PRACTICE BULLETIN

CLINICAL MANAGEMENT GUIDELINES FOR OBSTETRICIAN–GYNECOLOGISTS

Thromboembolism in Pregnancy

Pregnant women have a fourfold to fivefold increased risk of thromboembolism compared with nonpregnant women (1, 2). Approximately 80% of thromboembolic events in pregancy are venous (3), with a prevalence of 0.5–2.0 per 1,000 pregnant women (4–9). Venous thromboembolism, including pulmonary embolism, accounts for 1.1 deaths per 100,000 deliveries (3), or 9 % of all maternal deaths in the United States (10). In the developing world, the leading cause of maternal death is hemorrhage (11); however, in developed nations, where hemorrhage is more success-fully treated and prevented, thromboembolic disease is one of the leading causes of death (12).

The prevalence and severity of this condition during pregnancy and the peripartum period warrant special consider-ation of management and therapy. Such therapy includes the treatment of acute thrombotic events and prophylaxis for those at increased risk of thrombotic events. The purpose of this document is to provide information regarding the risk factors, diagnosis, management, and prevention of thromboembolism, particularly venous thromboembolism in pregnancy.

Background

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are collectively referred to as venous thromboem-bolic events. Approximately 75–80% of cases of preg-nancy-associated venous thromboembolism are caused by DVT, and 20–25% of cases are caused by PE (3, 7, 13). One half of these events occur during pregnancy and one half occur during the postpartum period (3–8).

Pregnancy-Associated Changes and Venous Thromboembolism

Pregnancy is associated with physiologic and anatomic changes that increase the risk of thromboembolism, including hypercoagulability, increased venous stasis, decreased venous outflow (14, 15), compression of the inferior vena cava and pelvic veins by the enlarging uterus (16), and decreased mobility (17–20). Pregnancy alters the levels of coagulation factors normally respon-sible for hemostasis. The overall effect of these changes is an increased thrombogenic state (see Table 1). When DVT occurs during pregnancy, it is more likely to involve the left lower extremity (21–23).

Risk Factors

The risk of venous thromboembolism may be higher in the third trimester compared with the first and second trimesters (2), but the increased risk of venous throm-boembolism is present from the first trimester (22, 23), often before many of the anatomic changes of pregnancy occur. The risk of venous thromboembolism is higher during the postpartum period than it is during pregnancy, especially during the first week postpartum (1).

The most important individual risk factor for venous thromboembolism in pregnancy is a personal history of thrombosis. The risk of recurrent venous thromboembo-

Table 1. Changes in the Normal Functioning of the Coagulation System During Pregnancy

Coagulant Factors	Change in Pregnancy
Procoagulants	
Fibrinogen	Increased
Factor VII	Increased
Factor VIII	Increased
Factor X	Increased
Von Willebrand factor	Increased
Plasminogen activator inhibitor-1	Increased
Plasminogen activator inhibitor-2	Increased
Factor II	No change
Factor V	No change
Factor IX	No change
Anticoagulants	
Free Protein S	Decreased
Protein C	No change
Antithrombin III	No change

Data from Bremme KA. Haemostatic changes in pregnancy. Best Practice & Research Clinical Haematology. 2003;16:153–68 *and* Medcalf RL, Stasinopoulos SJ. The undecided serpin: the ins and outs of plasminogen activator inhibitor type 2. FEBS J 2005;272:4858–67.

lism during pregnancy is increased threefold to fourfold (relative risk, 3.5; 95% confidence interval, 1.6–7.8), and 15–25% of all cases of venous thromboembolism in pregnancy are recurrent events (24). The next most important individual risk factor for venous thromboembolism in pregnancy is the presence of a thrombophilia (3, 23). Thrombophilia is present in 20–50% of women who experience venous thromboembolism during pregnancy and the postpartum period (25). Both acquired and inherited thrombophilias increase the risk of venous thromboembolism (26).

Besides a personal history of thrombosis, other risk factors for the development of pregnancy-associated venous thromboembolism include the physiologic changes that accompany pregnancy and childbirth, medical factors (such as obesity, hemoglobinopathies, hypertension, and smoking), and pregnancy complications (including operative delivery) (3, 6–8, 17, 27, 28).

