Inherited Thrombophilias in Pregnancy

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Inherited Thrombophilias in Pregnancy

Inherited thrombophilias are associated with an increased risk of venous thromboembolism and have been linked to adverse outcomes in pregnancy. However, there is limited evidence to guide screening for and management of these conditions in pregnancy. The purpose of this document is to review common thrombophilias and their association with maternal venous thromboembolism risk and adverse pregnancy outcomes, indications for screening to detect these conditions, and management options in pregnancy. This Practice Bulletin has been revised to provide additional information on recommendations for candidates for thrombophilia evaluation, updated consensus guidelines regarding the need for prophylaxis in women with an inherited thrombophilia during pregnancy and the postpartum period, and discussion of new published consensus guidelines from the Society for Obstetric Anesthesia and Perinatology addressing thromboprophylaxis and neuraxial anesthetic considerations in the obstetric population.

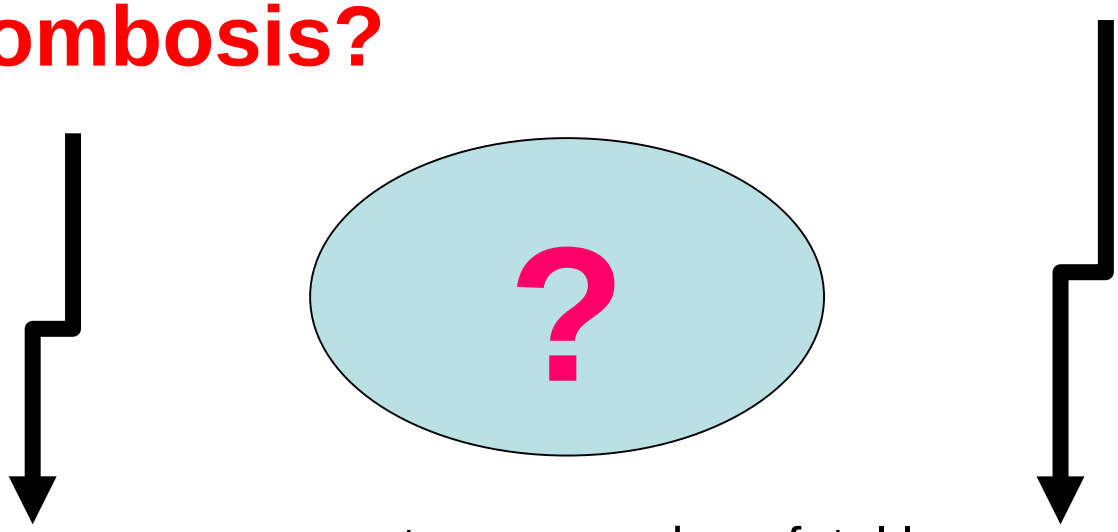
Pregnancy and VTE

- pregnancy or postpartum period: fourfold to fivefold increased risk of thromboembolism
- The risk of recurrent VTE is increased threefold to fourfold
- 50% of women with VTE during pregnancy have an acquired or inherited thrombophilia

Marik PE, Plante LA. Venous thromboembolic disease and pregnancy. *N Engl J Med*. 2008;359(19):2025-2033. doi:10.1056/NEJMra0707993

Pregnancy and VTE

Is there any association between inherited thrombophilias and uteroplacental thrombosis?

