTE was associated with a temporary risk factor, such as trauma, antenatal anticoagulation is not required.[12] Although pregnancy may be associated with a more than three-fold increase in the risk of recurrent VTE,[11] the evidence is conflicting. In a study of 125 pregnant women with a single previous VTE, none of the 44 women without thrombophilia whose previous VTE occurred in association with a temporary risk factor had a recurrence.[12] Of the 51 women with unprovoked first VTE or a thrombophilia, three[3] (6%) had an antepartum recurrence, although the numbers were small and the analysis *post hoc*.[12] In addition, if the previous VTE was oestrogen-related (pregnancy or the combined oral contraceptive pill) or if there are additional risk factors such as obesity,[5] thromboprophylaxis with LMWH has been advocated.

Women with previous VTE should be offered postpartum thromboprophylaxis with LMWH. It may be reasonable not to use antenatal thromboprophylaxis with heparin in women with a single previous VTE associated with a temporary risk factor that has now resolved. **C**

Women who have had more than one previous episode of VTE, who have had one episode and in addition have a family history of VTE in a first degree relative or whose episode of VTE was in an unusual site (such as the axillary vein), all of which are markers for a thrombophilic state, should be considered for antenatal thromboprophylaxis with LMWH.[6,7]

Women with previous recurrent VTE or a previous VTE and a family history of VTE in a first-degree relative should be offered thromboprophylaxis with LMWH antenatally and for at least six weeks postpartum. **C**

5.2 Women with a previous VTE who have inherited thrombophilia

Women with thrombophilias have an increased risk of VTE in pregnancy[12-14] but this risk varies depending

upon the specific thrombophilia.[13] For example, in a case–control study, the relative risk for VTE was 7.0 for factor V Leiden, 9.5 for prothrombin G20210A, 10.0 for antithrombin deficiency and 107 for the combination of factor V Leiden and prothrombin.[13] The relative risk of VTE due to the prothrombin mutation as outlined in this study[13] is high compared with nonpregnant data and to a more recent case–control study.[15] In this study of 119 consecutive women with a first VTE in pregnancy, the relative risks were 9.1 for factor V Leiden, 2.9 for prothrombin G20210A and 13.1 for deficiencies of antithrombin, protein C or S.[15] The risk also depends on whether the woman or her close family have had a previous VTE.[16–18] Current evidence supports, and existing guidelines recommend, that women with previous VTE and an identifiable thrombophilia should receive antenatal thromboprophylaxis with LMWH; prophylaxis should continue for six weeks postpartum.[5–7,12–17]

Expert haematological advice should be sought for women with symptomatic thrombophilia, as specific thrombophilias, particularly AT deficiency, merit higher doses of LMWH (see Table 2) for thromboprophylaxis.

Women with previous VTE and thrombophilia should be offered thromboprophylaxis with LMWH antenatally and for at least six weeks postpartum. **B**

Table 2. Antenatal prophylactic and therapeutic doses of low-molecular-weight heparin

Prophylaxis	Enoxaparin (100 units/mg)	Dalteparin	Tinzaparin[b]
Normal body weight (50–90 kg)	40 mg daily	5000 units daily	4500 units daily
Body weight < 50 kg	20 mg daily	2500 units daily	3500 units daily
Body weight > 90 kga	40 mg 12-hourly	5000 units 12-hourly	4500 units 12-hourly
Higher prophylactic dose	40 mg 12-hourly	5000 units 12-hourly	4500 units 12-hourly
Therapeutic dose	1 mg/kg 12-hourly	90units/kg 12-hourly	90units/kg 12-hourly

[a] Body mass index > 30 in early pregnancy

[b] The dosage schedules for tinzaparin differ from the manufacturer's recommendation of once-daily dosage

5.3 Women with inherited thrombophilia without previous VTE

Increasingly, women present in pregnancy with a known thrombophilia, usually detected because of screening following identification of inherited thrombophilia in a family member. The risk of VTE associated with thrombophilia varies considerably.[14,17] Antithrombin deficiency is associated with a high risk (30%)[18] of VTE in pregnancy.[19] Asymptomatic women with protein C or protein S deficiencies have an eight-fold increased risk of VTE associated with pregnancy but most events occur postpartum.[20] Data from retrospective family studies[21,22] confirm a high risk of VTE for women with homozygous factor V Leiden (prevalence 15.8%[21] to 17.0%;[22] relative risk 41.3[21]) and combined defects of factor V Leiden and prothrombin gene mutation (prevalence 4.0%; relative risk 9.2[21]). Women heterozygous for the factor V Leiden mutation or the prothrombin gene variant are at considerably lower risk.[13] Data from a case–control study` would suggest an estimated risk of VTE in pregnancy of 1.2 in 100 for heterozygous factor V Leiden and one in 500 for heterozygous prothrombin G20210A. Prospective data examining the incidence of VTE in pregnant women with thrombophilia and no prior VTE are lacking.