Anticoagulation Medications in Pregnancy

The use of anticoagulation therapy in women during pregnancy warrants special consideration for both mother and fetus. Most women who require anticoagulation therapy before conception will need to continue this therapy during pregnancy and the postpartum period. Common anticoagulation medications include unfractionated heparin, low molecular weight heparin (LMWH), and warfarin. The preferred anticoagulants in pregnancy are heparin compounds.

Heparin Compounds

Neither unfractionated heparin nor LMWH crosses the placenta (29, 30) and both are considered safe in pregnancy (31). Unique considerations regarding the use of anticoagulation therapy in pregnancy include a 40–50% increase in maternal blood volume; an increase in glomerular filtration, which results in increased renal excretion of heparin compounds; and an increase in protein binding of heparin (32). During pregnancy, both unfractionated heparin and LMWH have shorter half-lives and lower peak plasma concentrations, usually necessitating higher doses and more frequent administration in order to maintain effective concentrations (33–39).

There are few comparative studies of LMWH use in pregnancy, but in nonpregnant patients, LMWH has been associated with fewer adverse effects than unfractionated heparin (40). Potential advantages of LMWH include fewer bleeding episodes, a more predictable therapeutic response, a lower risk of heparin-induced thrombocytopenia, a longer half-life, and less bone mineral density loss (31, 41, 42).

Importantly, neither LMWH nor unfractionated heparin is associated with significant bone loss when used in prophylactic doses during pregnancy (43–45). Unfractionated heparin, which is associated with increased bruising at the injection sites, also has been associated with other skin reactions and serious allergic reactions (46). Moreover, unfractionated heparin is dispensed in multiple-dose vials, which are potentially vulnerable to contamination (47). Besides its greater cost, a relative disadvantage of LMWH at the time of delivery is its longer half-life, which is an important consideration for both neuraxial anesthesia and peripartum bleeding risk.

Warfarin

Warfarin, a common agent for long-term anticoagulation therapy outside of pregnancy, has been associated with potentially harmful fetal effects, especially with first-trimester exposure (48–54). Warfarin embryopathy has been linked with exposure at 6–12 weeks of gestation, highlighting the importance of early pregnancy care in such patients (55). Therefore, for most women receiving prolonged anticoagulation therapy who become pregnant, it is recommended that unfractionated heparin or LMWH be used in place of warfarin.

Although rarely prescribed in pregnancy, warfarin is still considered in pregnancy for women with mechanical heart valves because of their high risk of thrombosis

even with heparin or LMWH anticoagulation therapy (56). The management of such women requires a multidisciplinary care approach, and the decision regarding optimal anticoagulation therapy merits a detailed discussion with the patient and her health care providers regarding the risks and benefits of the various treatment options.

Clinical Considerations and Recommendations

▶ *What is the appropriate evaluation of women with a prior venous thromboembolism?*

Women with a history of thrombosis who have not had a complete evaluation of possible underlying etiologies should be tested for both antiphospholipid antibodies (57) and for inherited thrombophilias (58). The results of thrombophilia testing in women with a prior venous thromboembolism may alter the need for treatment or the intensity of treatment from a prophylactic to a therapeutic dose (also known as adjusted-dose or weight-based dose) of LMWH or unfractionated heparin (59).

▶ *How is a venous thromboembolism diagnosed in pregnancy?*

Deep Vein Thrombosis

The two most common initial symptoms of DVT, present in more than 80% of women with pregnancy-associated DVT, are pain and swelling in an extremity (23). A difference in calf circumference of 2 cm or more is particularly suggestive of DVT in a lower extremity (60). When signs or symptoms suggest new-onset DVT, the recommended initial diagnostic test is compression ultrasonography of the proximal veins (40). When results are negative and iliac vein thrombosis is not suspected, routine surveillance may be a reasonable option (see Fig. 1). When results are negative or equivocal and iliac vein thrombosis is suspected, additional confirmatory imaging with magnetic resonance imaging is recommended (61). Alternatively, depending on the clinical circumstances, empiric anticoagulation may be a reasonable option (see Fig. 1). Although measurement of D-dimer levels is a useful screening tool to exclude venous thromboembolism in the nonpregnant population, pregnancy is accompanied by a progressive increase in D-dimer levels, even a high D-dimer level does not predict venous thromboembolism in pregnancy (62–64).