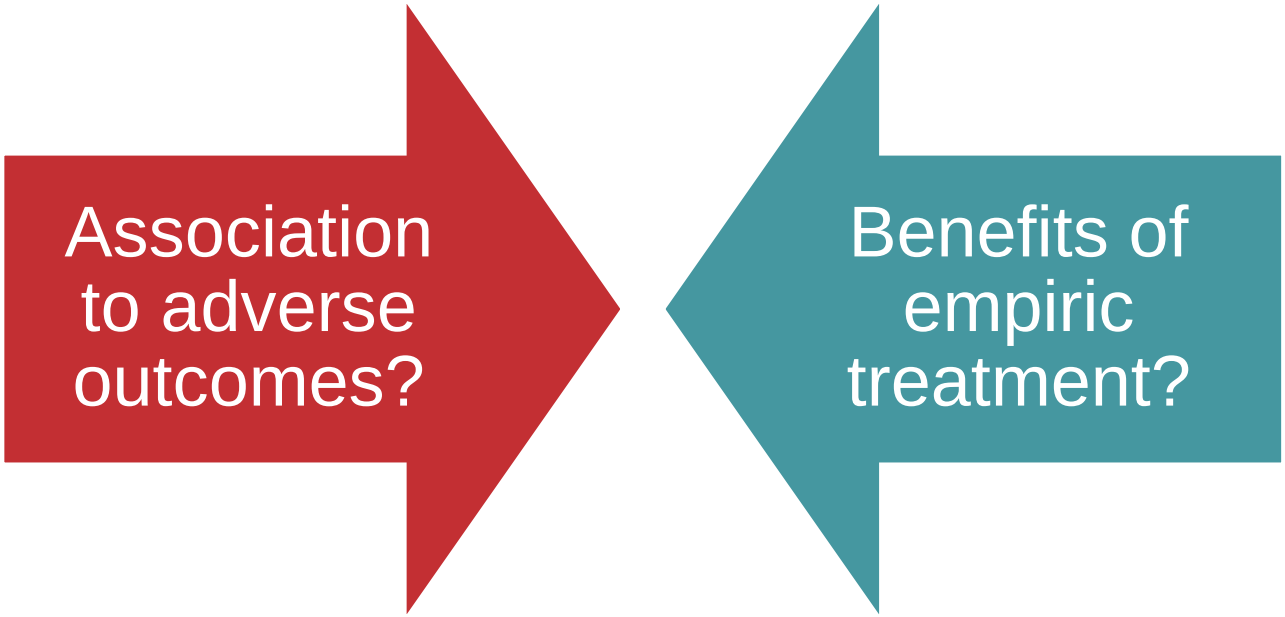


Adverse pregnancy outcomes such as fetal loss, preeclampsia, fetal growth restriction, and placental abruption

Dizon-Townson D, Miller C, Sibai B, et al. The relationship of the factor V Leiden mutation and pregnancy outcomes for mother and fetus. Obstet Gynecol. 2005;106(3):517-524. doi:10.1097/01.AOG.0000173986.32528.ca

Conflicts

Screening for thrombophilias in pregnancy?



Rodger MA, Hague WM, Kingdom J, et al. Antepartum dalteparin versus no antepartum dalteparin for the prevention of pregnancy complications in pregnant women with thrombophilia (TIPPS): a multinational open-label randomised trial. *Lancet*. 2014;384(9955):1673-1683. doi:10.1016/S0140-6736(14)60793-5

Conflicts

While there are clear differences in the definition of losses between the meta-analysis and the EPCOT study, both show a stronger association between thrombophilia and isolated late, rather than early, pregnancy losses.

- Rey E, Kahn SR, David M, Shrier I. Thrombophilic disorders and fetal loss: a meta-analysis. Lancet. 2003;361(9361):901-908. doi:10.1016/S0140-6736(03)12771-7
- Preston FE, Rosendaal FR, Walker ID, et al. Increased fetal loss in women with heritable thrombophilia. *Lancet*. 1996;348(9032):913-916. doi:10.1016/s0140-6736(96)04125-6

Thus, the adverse effect of maternal thrombophilias on uteroplacental blood flow and oxygen delivery would be expected to be harmful to the late, but not early, first-trimester pregnancy.

- Rodesch F, Simon P, Donner C, Jauniaux E. Oxygen measurements in endometrial and trophoblastic tissues during early pregnancy. Obstet Gynecol. 1992;80(2):283-285.
- Jaffe R. Investigation of abnormal first-trimester gestations by color Doppler imaging. *J Clin Ultrasound*. 1993;21(8):521-526. doi:10.1002/jcu.1870210809

Prevalence of Common Inherited Thrombophilias

Table 1. Risk of Venous Thromboembolism With Different Inherited Thrombophilias

	Prevalence in General Population (%)	VTE Risk Per Pregnancy (No History) (%)	VTE Risk Per Pregnancy (Previous VTE) (%)	Percentage of All VTE	References
Factor V Leiden heterozygote	1–15	0.5–3.1	10	40	1–4, 11, 12
Factor V Leiden homozygote	<1	2.2–14.0	17	2	1–4, 11, 12
Prothrombin gene heterozygote	2–5	0.4–2.6	>10	17	1–4, 11, 12
Prothrombin gene homozygote	<1	2–4	>17	0.5	1–4, 11, 12
Factor V Leiden/ prothrombin double heterozygote	0.01	4–8.2	>20	1–3	1–4, 12
Antithrombin deficiency	0.02	0.2–11.6 pp	40	1	1, 5, 6, 11, 12
Protein C deficiency	0.2–0.4	0.1–1.7	4–17	14	1, 5, 7, 11, 12
Protein S deficiency	0.03–0.13	0.3–6.6	0–22	3	1, 8–12

Abbreviation: VTE, venous thromboembolism.

