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Clinical Management Guidelines for Obstetrician–Gynecologists

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For a comprehensive overview of these recommendations, the full-text version of this Practice Bulletin is available at <http://dx.doi.org/10.1097/AOG.0000000000002703>.



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Committee on Practice Bulletins—Obstetrics. This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics with the assistance of Torri D. Metz, MD, and Neil S. Silverman, MD.

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.

Clinical Management Questions

- ▶ Who are candidates for thrombophilia evaluation?
- ▶ What laboratory tests are recommended for thrombophilia screening among women with personal histories of venous thromboembolism and no prior thrombophilia testing?
- ▶ In which patients should anticoagulants be considered to prevent venous thromboembolism?
- ▶ What anticoagulant regimens are available for pregnant women?
- ▶ What is appropriate peripartum management for thrombophilic patients?
- ▶ What is the appropriate management of thrombophilic patients who require postpartum anticoagulation therapy?
- ▶ What postpartum contraceptive options are appropriate for women with thrombophilias?



[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.

Recommendations

The following recommendations are based on limited or inconsistent scientific evidence (Level B):

- ▶ Screening for inherited thrombophilias is not recommended for women with a history of fetal loss or adverse pregnancy outcomes including abruption, preeclampsia, or fetal growth restriction because
- ▶ there is insufficient clinical evidence that antepartum prophylaxis with unfractionated heparin or low-molecular-weight heparin prevents recurrence in these patients.
- ▶ 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, low-molecular-weight heparin, and unfractionated heparin 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.

The following recommendations are based primarily on consensus and expert opinion (Level C):

- ▶ 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.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force. Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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American College of Obstetricians and Gynecologists
409 12th Street, SW, PO Box 96920, Washington, DC 20090-6920

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