Women should be stratified according to the level of risk associated with their thrombophilia. Since the risk of VTE is lower in women with no history of VTE, antenatal thromboprophylaxis is not always necessary, except in those with combined defects, those homozygous for defects or those with antithrombin deficiency.[13,16,21–23] Women with antithrombin deficiency should always receive thromboprophylaxis in pregnancy and the puerperium.[18]

Women with known inherited or acquired thrombophilia may qualify for LMWH or warfarin for six weeks following delivery, even if they were not receiving antenatal thromboprophylaxis if they have other risk factors (see Table 1).

Women with asymptomatic inherited or acquired thrombophilia may qualify for antenatal or postnatal thromboprophylaxis, depending on the specific thrombophilia and the presence of other risk factors. C

5.4 Women with acquired thrombophilia (antiphospholipid syndrome)

Antiphospholipid syndrome (APS) is defined as the presence of lupus anticoagulant or anticardiolipin antibodies of medium–high titre on two occasions eight weeks apart, found in association with a history of thrombosis (arterial or venous) or adverse pregnancy outcome (three or more unexplained miscarriages before ten weeks of gestation, a fetal death after ten weeks of gestation or a premature {less than 35 weeks} birth due to severe pre-eclampsia or intrauterine growth restriction).[24]

The risk of recurrent thromboses in women with APS is up to 70%[25] and may be even higher in pregnancy. Therefore, pregnant women with APS and previous thromboses should receive antenatal and postnatal thromboprophylaxis with LMWH.[26]

The management of women with obstetric manifestations of APS is more controversial. Low-dose aspirin has been shown to improve pregnancy outcome in APS and is recommended for all women with APS.[26] However, the presence of antiphospholipid antibodies with no previous 'APS classifiable' pregnancy loss[24] or thrombosis does not equate to APS[27] and such women do not require LMWH (or low-dose aspirin).[28,29]

Women with antiphospholipid syndrome identified because of recurrent miscarriage may not require LMWH for six weeks postpartum but should receive LMWH for at least three to five days, especially if they have other risk factors.

5.5 Women without previous VTE or thrombophilia

There are few data to support recommendations for many of the individual risk factors listed in Table 1. In general, women with three or more current or persisting risk factors (other than those with a previous VTE or a thrombophilia discussed in sections 5.1–5.4) should be considered for prophylactic LMWH antenatally and for at least three to five days postpartum.

A woman with two current or persisting risk factors should be considered for prophylactic LMWH for three to five days after vaginal delivery.

Clinical judgement is required with regard to the weighting of the above risk factors.There are circumstances where one or two risk factors alone may be sufficient to justify antenatal thromboprophylaxis with LMWH, for example an extremely obese woman admitted to the antenatal ward.

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

Women with three or more persisting risk factors should be considered for thromboprophylaxis with LMWH antenatally and for three to five days postpartum. ✓

Women should be reassessed before or during labour for risk factors for VTE. Age over 35 years and BMI greater than 30/body weight greater than 90 kg are important independent risk factors for postpartum VTE even after vaginal delivery. The combination of either of these risk factors with any other risk factor for VTE (such as pre-eclampsia or immobility) or the presence of two other persisting risk factors should lead the clinician to consider the use of LMWH for three to five days postpartum. ✓

6. Timing and duration of thromboprophylaxis

6.1 Antepartum

As VTE during pregnancy has an equal distribution throughout gestation,[4] if a decision is made to initiate thromboprophylaxis antenatally, this should begin as early in pregnancy as practical.[5] Once antenatal treatment is initiated it should continue until delivery unless a specific risk factor is removed or disappears.

Women with ovarian hyperstimulation syndrome (OHSS) require thromboprophylaxis for at least the period of inpatient stay. Similarly, women with multiple risk factors for VTE and at risk of OHSS undergoing ovulation induction may also be considered for thromboprophylaxis. Advice for pregnant women travelling by air is available.[30]

6.2 Postpartum

Postpartum thromboprophylaxis should be given as soon as possible after delivery, provided that there is no postpartum haemorrhage. Those with postpartum haemorrhage should be fitted with thromboembolic-deterrent stockings. If the woman has been given regional analgesia, LMWH should be withheld until four hours after insertion or removal of the epidural catheter (or six hours if either insertion or removal were traumatic). The first postpartum dose can be given after insertion but before removal of the epidural catheter.