Protein C deficiency

- Linked to more than 160 distinct mutations that produce a highly variable phenotype
- Cut off : less than 65%
  heterozygosity 55-65%
- Homozygous newborn: purpura fulminans

Protein S deficiency

Activity assays alone → substantial variability because of fluctuating levels of protein S binding protein in pregnancy

Screening in nonpregnant women is more reliable, and planned testing should be deferred until remote from a recent birth

Homozygous protein S deficiency may result in neonatal purpura fulminans.

Antithrombin Deficiency

Highly thrombogenic (25 fold) but rare.

More than 250 associated mutations leading to reductions in antigen level and activity

Mild antithrombin deficiency (activity between 70% and 85%)

Severe antithrombin deficiency (less than 60% activity)

Methylenetetrahydrofolate Reductase Mutations

Insufficient evidence to support assessment of MTHFR or fasting homocysteine levels in the evaluation of VTE (a weak risk factor).

Homozygosity for the MTHFR mutation is the most common cause of hyperhomocysteinemia.

Rx: folate, B6 (?)

Other Thrombophilias

- Mutations in the factor V gene
- Promoter mutation in the PAI-1 gene
- Protein Z deficiency

* *There is **insufficient evidence** to recommend testing for these thrombophilias even in the setting of diagnosed VTE.*

Inherited Thrombophilias and Adverse Pregnancy Outcomes

* ***A definitive causal link cannot be made between inherited thrombophilias and adverse pregnancy outcomes.***

Adverse pregnancy outcome:

- pregnancy loss, preeclampsia, fetal growth restriction, placental abruption

Level II-2

Anticoagulation for Prevention of Adverse Pregnancy Outcomes

* *There is insufficient evidence to recommend anticoagulation as an intervention to prevent adverse pregnancy outcomes among women with inherited thrombophilias.*

Level I

Recommendations

*Who are **candidates** for thrombophilia evaluation?*

1. A personal history of VTE, with or without a recurrent risk factor, and no prior thrombophilia testing. In a population-based study, the recurrence risk of VTE in untreated pregnant women differed based on whether the prior embolism was associated with a recurrent (eg, pregnancy, estrogen containing contraceptives) or nonrecurrent (eg, fractures, surgery, prolonged immobilization) risk factor.

2. A first-degree relative (eg, parent or sibling) with a history of high-risk inherited thrombophilia.

ACOG Practice Bulletin No. 197: Inherited Thrombophilias in Pregnancy [published correction appears in Obstet Gynecol. 2018 Oct;132(4):1069]. Obstet Gynecol. 2018;132(1):e18-e34. doi:10.1097/AOG.0000000000002703

Recommendations

Screening for inherited thrombophilias is not recommended for women with a history of fetal loss or adverse pregnancy outcomes.

Testing for the acquired antibodies present in antiphospholipid syndrome should be considered in the setting of recurrent pregnancy loss or stillbirth.

Level iii

Recommendations

- If the ***asymptomatic patient + heterozygous defects*** → thromboprophylaxis is indicated in the presence of other risk factors for VTE (eg, C/S, prolonged immobilization, severe obesity, or a first-degree relative with VTE before age 50 years).
- ***Couples with IVF failure:*** We would **not** screen

updated: Nov 25, 2019

Recommendations

What laboratory tests are recommended for thrombophilia screening with personal histories of VTE and no prior thrombophilia testing?

1. **APC resistance and Factor V Leiden mutation***
2. **Prothrombin G20210A mutation**
3. **Antithrombin deficiency**
4. **Protein C deficiency**
5. **Protein S deficiency**
6. Thrombophilia screening includes testing for **acquired thrombophilia with antiphospholipid antibodies.**

consensus and expert opinion (Level C)

Recommendations

Protein S assay

- Ideally, protein S deficiency should be assessed initially by a functional assay remote from pregnancy.
- A value less than 55% should be followed up by assessing free protein S levels.
- In the nonpregnant state, a free protein S antigen value **less than 55%** (65%) is consistent with protein S deficiency.
- In pregnancy, it is unclear what protein S activity value is diagnostic, but free protein S cutoffs of **less than 30% and less than 24% may be used in the second and third trimesters**, respectively.