Pulmonary Embolism

The diagnosis of new-onset PE is similar to that in the nonpregnant individual. Both ventilation–perfusion
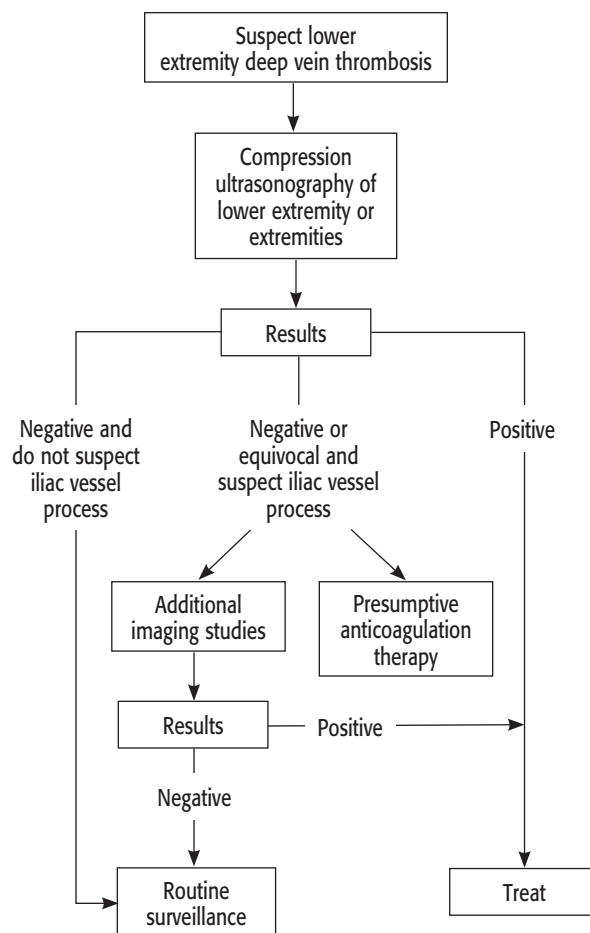
Fig. 1. Diagnosis of deep vein thrombosis during pregnancy. Figure provided courtesy of Leo R. Brancazio, MD.

scanning and computed tomographic (CT) angiography are associated with relatively low radiation exposure for the fetus (65). The concerns about maternal breast radiation exposure with CT angiography must be weighed against the potential consequences of withholding appropriate imaging and failing to make a proper diagnosis. A recent study concluded that a chest X-ray could be used as a discriminator to reduce the likelihood of nondiagnostic ventilation–perfusion scanning and CT angiography in this setting (66).

▶ *Who are candidates for anticoagulation therapy during pregnancy?*

Therapeutic anticoagulation is recommended for all women with acute venous thromboembolism during pregnancy. Other candidates for either prophylactic or therapeutic anticoagulation during pregnancy include women with a history of thrombosis or those who are at significant risk of venous thromboembolism during pregnancy or the postpartum period, such as those with

high-risk acquired or inherited thrombophilias (see Table 2).

Despite the increased risk of venous thromboembolism during pregnancy and the postpartum period, routine anticoagulation therapy for all pregnant women is not warranted (67, 68). Bleeding complications can arise from administration of unfractionated heparin or LMWH, and this complication should be considered before initiating anticoagulation therapy (31, 41, 69, 70).