As the prothrombotic changes of pregnancy do not revert completely to normal until several weeks after delivery, postpartum thromboprophylaxis is normally continued for six weeks in high-risk women.[3] In practice, this will mean women learning to inject themselves if they have not already commenced heparin antenatally. However, for women at lower risk prophylaxis for three to five days is usually recommended, despite the lack of evidence in this area. Low risk includes those with two current or persisting risk factors as discussed above (Table 1) and asymptomatic thrombophilias with low thrombotic risk (heterozygous factor V Leiden and prothrombin gene variant). The risk of VTE reduces when women are mobile postpartum but does not disappear. If the woman is discharged home early, her thromboprophylaxis should be continued at home, to complete the course of three to five days. The combined oral contraceptive pill should not be prescribed during the first three months postpartum for women with other risk factors for VTE.

Just as circumstances and risk factors can change antenatally so too may they in the puerperium. Therefore, puerperal women undergoing surgery for any reason or those who develop severe infection or who choose to travel long-haul are at increased risk of VTE even though they may have been discharged from hospital following vaginal delivery several weeks before.

Antenatal thromboprophylaxis should begin as early in pregnancy as practical. Postpartum prophylaxis should begin as soon as possible after delivery (but see precautions after use of regional anaesthesia). **B**

7. Agents for thromboprophylaxis

The different options for and types of treatment should be discussed with the mother.

7.1 Low molecular weight heparin

Low molecular weight heparins are the agents of choice for antenatal thromboprophylaxis. They are as effective as and safer than unfractionated heparin in pregnancy. **B**

LMWHs are at least as effective as unfractionated heparin for the prevention of deep vein thrombosis in nonpregnant women undergoing surgery.[31] Systematic reviews and retrospective studies have concluded that LMWH is a safe alternative to unfractionated heparin as an anticoagulant during pregnancy[32–34] and from a safety perspective LMWH is preferred.

Evidence level Ia supported by levels II and III

The risk of heparin-induced thrombocytopenia is reduced with LMWH.[35,36] Prolonged unfractionated heparin use during pregnancy may result in osteoporosis and fractures[35] but this risk is low with LMWH.[32,34,37–40] Allergic skin reactions to heparin can occur[35] and may require a change of heparin preparation or conversion to a heparinoid (danaparoid sodium).[41]

See Table 2 (page 4) for suggested antenatal prophylactic and therapeutic doses of LMWH.

Experience indicates that, provided that the woman has normal renal function, monitoring of anti-Xa levels is not required when LMWH is used for thromboprophylaxis. In antithrombin deficiency, anti-Xa monitoring is critical, higher doses of LMWH may be necessary and these patients should be monitored by a haemostatic expert. Antithrombin concentrates may be required. Although the risk of heparin-induced thrombocytopenia is extremely low with LMWH[36] and has never been reported in pregnancy, current guidelines[5,23] still recommend checking the platelet count one week after starting LMWH.

Where antenatal thromboprophylaxis with LMWH is given to women who are normally on long-term oral anticoagulants, usually because of previous recurrent VTE and/or a thrombophilia, higher prophylactic doses or therapeutic doses of LMWH may be appropriate (see Table 2). Whether high prophylactic doses or therapeutic doses are required is controversial and there is some evidence from nonpregnant[42] and pregnant[43] data that the former may suffice.

For postpartum thromboprophylaxis, LMWH is probably the agent of choice for women who had LMWH antenatally or for those requiring only three to five days of postpartum treatment. Experience of enoxaparin in the puerperium reports no adverse effects on the baby resulting from breastfeeding.[35]

7.2 Low-dose aspirin

Low-dose aspirin is safe in pregnancy,[44] although its use for thromboprophylaxis in this setting has never been assessed by a controlled trial. A much criticised trial suggested that low-dose aspirin, compared with placebo, reduces by 36% the risk of VTE after orthopaedic surgery, even in some women taking concomitant heparin therapy.[45] Meta-analysis of trials in surgical and medical patients also shows a significant reduction in deep vein thrombosis and pulmonary embolism with antiplatelet prophylaxis.[45] Therefore, the use of low-dose aspirin (75 mg daily) may be appropriate in situations where the risk of VTE is increased[30] but is not deemed high enough to warrant the use of antenatal LMWH; for example, in women with previous provoked VTE without thrombophilia.[47] Women should be advised of the lack of evidence for benefit of aspirin use for thromboprophylaxis in pregnancy.