Level II-3

Recommendations

Whenever possible, laboratory testing should be performed remote ***(after 6 weeks) from the thrombotic event*** and while the patient is not pregnant and not taking anticoagulation or hormonal therapy.

Haemostasis and Thrombosis Task Force, British Committee for Standards in Haematology. Investigation and management of heritable thrombophilia. Br J Haematol. 2001;114(3):512-528. doi:10.1046/j.1365-2141.2001.02981.x

Recommendations

Postpartum, normalization of coagulation parameters and factor levels return to baseline by ***6 - 8 weeks after delivery***. Hemostasis is not evaluated by functional assays earlier than ***3 months following delivery and after terminating breastfeeding*** to exclude pregnancy-related effects.

Saha P, Stott D, Atalla R. Haemostatic changes in the puerperium '6 weeks postpartum' (HIP Study) - implication for maternal thromboembolism. BJOG. 2009;116(12):1602-1612. doi:10.1111/j.1471-0528.2009.02295.x

Table 2. How to Test for Inherited Thrombophilias

Thrombophilia	Testing Method	Is Testing Reliable During Pregnancy?	Is Testing Reliable During Acute Thrombosis?	Is Testing Reliable With Anti-coagulation?
Factor V Leiden mutation	Activated protein C resistance assay (second generation)	Yes	Yes	No
	If abnormal: DNA analysis	Yes	Yes	Yes
Prothrombin G20210A mutation	DNA analysis	Yes	Yes	Yes
Protein C deficiency	Protein C activity (<65%)	Yes	No	No
Protein S deficiency	Functional assay (<55%)	No*	No	No
Antithrombin deficiency	Antithrombin activity (<60%)	Yes	No	No

*If screening in pregnancy is necessary, cutoff values for free protein S antigen levels in the second and third trimesters have been identified at less than 30% and less than 24%, respectively.

Recommendations

In which patients should anticoagulants be considered to prevent VTE?

- All patients with inherited thrombophilias should undergo individualized **risk assessment.**
- The decision to use anticoagulants is influenced by personal history of VTE, severity of inherited thrombophilia, family history of VTE, and additional risk factors such as cesarean delivery, obesity, and prolonged immobility. *consensus and expert opinion (Level C)*
- **These authors recommended prophylaxis if the risk of VTE was 3% or greater.**

High risk?

- Women who are known to be **homozygous** for the factor V Leiden mutation or prothrombin gene mutation should receive pharmacologic prophylaxis **during pregnancy and the postpartum period**
- Women with antithrombin deficiency and women who are heterozygous for factor V and the prothrombin gene mutation

Lower risk?

- Factor V Leiden heterozygous
- Prothrombin G20210A heterozygous
- Protein C or S deficiency

Recommendations

What anticoagulant regimens?

- **LMWH** is preferred over UFH
- Vitamin K antagonists should be avoided in pregnancy (exception of prophylaxis in women with a mechanical heart valve)

Recommendations

Dosage?

- Depending on severity of thrombophilia, obesity, cesarean delivery, family history, history of VTE
- Antithrombin concentrates can be used in antithrombin-deficient patients who are refractory to standard anticoagulant therapy or as part of a multidisciplinary plan
- There is insufficient evidence to recommend changing the prophylactic dose based on weight.

Table 4. Anticoagulation Regimen Definitions

Anticoagulation Regimen	Anticoagulation Dosage
Prophylactic LMWH*	Enoxaparin, 40 mg SC once daily Dalteparin, 5,000 units SC once daily Tinzaparin, 4,500 units SC once daily Nadroparin 2,850 units SC once daily
Intermediate-dose LMWH	Enoxaparin 40 mg SC every 12 hours Dalteparin 5,000 units SC every 12 hours
Adjusted-dose (therapeutic) LMWH†	Enoxaparin, 1 mg/kg every 12 hours Dalteparin, 200 units/kg once daily Tinzaparin, 175 units/kg once daily Dalteparin, 100 units/kg every 12 hours Target an anti-Xa level in the therapeutic range of 0.6–1.0 units/mL 4 hours after last injection for twice-daily regimen; slightly higher doses may be needed for a once-daily regimen.
Prophylactic UFH	UFH, 5,000–7,500 units SC every 12 hours in first trimester UFH, 7,500–10,000 units SC every 12 hours in the second trimester UFH, 10,000 units SC every 12 hours in the third trimester, unless the aPTT is elevated
Adjusted-dose (therapeutic) UFH†	UFH, 10,000 units or more SC every 12 hours in doses adjusted to target aPTT in the therapeutic range (1.5–2.5 × control) 6 hours after injection
Postpartum anticoagulation	Prophylactic, intermediate, or adjusted dose LMWH for 6–8 weeks as indicated. Oral anticoagulants may be considered postpartum based upon planned duration of therapy, lactation, and patient preference.
Surveillance	Clinical vigilance and appropriate objective investigation of women with symptoms suspicious of deep vein thrombosis or pulmonary embolism. VTE risk assessment should be performed prepregnancy or early in pregnancy and repeated if complications develop, particularly those necessitating hospitalization/prolonged immobility.