▶ *How should anticoagulation therapy be administered?*

There are no large trials regarding the optimal dose of anticoagulants in pregnancy, and recommendations for their use are based on case series and expert opinion. Therapeutic anticoagulation is recommended for women with acute thromboembolism during the current pregnancy or those at high risk of thrombosis, such as women with mechanical heart valves (40). The decision regarding intensity of treatment may be shaped by other risk factors such as cesarean delivery, prolonged immobility, obesity, and family history of thrombophilias or venous thromboembolism (see Table 3). For women with a history of idiopathic thrombosis or those with transient risk factors who are not taking anticoagulants as a lifelong treatment and have either no thrombophilia or a low-risk thrombophilia, experts recommend antepartum prophylactic anticoagulation or antepartum surveillance

Table 2. Recommended Thromboprophylaxis for Pregnancies Complicated by Inherited Thrombophilias*

Clinical Scenario	Antepartum Management	Postpartum Management
Low-risk thrombophilia† without previous VTE	Surveillance without anticoagulation therapy or prophylactic LMWH or UFH	Surveillance without anticoagulation therapy or postpartum anticoagulation therapy if the patient has additional risks factors‡
Low-risk thrombophilia† with a single previous episode of VTE—Not receiving long-term anticoagulation therapy	Prophylactic or intermediate-dose LMWH/UFH or surveillance without anticoagulation therapy	Postpartum anticoagulation therapy or intermediate-dose LMWH/UFH
High-risk thrombophilia§ without previous VTE	Prophylactic LMWH or UFH	Postpartum anticoagulation therapy
High-risk thrombophilia§ with a single previous episode of VTE—Not receiving long-term anticoagulation therapy	Prophylactic, intermediate-dose, or adjusted-dose LMWH/UFH regimen	Postpartum anticoagulation therapy or intermediate or adjusted-dose LMWH/UFH for 6 weeks (therapy level should be at least as high as antepartum treatment)
No thrombophilia with previous single episode of VTE associated with transient risk factor that is no longer present—Excludes pregnancy- or estrogen-related risk factor	Surveillance without anticoagulation therapy	Postpartum anticoagulation therapy‖
No thrombophilia with previous single episode of VTE associated with transient risk factor that was pregnancy- or estrogen-related	Prophylactic-dose LMWH or UFH‖	Postpartum anticoagulation therapy
No thrombophilia with previous single episode of VTE without an associated risk factor (idiopathic)—Not receiving long-term anticoagulation therapy	Prophylactic-dose LMWH or UFH‖	Postpartum anticoagulation therapy
Thrombophilia or no thrombophilia with two or more episodes of VTE—Not receiving long-term anticoagulation therapy	Prophylactic or therapeutic-dose LMWH or Prophylactic or therapeutic-dose UFH	Postpartum anticoagulation therapy or Therapeutic-dose LMWH/UFH for 6 weeks
Thrombophilia or no thrombophilia with two or more episodes of VTE—Receiving long-term anticoagulation therapy	Therapeutic-dose LMWH or UFH	Resumption of long-term anticoagulation therapy

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

*Postpartum treatment levels should be greater or equal to antepartum treatment. Treatment of acute VTE and management of antiphospholipid syndrome are addressed in other Practice Bulletins.

†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 before age 50 years, or other major thrombotic risk factors (eg, obesity, prolonged immobility).

§High-risk thrombophilia: antithrombin deficiency; double heterozygous for prothrombin *G20210A* mutation and factor V Leiden; factor V Leiden homozygous or prothrombin *G20210A* mutation homozygous.

‖Surveillance without anticoagulation is supported as an alternative approach by some experts.

Table 3. Anticoagulation Regimens

Management Type	Dosage
Prophylactic LMWH*	Enoxaparin, 40 mg SC once daily Dalteparin, 5,000 units SC once daily Tinzaparin, 4,500 units SC once daily
Therapeutic LMWH† (Also referred to as weight-adjusted, full-treatment dose)	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
Minidose prophylactic UFH	UFH, 5,000 units SC every 12 hours
Prophylactic UFH	UFH, 5,000–10,000 units SC every 12 hours 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
Therapeutic UFH (Also referred to as weight-adjusted, full-treatment dose)	UFH, 10,000 units or more SC every 12 hours in doses adjusted to target aPTT in the therapeutic range (1.5–2.5, 6 hours after injection)
Postpartum anticoagulation	Prophylactic LMWH/UFH for 4–6 weeks or Vitamin K antagonists for 4–6 weeks with a target INR of 2.0–3.0, with initial UFH or LMWH therapy overlap until the INR is 2.0 or more for 2 days
Surveillance‡	

Abbreviations: LMWH, low molecular weight heparin; SC, subcutaneously; UFH, unfractionated heparin; aPTT, activated partial thromboplastin time; INR, international normalized ratio.