7.3 Warfarin

Warfarin should be avoided if possible during pregnancy,[5] especially between 6 and 12 weeks of gestation, because it is associated with an up to 5% risk of teratogenesis and increases the risk of miscarriage, fetal and maternal haemorrhage, neurological problems in the baby and stillbirth.[48]

Warfarin is safe after delivery and for breastfeeding, although it requires close monitoring, frequent visits to an anticoagulant clinic and carries an increased risk of postpartum haemorrhage and perineal haematoma compared with LMWH. It is not appropriate for women requiring only three to five days of postpartum prophylaxis.

If the woman chooses to commence warfarin postpartum, this can usually be initiated on the second or third postnatal day. LMWH should be continued until the international normalised ratio is greater than 2.0. The dosage regimens are the same as for women converting to warfarin postpartum following an acute VTE in pregnancy.[2]

Warfarin should usually be avoided during pregnancy. It is safe after delivery and during breastfeeding. **B**

7.4 Dextran

Dextran should not be used primarily because of the risk of anaphylaxis, which has killed fetuses by causing massive histamine release and uterine hypertonus.

7.5 Graduated elastic compression stockings

Graduated elastic compression stockings may be used antenatally. There are no trials to support such practice but the British Society for Haematology guidelines[23] give a grade C recommendation (evidence level IV) that all women with previous VTE or a thrombophilia should be encouraged to wear class-II graduated elastic compression below knee stockings throughout their pregnancy and for 6–12 weeks after delivery. Class-I thromboelastic stockings are appropriate for hospital inpatients at increased risk of VTE and may be combined with LMWH. Their use is also recommended for pregnant women travelling by air.[30]

8. Care during labour and delivery for women on thromboprophylaxis

Once the woman is in labour or thinks she is in labour, she should be advised not to inject any further heparin. She should be reassessed on admission to hospital and further doses should be prescribed by medical staff. ✓

The pregnancy-associated prothrombotic changes in the coagulation system are maximal immediately following delivery. Therefore, it is desirable to continue LMWH during labour or delivery in women receiving antenatal thromboprophylaxis with LMWH. For women receiving high prophylactic or therapeutic doses of LMWH, the dose of heparin should be withheld if the woman goes into labour or reduced to its thromboprophylactic dose on the day before induction of labour or elective caesarean section and continued in this dose during labour. If the woman is of normal weight, the dose for unfractionated heparin should be 5000 units 12 hourly. For LMWH preparations, a once-daily regimen should be adopted using the following doses: enoxaparin 40 mg, dalteparin 5000 iu, tinzaparin 50 units/kg.[49,50]

Epidural anaesthesia can be sited only after discussion with a senior anaesthetist, in keeping with local anaesthetic protocols.[2] It is important to discuss the implication of treatment with heparin or LMWH for epidural or spinal anaesthesia with the woman before labour or caesarean section. To minimise the risk of epidural haematoma, regional techniques should not be used until at least 12 hours after the previous prophylactic dose of LMWH. When a woman presents while on a therapeutic regimen of LMWH, regional techniques should not be employed for at least 24 hours after the last dose of LMWH.[51] LMWH should not be given for at least four hours after the epidural catheter has been inserted or removed and the cannula should not be removed within 10–12 hours of the most recent injection.[52]

For delivery by elective caesarean section, the woman should receive a thromboprophylactic dose of LMWH on the day before delivery. On the day of delivery, the morning dose should be omitted and the operation performed that morning. The thromboprophylactic dose of LMWH should be given by three hours postoperatively (or four hours after insertion or removal of the epidural catheter, if appropriate). There is an

increased risk of around 2% of wound haematoma following caesarean section with both unfractionated heparin and LMWH.

Women at high risk of haemorrhage with risk factors including major antepartum haemorrhage, coagulopathy, progressive wound haematoma, suspected intraabdominal bleeding and postpartum haemorrhage may be more conveniently managed with unfractionated heparin. Unfractionated heparin has a shorter half-life than LMWH and there is more experience in the use of protamine sulphate to reverse its activity. If a woman develops a haemorrhagic condition while taking LMWH, the treatment should be stopped and expert haematological advice sought.[2] It should be remembered that excess blood loss and blood transfusion are risk factors for VTE, so thromboprophylaxis should be commenced or reinstituted as soon as the immediate risk of haemorrhage is reduced.