Recommendations

How long?

Women deemed to require pharmacologic prophylaxis during pregnancy will typically continue anticoagulation for at least 6 weeks postpartum. *Level III*

Women with recurrent VTE events or other indications for life-long full anticoagulation should receive adjusted-dose LMWH throughout pregnancy with transition back to maintenance anticoagulation postpartum. *Level III*

Table 3. Recommended Thromboprophylaxis for Pregnancies Complicated by Inherited Thrombophilias*

Clinical Scenario	Antepartum Management	Postpartum Management
Low-risk thrombophilia† without previous VTE	Surveillance without anticoagulation therapy	Surveillance without anticoagulation therapy or postpartum prophylactic anticoagulation therapy if the patient has additional risks factors‡
Low-risk thrombophilia† with a family history (first-degree relative) of VTE	Surveillance without anticoagulation therapy or prophylactic LMWH/UFH	Postpartum prophylactic anticoagulation therapy or intermediate-dose LMWH/UFH
Low-risk thrombophilia† with a single previous episode of VTE—Not receiving long-term anticoagulation therapy	Prophylactic or intermediate-dose LMWH/UFH	Postpartum prophylactic anticoagulation therapy or intermediate-dose LMWH/UFH
High-risk thrombophilia§ without previous VTE	Prophylactic or intermediate-dose LMWH/UFH	Postpartum prophylactic anticoagulation therapy or intermediate-dose LMWH/UFH
High-risk thrombophilia§ with a single previous episode of VTE or an affected first-degree relative—Not receiving long-term anticoagulation therapy	Prophylactic, intermediate-dose, or adjusted-dose LMWH/UFH	Postpartum prophylactic anticoagulation therapy, or intermediate or adjusted-dose LMWH/UFH for 6 weeks (therapy level should be equal to the selected antepartum treatment)
Thrombophilia with two or more episodes of VTE—Not receiving long-term anticoagulation therapy	Intermediate-dose or adjusted-dose LMWH/UFH	Postpartum anticoagulation therapy with intermediate-dose or adjusted-dose LMWH/UFH for 6 weeks (therapy level should be equal to the selected antepartum treatment)
Thrombophilia with two or more episodes of VTE—Receiving long-term anticoagulation therapy	Adjusted-dose LMWH/UFH	Resumption of long-term anticoagulation therapy. Oral anticoagulants may be considered postpartum based upon planned duration of therapy, lactation, and patient preference.

Abbreviations: LMWH, low-molecular-weight heparin; UFH, unfractionated heparin; VTE, venous thromboembolism.

*Postpartum treatment levels should be equal to antepartum treatment.

†Low-risk thrombophilia: factor V Leiden heterozygous; prothrombin G20210A heterozygous; protein C or protein S deficiency.

‡First-degree relative with a history of a thrombotic episode or other major thrombotic risk factors (eg, obesity, prolonged immobility, cesarean delivery).

§High-risk thrombophilias include factor V Leiden homozygosity, prothrombin gene G20210A mutation homozygosity, heterozygosity for factor V Leiden and prothrombin G20210A mutation, or antithrombin deficiency.

Approach to VTE prophylaxis in pregnant women with inherited thrombophilias

Approach to VTE prophylaxis in pregnant women with inherited thrombophilias

Clinical setting	Antepartum management	Postpartum management
Lower-risk thrombophilia* with personal history of previous VTE or Higher-risk thrombophilia¶ without personal history of previous VTE	Anticoagulation therapy (intermediate dose)	Anticoagulation therapy (intermediate dose)
Lower-risk thrombophilia* without personal history of VTE	Surveillance for VTE without anticoagulation therapy. Anticoagulation may be warranted for individual patients with additional factors that place them at greater risk of thrombosis (eg, prolonged immobility, first-degree relative with unprovoked VTE at age <50 years).	Anticoagulation therapy (prophylactic dose) for women who deliver by cesarean
Higher-risk thrombophilia¶ with previous VTE on chronic anticoagulation	Anticoagulation therapy (therapeutic dose)	Anticoagulation therapy (therapeutic dose)

Postpartum anticoagulation can generally be started four to six hours after vaginal delivery or 6 to 12 hours after cesarean delivery, unless there is significant bleeding or risk for significant bleeding.