*Although at extremes of body weight, modification of dose may be required.

†May target an anti-Xa level in the therapeutic range of 0.6–1.0 units/mL for twice daily regimen; slightly higher doses may be needed for a once-daily regimen.

‡Clinical vigilance and appropriate objective investigation of women with symptoms suspicious of deep vein thrombosis or pulmonary embolism may be needed.

and postpartum prophylaxis (40). Patients with an incidentally discovered low-risk thrombophilia who have not had a prior venous thromboembolism can be managed antepartum with either surveillance or prophylactic LMWH or unfractionated heparin, and in the postpartum period with either LMWH and unfractionated heparin prophylaxis or with surveillance if the patient has no additional risk factors for DVT.

Based on the pharmacokinetics of the heparin agents in pregnancy, therapeutic LMWH should be administered once or twice daily and unfractionated heparin, every 12 hours (Table 3) (34–38). A retrospective study of once daily versus twice daily doses of various heparins for venous thromboembolism in pregnancy found no cases of recurrent venous thromboembolism in 126 women,

66% of whom received once daily LMWH (71). Another study comparing once daily tinzaparin versus twice daily tinzaparin for the treatment of venous thromboembolism in pregnancy found that a higher-than-recommended dosage was required to maintain anti-Xa activity in the target range in women who took tinzaparin only once a day (36). Another retrospective study of the once-a-day tinzaparin regimen found two unusual thrombotic complications among 37 pregnancies (72). Any adjustment for obesity is incorporated into therapeutic-dose regimens. There is no evidenced-based protocol for adjusting prophylactic doses in women who are obese, thus adjustments can be made on a case-by-case basis.

▶ *Which anticoagulants should be used in cases of heparin allergy?*

In cases of severe cutaneous allergies or heparin-induced thrombocytopenia in pregnancy, fondaparinux (a synthetic pentasaccharide) may be the preferred anticoagulant because danaparoid, an LMWH with minimal cross-reactivity in heparin-sensitive patients, is currently unavailable in the United States (73). However, there are insufficient data to justify the routine use of fondaparinux as an alternative to heparins for prophylaxis of venous thromboembolism in pregnancy. Although a recent retrospective study comparing fondaparinux with enoxaparin administered between day 6 of the conception cycle and continued until 12 weeks of gestation found no untoward effects of fondaparinux on mother or infant (74), anticoagulant activity has been detected in umbilical cord blood of exposed fetuses (75).

▶ *How is newly diagnosed venous thromboembolism in pregnancy managed?*

Management of newly diagnosed venous thromboembolism requires therapeutic anticoagulation with either unfractionated heparin or LMWH (Table 3). Hospitalization for the initiation of anticoagulation therapy may be indicated in cases of hemodynamic instability, large clots, or maternal comorbidities. Intravenous unfractionated heparin can be considered in the initial treatment of PE and in situations in which delivery, surgery, or thrombolysis (indicated for life-threatening or limb-threatening thromboembolism) may be necessary. When patients appear to be hemodynamically stable, therapeutic LMWH can be substituted in anticipation of discharge from the hospital.

▶ *How should anticoagulation therapy be monitored during pregnancy?*

Data are unclear regarding optimal surveillance of anticoagulation therapy during pregnancy. When used in

therapeutic doses to treat or prevent venous thromboembolism, it is not clear whether the dose of LMWH needs to be adjusted. On the basis of small studies demonstrating the need for increased LMWH to maintain antifactor Xa levels between 0.6 units/mL and 1.0 units/mL, some advocate periodic measurement of antifactor Xa levels 4–6 hours after injection, but other studies have shown that few women actually require increased doses when weight-based doses are used (40). Patients converted to a subcutaneous therapeutic dose of unfractionated heparin in the last month of pregnancy should have an activated partial thromboplastin time (aPTT) checked (aPTT of 1.5–2.5, 6 hours after injection) and their dose of heparin adjusted to maintain the aPTT in the therapeutic range.