9. Topics suitable for audit

- Proportion of women with previous venous thromboembolism who undergo screening for thrombophilia
- Proportion of women with previous venous thromboembolism who receive six weeks postnatal LMWH

Key recommendations

All women should undergo an assessment of risk factors for VTE in early pregnancy or before pregnancy. This assessment should be repeated if the woman is admitted to hospital or develops other intercurrent problems. C

Women with previous VTE should be screened for inherited and acquired thrombophilia, ideally before pregnancy. B

Regardless of their risk of VTE, immobilisation of women during pregnancy, labour and the puerperium should be minimised and dehydration should be avoided. ✓

Women with previous VTE should be offered postpartum thromboprophylaxis with LMWH. It may be reasonable not to use antenatal thromboprophylaxis with heparin in women with a single previous VTE associated with a temporary risk factor that has now resolved. C

Women with previous recurrent VTE or a previous VTE and a family history of VTE in a first-degree relative should be offered thromboprophylaxis with LMWH antenatally, and for at least six weeks postpartum. C

Women with previous VTE and thrombophilia should be offered thromboprophylaxis with LMWH antenatally and for at least six weeks postpartum. B

Women with asymptomatic inherited or acquired thrombophilia may qualify for antenatal or postnatal thromboprophylaxis, depending on the specific thrombophilia and the presence of other risk factors. C

Women with three or more persisting risk factors should be considered for thromboprophylaxis with LMWH antenatally and for three to five days postpartum. ✓

Women should be reassessed before or during labour for risk factors for VTE. Age over 35 years and BMI greater than30/body weight greater than 90 kg are important independent risk factors for postpartum VTE even after vaginal delivery. The combination of either of these risk factors with any other risk factor for VTE (such as pre-eclampsia or immobility) or the presence of two other persisting risk factors should lead the clinician to consider the use of LMWH for three to five days postpartum. ✓

Antenatal thromboprophylaxis should begin as early in pregnancy as practical. Postpartum prophylaxis should begin as soon as possible after delivery (but see precautions after use of regional anaesthesia). B

LMWHs are the agents of choice for antenatal thromboprophylaxis. They are as effective as and safer than unfractionated heparin in pregnancy. B

Warfarin should usually be avoided during pregnancy. It is safe after delivery and during breastfeeding. B

Once the woman is in labour or thinks she is in labour, she should be advised not to inject any further heparin. She should be reassessed on admission to hospital and further doses should be prescribed by medical staff. ✓

Table 3. Summary of protocol for thromboprophylaxis in women with previous VTE and/or thrombophilia[a]

Risk	Previous VTE and/or thrombophilia status	Prophylaxis
Very high	Previous VTE (± thrombophilia) on long-term warfarin	Antenatal high prophylactic or therapeutic dose LMWH and at least six weeks of postnatal warfarin
High	Previous recurrent VTE not on long-term warfarin	Antenatal and six weeks postnatal prophylactic LMWH
	Previous VTE + thrombophilia	
	Previous VTE + family history of VTE	
	Asymptomatic thrombophilia (antithrombin deficiency, combined defects, homozygous factor V Leiden or prothrombin gene defect)	
Moderate	Single previous provoked VTE without thrombophilia, family history or other risk factors	Six weeks of postnatal prophylactic LMWH ± antenatal low-dose aspirin
	Asymptomatic thrombophilia (except antithrombin deficiency, combined defects, homozygous FVL or prothrombin gene defect)	

[a] These women require joint specialist management by obstetricians and experts in haemostasis and pregnancy

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APPENDIX

Clinical guidelines are: 'systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions'. Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No. 1: *Guidance for the Development of RCOG Green-top Guidelines* (available on the RCOG website at www.rcog.org.uk/clingov1). These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research may be indicated.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

Classification of evidence levels

Ia	Evidence obtained from meta-analysis of randomised controlled trials.
Ib	Evidence obtained from at least one randomised controlled trial.
IIa	Evidence obtained from at least one well-designed controlled study without randomisation.
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study.
III	vidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

Grades of recommendations

A	Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)
B	Requires the availability of well controlled clinical studies but no randomised clinical trials on the topic of recommendations. (Evidence levels IIa, IIb, III)
C	Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)

Good practice point

✓	Recommended best practice based on the clinical experience of the guideline development group.

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The final version is the responsibility of the Guidelines and Audit Committee of the RCOG.

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