VTE: venous thromboembolism.

* Lower-risk thrombophilias include women who are heterozygotes for factor V Leiden (FVL) or prothrombin G20210A gene mutation (PGM) and women with deficiencies of protein C or protein S.

¶ Higher-risk thrombophilias include women with antithrombin (AT) deficiency, homozygotes for the FVL mutation, homozygotes for the PGM mutation, double heterozygotes for FVL and PGM.

Use of heparins during pregnancy

Heparin	Dose level	Dosage
LMW heparin	Prophylactic*	Enoxaparin 40 mg SC once daily
		Dalteparin 5000 units SC once daily
	Intermediate¶	Enoxaparin 40 mg SC once daily, increase as pregnancy progresses to 1 mg/kg once daily
		Dalteparin 5000 units SC once daily, increase as pregnancy progresses to 100 units/kg once daily
	Therapeutic	Enoxaparin 1 mg/kg SC every 12 hours
		Dalteparin 100 units/kg SC every 12 hours
Unfractionated heparin	Prophylactic	5000 units SC every 12 hours
	Intermediate¶	First trimester: 5000 to 7500 units SC every 12 hours
		Second trimester: 7500 to 10,000 units SC every 12 hours
		Third trimester: 10,000 units SC every 12 hours
	Therapeutic	Can be given as a continuous IV infusion or a SC dose every 12 hours. Titrated to keep the aPTT in the therapeutic range.

Doses apply to pregnant women receiving heparin for venous thromboembolism prophylaxis. Therapeutic dose level refers to doses used both for prophylaxis in individuals at especially high risk and for treatment of venous thromboembolism. This dosing table should **not** be used in women with prosthetic heart valves. Refer to the UpToDate topic on anticoagulant use in pregnancy for details of administration and monitoring. Refer to UpToDate topics on specific pregnant patient populations for other dosing recommendations (eg, prosthetic heart valve, atrial fibrillation, treatment of deep vein thrombosis or pulmonary embolism).

LMW: low molecular weight; IV: intravenous; SC: subcutaneously; aPTT: activated partial thromboplastin time.

* Prophylactic dosing may require modifications for extremes of body weight; refer to the UpToDate table on LMW heparin dosing in obesity for details.

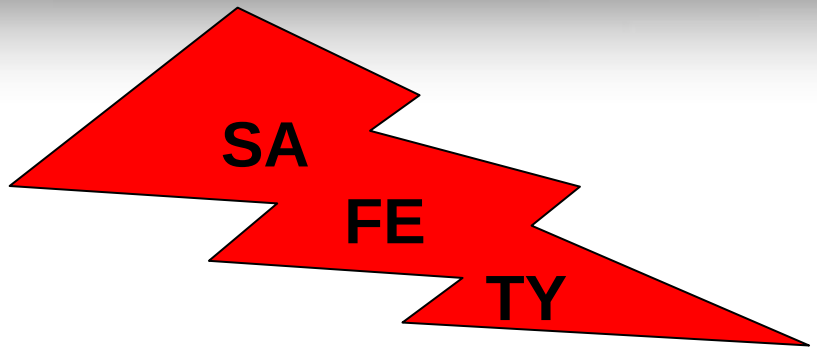
¶ Our "intermediate" dose level differs from that used in society guidelines (eg, ACCP, ACOG). Some clinicians prefer to use a different "intermediate" dose level such as enoxaparin 40 mg SC every 12 hours; however, this entails a significant increase in the number of injections over the course of the pregnancy.

Recommendations

Level assessment

- Goal anti-Xa level of 0.6–1.0 units/mL 4 hours after injection
- Routine assessment Of anti-Xa levels in the setting of prophylactic anticoagulation is not recommended.
- Routine anti-Xa levels is controversial even in the setting of adjusted-dose therapy.
- If using UFH, mid-interval aPTT should be checked in order to ensure therapeutic dosage.