Patients receiving prophylactic anticoagulation do not require monitoring, but measurement of antifactor Xa levels or aPTT may be warranted in cases in which prophylaxis levels outside of the recommended range are clinically suspected (39). In one study, approximately 40% of women taking prophylactic LMWH had levels outside of the prophylactic range (39).

Guidelines recommend obtaining platelet counts when initiating therapeutic unfractionated heparin therapy in order to monitor for heparin-induced thrombocytopenia (76). The data are less clear about measuring platelet levels when initiating LMWH, but case reports of heparin-induced thrombocytopenia have been described (77).

▶ *How is anticoagulation therapy managed at the time of delivery?*

Women receiving either therapeutic or prophylactic anticoagulation therapy may be converted from LMWH to the shorter half-life unfractionated heparin in the last month of pregnancy or sooner if delivery appears imminent. An alternative option may be to stop therapeutic anticoagulation and induce labor within 24 hours, if clinically appropriate. The purpose of conversion to unfractionated heparin has less to do with any risk of maternal bleeding at the time of delivery, but rather the risk of an epidural or spinal hematoma with regional anesthesia. The American Society of Regional Anesthesia and Pain Medicine guidelines recommend withholding neuraxial blockade for 10–12 hours after the last prophylactic dose of LMWH or 24 hours after the last therapeutic dose of LMWH (78). These guidelines support the use of neuraxial anesthesia in patients receiving dosages of 5,000 units of unfractionated heparin twice daily, but the safety in patients receiving 10,000 units twice daily or more is unknown. In such cases, the American Society of Regional Anesthesia and Pain Medicine recommends assessment on an individual basis (78). If a woman goes into labor while taking unfractionated heparin, clearance can be verified by an aPTT. Reversal of heparin is rarely

required and is not indicated with a prophylactic dose of heparin. For women in whom anticoagulation therapy has temporarily been discontinued, pneumatic compressions devices are recommended.

▶ *Should patients undergoing cesarean delivery receive DVT prophylaxis?*

Cesarean delivery approximately doubles the risk of venous thromboembolism (6), but in the otherwise normal patient, this risk is still low (approximately 1 per 1,000 patients) (79). Given this increased risk, and based on extrapolation from perioperative data, placement of pneumatic compression devices before cesarean delivery is recommended for all women not already receiving thromboprophylaxis. Studies of routine thromboprophylaxis for cesarean delivery have been small and not adequately powered to assess a decrease in the risk of DVT or PE with anticoagulation therapy (80–82). One published decision analysis concluded that if thromboprophylaxis was elected, pneumatic compression devices were preferred to unfractionated heparin because of the risk of bleeding complications and heparin-induced thrombocytopenia (83). Another decision analysis concluded that pneumatic compression devices were cost effective if the incidence of postcesarean venous thromboembolism in the population was at least 6.8 per 1,000 patients (84).

For patients undergoing cesarean delivery with additional risk factors for thromboembolism, individual risk assessment may require thromboprophylaxis with both pneumatic compression devices and unfractionated heparin or LMWH (40). However, cesarean delivery in the emergency setting should not be delayed because of the timing necessary to implement thromboprophylaxis. Most patients receiving thromboprophylaxis during pregnancy will benefit from postpartum thromboprophylaxis, but the dose and route will vary by indication (85).

Additional measures should be considered for certain women at particularly high risk of thrombosis at the time of delivery. Women who have antithrombin deficiency may be candidates for antithrombin concentrates peripartum. Women who have had DVT in the 2–4 weeks before delivery may be candidates for placement of a retrievable vena caval filter, with removal postpartum (86, 87). Other women who may be candidates for vena caval filter placement during pregnancy include women with recurrent venous thromboembolism despite therapeutic anticoagulation (87).