Recommendations



- **UFH, LMWH, and Warfarin are compatible with breastfeeding**.
- Oral direct thrombin inhibitors (Dabigatran) and anti Xa inhibitors (Rivaroxaban, Apixaban) should be avoided in pregnancy and lactation because there are insufficient data

Level III

Fetal surveillance and timing of delivery

- Given that there may be a small absolute increase in risk of stillbirth in women with inherited thrombophilias who are receiving or not receiving prophylactic anticoagulation, we suggest ***weekly fetal assessment with NST beginning at ≥36 weeks***.

Recommendations

What is appropriate peripartum management for thrombophilic patients?

- The presence of a thrombophilia alone is **not an indication for induction** outside of standard obstetric indications.
- **Adjusted dose** LMWH should be held for **24 hours**, and **prophylactic LMWH for 12 hours** before induction of labor to facilitate neuraxial anesthesia placement.

SOAP 2017

Recommendations

- Consideration can be given to **substituting a comparable dose of UFH** as delivery approaches (because of its shorter half-life).
- A **12-hour interval** from last dose of **UFH** if the dose is **more than 7,500 units**, in addition to **laboratory testing** to verify normal aPTT.

SOAP 2017

Recommendations

- All women undergoing C/S should have sequential compression devices at a minimum, with consideration for pharmacologic prophylaxis depending on the type of thrombophilia and other risk factors.
- Patients receiving UFH or LMWH who require rapid reversal of the anticoagulant effect for delivery can be treated with protamine sulfate.

Recommendations

What is the appropriate management of thrombophilic patients who require postpartum anticoagulation therapy?

- Postpartum doses of UFH or LMWH → equal to antepartum
- The optimal time to restart postpartum anticoagulation is unclear:

- **No sooner than 4–6 hours after vaginal delivery**
- **6–12 hours after cesarean delivery**

ACOG 2018 level III

Recommendations

- Warfarin therapy can begin immediately after delivery since it takes a few days to achieve anticoagulation.
- To avoid paradoxical thrombosis and skin necrosis from the early anti-protein C effect of warfarin, women who will be treated with Warfarin should be bridged with adjusted-dose LMWH or UFH until an INR in the therapeutic range (2.0–3.0) is achieved for 2 consecutive days. Initial dose of warfarin is 5 mg daily for 2 days, with subsequent doses determined by monitoring the INR.

Recommendations

What postpartum contraceptive options are appropriate for women with thrombophilias?

Screening all women for thrombophilias before initiating combination contraception is not recommended.

Alternative methods of contraception such as **IUD (containing progestin), progestin-only pills or implants, and barrier methods** should be considered for women with known inherited thrombophilias.

Level III

Society for Maternal-Fetal Medicine (SMFM) Recommendations

1. ***Don’t do an inherited thrombophilia evaluation for women with histories of pregnancy loss, IUGR, preeclampsia and abruption.***
2. ***Don't test women for MTHFR mutations.***
3. All women who undergo C/S receive sequential compression devices starting prior to surgery and that they be continued until the patient is fully ambulatory (GRADE 1C).
4. Women with a previous personal history of a DVT or PE who undergo C/S receive both mechanical (starting preoperatively and continuing until ambulatory) and pharmacological (for 6 weeks postoperatively) prophylaxis (GRADE 2C).

Society for Maternal·Fetal Medicine

Society for Maternal-Fetal Medicine (SMFM) Recommendations

5. Women with a personal history of an ***inherited thrombophilia (high risk and low risk) but no previous thrombosis*** who undergo C/S receive ***both mechanical (starting preoperatively and continuing until ambulatory) and pharmacological (for 6 weeks postoperatively) prophylaxis*** (GRADE 2C).
6. The use of LMWH as the preferred thromboprophylactic agent in pregnancy and the postpartum period (GRADE 1C).
7. When pharmacologic thromboprophylaxis is needed in women with class III obesity, we suggest the use of intermediate doses of enoxaparin (GRADE 2C).

Society for Maternal·Fetal Medicine

Society for Maternal-Fetal Medicine (SMFM) Recommendations

8. Each institution develop a patient safety bundle with an institutional protocol for VTE prophylaxis among women who undergo C/S (Best Practice).