▶ *When is the optimal time to resume anticoagulation therapy postpartum?*

The optimal time to restart anticoagulation therapy postpartum is unclear. A reasonable approach to mini-

mize bleeding complications is to restart unfractionated heparin or LMWH no sooner than 4–6 hours after vaginal delivery or 6–12 hours after cesarean delivery. One study of 95 women treated with peripartum enoxaparin compared with 303 controls found no significant increase in the rate of severe postpartum hemorrhage when enoxaparin was restarted between 5 hours and 24 hours after a vaginal delivery and between 12 hours and 36 hours after a cesarean delivery (88). Current recommendations by American Society of Regional Anesthesia and Pain Medicine are for resumption of prophylactic LMWH no sooner than 2 hours after epidural removal (78). Because the optimal interval for resumption of therapeutic anticoagulation after epidural removal is unclear, 12 hours may be a reasonable approach. When reinstitution of anticoagulation therapy is planned postpartum, pneumatic compression devices should be left in place until the patient is ambulatory and until anticoagulation therapy is restarted.

Women who require more than 6 weeks of therapeutic anticoagulation may be bridged to warfarin (89–91). Bridging to warfarin requires women to take two anticoagulants simultaneously. For women who require only 6 weeks of anticoagulation therapy postpartum, the utility of warfarin is limited because it frequently requires 1–2 weeks of administration before a therapeutic range is attained. Consequently, many patients opt to continue LMWH for the 6-week period. Women who have experienced venous thromboembolism during the current pregnancy, especially those in the third trimester, will likely need to continue taking warfarin for more than 6 weeks after delivery; some experts recommend taking warfarin for at least 3–6 months depending on the circumstances (92). Because warfarin, LMWH, and unfractionated heparin do not accumulate in breast milk and do not induce an anticoagulant effect in the infant, these anticoagulants are compatible with breastfeeding (89, 93, 94).

▶ *What postpartum hormonal contraceptive options are appropriate for women with thrombophilias?*

The risk of venous thromboembolism among women taking estrogen-containing oral contraceptives increases 35-fold to 99-fold and increases 16-fold among women heterozygous for factor V Leiden and prothrombin *G20210A* mutations (95). The annual risk of venous thromboembolism is 5.7 per 10,000 among factor V Leiden carriers but increases to 28.5 per 10,000 among factor V Leiden heterozygous women using estrogen-containing contraceptives (relative risk, 34.7) (96). Therefore, alternative methods, such as intrauterine devices (including those containing progestin), progestin-only pills or implants, and barrier methods should be used

(97). However, screening all women for thrombophilias before initiating combination contraception is not recommended (97–99).

Summary of Recommendations and Conclusions

The following recommendation is based on good and consistent scientific evidence (Level A):

▶ When signs or symptoms suggest new onset DVT, the recommended initial diagnostic test is compression ultrasonography of the proximal veins.

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

▶ The preferred anticoagulants in pregnancy are heparin compounds.

▶ A reasonable approach to minimize postpartum bleeding complications is resumption of anticoagulation therapy no sooner than 4–6 hours after vaginal delivery or 6–12 hours after cesarean delivery.

▶ Because warfarin, LMWH, and unfractionated heparin do not accumulate in breast milk and do not induce an anticoagulant effect in the infant, these anticoagulants are compatible with breastfeeding.

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

▶ Women with a history of thrombosis who have not had a complete evaluation of possible underlying etiologies should be tested for both antiphospholipid antibodies and for inherited thrombophilias.

▶ Therapeutic anticoagulation is recommended for women with acute thromboembolism during the current pregnancy or those at high risk of venous thromboembolism, such as women with mechanical heart valves.

▶ When reinstitution of anticoagulation therapy is planned postpartum, pneumatic compression devices should be left in place until the patient is ambulatory and until anticoagulation therapy is restarted.

▶ Women receiving either therapeutic or prophylactic anticoagulation may be converted from LMWH to the shorter half-life unfractionated heparin in the last month of pregnancy or sooner if delivery appears imminent.

▶ It is recommended to withhold neuraxial blockade for 10–12 hours after the last prophylactic dose of LMWH or 24 hours after the last therapeutic dose of LMWH.

▶ Placement of pneumatic compression devices before cesarean delivery is recommended for all women not already receiving thromboprophylaxis.

Proposed Performance Measure

Percentage of patients assessed for risk factors for thrombosis at the beginning of pregnancy, during pregnancy, and at the time of delivery

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The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985–December 2010. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

I   Evidence obtained from at least one properly designed randomized controlled trial.

II-1 Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

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.