Society for Maternal·Fetal Medicine

Released February 3, 2014 (1–5); February 1, 2016 (6–10) and May 1, 2019 (11–15

	امتیاز
عوامل خطر مرتبط با شرایط طبی	
سابقه VTE قبلی (به جز موارد VTE به علت جراحی بزرگ)	٤
ترومبوفیلی اکتسابی (سندرم آنتی فسفولیپید آنتی بادی): حداقل یک معیار آزمایشگاهی و حداقل یک معیار بالینی	٤
سابقه VTE قبلی به علت جراحی بزرگ	٣
هر یک از مشکلات طبی: سرطان، بیماری قلبی، لوپوس فعال، پلی آرتروپاتی التهابی یا بیماری التهابی روده ، سندرم نفروتیک، دیابت ملیتوس نوع یک با نفروپاتی، بیماری سیکل سل، اعتیاد تزریقی وریدی کنونی	٣
ترومبوفیلی ارثی پر خطر (کمبود آنتی ترومبین، کمبود پروتیین C یا S ، ترومبوفیلی کم خطر هموزیگوت یا همراه)	٣
ترومبوفیلی ارثی کم خطر (فاکتور ٥لیدن هتروزیگوت، جهش ژن پروترومبین G٢٠٢١٠A)	١
تاریخچه خانوادگی VTE (بدون زمینه یا وابسته به استروژن) در بستگان درجه اول	١
وجود آنتی فسفولیپید آنتی بادی (فقط معیار آزمایشگاهی، بدون وجود معیار بالینی)	١
عوامل خطر مرتبط با شرایط عمومی	
چاقی (BMI مساوی یا بیشتر از ٤٠) قبل یا اوایل بارداری	٢
چاقی (BMI مساوی یا بیشتر از ٣٠ و کمتر از ٤٠) قبل یا اوایل بارداری	١
سن بیشتر از ٣٥ سال	١
سابقه سه بار یا بیشتر زایمان (para ≥ ٣) صرف نظر از بارداری فعلی	١
استعمال سیگار	١
وجود وریدهای واریسی واضح (علامتدار یا بالای زانو یا همراه با ظبیت، ادم، تغییرات پوستی)	١
عوامل خطر مامایی و زایمان	
سزارین اورژانس (در لیبر)	٢
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مرده زایی در بارداری کنونی	١
عوامل خطر موقت	
سندرم هیپراستیمولیشن تخمدان (فقط در سه ماهه اول در نظر گرفته شود)	٤
جراحی در دوران بارداری یا پس از زایمان (آپاندکتومی، بستن لوله ها، ...) به جز ترمیم فوری پرینه	٣
استفراغ شدید بارداری (به حدی که باعث از دست دادن وزن، دهیدراتاسیون، کتوز، آلکالوز به دلیل از دست دادن اسید کلریدریک و هیپوکالمی شود)	٣
عفونت سیستمیک (نیازمند تجویز آنتی بیوتیک یا بستری) مانند پنومونی، پیلونفریت، عفونت زخم بعد از زایمان	١
بستری در بیمارستان یا بی حرکتی (مساوی یا بیشتر از ٣ روز استراحت در بستر)، دهیدراتاسیون	١

ارزیابی عوامل خطر ایجاد ترومبوآمبولی وریدی (VTE) در بارداری و پس از زایمان

پروتکل کشوری

نکات مهم

- در موارد زیر تجویز داروی ضد انعقاد می بایست تا ٦ هفته پس از زایمان ادامه یابد:
  - سابقه VTE قبلی
  - ترومبوفیلی ارثی از نوع پرخطر بدون علامت که خود سابقه VTE دارند.
  - ترومبوفیلی اکتسابی (سندرم آنتی فسفولیپید آنتی بادی): یعنی وجود حداقل یک معیار آزمایشگاهی و حداقل یک معیار بالینی
  - ترومبوفیلی ارثی از نوع کم خطر که خود سابقه VTE ندارند ولی سابقه VTE در بستگان درجه اول وجود دارد.

Take home message

- Because there is insufficient clinical evidence that antepartum prophylaxis with UFH or LMWH prevents recurrence in women with a history of fetal loss or adverse pregnancy outcomes, screening for inherited thrombophilias is not recommended.
- Among women with personal histories of VTE, recommended screening tests for inherited thrombophilias should include factor V Leiden mutation; prothrombin G20210A mutation; and antithrombin, protein S, and protein C deficiencies.
- All patients with inherited thrombophilias should undergo individualized risk assessment, which may modify management decisions regarding VTE prevention.

Take home message

- Because of the lack of association between either heterozygosity or homozygosity for the MTHFR C677T polymorphism and any negative pregnancy outcomes, including any increased risk of VTE, screening with either MTHFR mutation analyses or fasting homocysteine levels is not recommended.
- Warfarin, LMWH, and UFH do not accumulate in breast milk and do not induce an anticoagulant effect in the infant; therefore, these anticoagulants may be used in women who breastfeed.

Thank you