# Chapter 6
# Thrombophilia and Thrombosis

**Courtney Bilodeau and Karen Rosene-Montella**

## Abbreviations

| | |
|---|---|
| APTT | Activated partial thromboplastin time |
| APC | Activated protein C |
| APS | Antiphospholipid antibody syndrome |
| CT | Computed topography |
| CVT | Cerebral vein thrombosis |
| DVT | Deep vein thrombosis |
| EKG | Electrocardiogram |
| FVL | Factor V Leiden |
| IUGR | Intrauterine growth restriction |
| IUFD | Intrauterine fetal demise |
| IVC | Inferior vena cava |
| LMWH | Low-molecular-weight heparin |
| MRI | Magnetic resonance imaging |
| MRV | Magnetic resonance venography |
| MTHFR | 5,10-Methylenetetrahydrofolate reductase |

C. Bilodeau, M.D. (✉)
Department of Obstetric Medicine, Women's Medicine Collaborative, Miriam Hospital, 146 West River Street, Ste 11C, Providence, RI 02904, USA

The Warren Alpert Medical School of Brown University, Providence, RI, USA
e-mail: cbilodeau1@lifespan.org

K. Rosene-Montella, M.D.
SVP Women's Services and Clinical Integration, Lifespan Corporation, Providence, RI 02903, USA

Obstetric Medicine, Women's Medicine Collaborative, The Miriam Hospital, Providence, RI 02903, USA

The Warren Alpert Medical School of Brown University, Providence, RI, USA



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| | |
|---|---|
| PAI | Plasminogen activator inhibitor |
| PE | Pulmonary embolism |
| PGM | Prothrombin gene mutation G20210A |
| PTS | Post-thrombotic syndrome |
| TAFI | Thrombin activatable fibrinolytic inhibitor |
| UFH | Unfractionated heparin |
| US | Ultrasonography |
| V/Q | Ventilation-perfusion |
| VTE | Venous thromboembolism |

## Thrombophilia

### *Background/Definition*

Thrombophilia is an inherited or acquired predisposition for thrombosis due to alterations in the coagulation system. Greater than 50 % of patients with thrombophilia who develop a VTE have additional thromboembolic risk factors. Pregnancy alone can be this additional risk factor. Addition of other factors such as advanced maternal age (>35 years), race (black), certain medical conditions (diabetes), and mode of delivery (cesarean section) further increases this risk [1]. Table 6.1 highlights the risk factors for thrombosis in pregnancy. Placenta-mediated pregnancy

**Table 6.1** Peripartum risk factors for VTE

| Maternal risk factors |
|---|
| Age >35 years |
| BMI > 30 kg/m$^2$ |
| Black race |
| Cigarette smoker |
| IV drug user |
| Medical comorbidities: |
| Infection, dehydration, diabetes, malignancy, autoimmune disease, varicose veins, sickle cell, nephrotic syndrome, hypertension |
| Personal or family history of VTE |
| Cesarean delivery or other surgery |
| Three or more previous deliveries |
| Obstetric hemorrhage |
| Preterm delivery (<37 weeks' gestation) |
| Stillbirth |
| Thrombophilia |
| Multiple pregnancy |
| Prolonged immobility |
| Prolonged labor (>24 h) |
| Preeclampsia/eclampsia |

Sources: [2, 3]

complications may also increase with certain thrombophilias. This potential correlation is controversial and will be further discussed below.

The inherited thrombophilias include factor V Leiden mutation (FVL), prothrombin gene mutation G20210A (PGM), protein C deficiency, and protein S deficiency. Antiphospholipid antibody syndrome (APS) is an acquired thrombophilia which may occur alone or in association with systemic lupus erythematosus (SLE) [4]. Antithrombin III deficiency can be either an inherited disorder or acquired, such as with nephrotic syndrome when levels fall via urinary excretion of the protein [5].

The 5,10-methylenetetrahydrofolate reductase (MTHFR) gene polymorphism is very common in individuals of European decent and causes modest elevations of plasma homocysteine. Elevated plasma homocysteine levels are themselves associated with a mild increased risk for VTE; however, studies in pregnant and nonpregnant individuals with the 5,10-MTHFR gene polymorphism do not reveal a significantly increased risk for VTE [6, 7]. Therefore, the 5,10-MTHFR gene polymorphism is no longer considered by many to be an inherited thrombophilia, and maternal evaluation for the gene mutation or homocysteine levels is not recommended [8].

## *Epidemiology*

The prevalence of inherited thrombophilias in the general population ranges between 0.03 and 15 %, with FVL being the most common [9]. One half of VTEs in pregnancy are associated with thrombophilia [10]. The absolute risk for VTE in pregnancy is 1–2:1,000 [2] in women with thrombophilia such as heterozygous FVL or PGM and no prior VTE, this risk rises to 1:400 [11]. Homozygous FVL is the highest risk inherited thrombophilia for VTE with an absolute VTE risk of 3.4 % [12]. Antithrombin deficiency and compound heterozygotes (e.g., FVL/PGM) represent higher-risk groups in pregnancy as well. Women with thrombophilia and a history of VTE are at even higher risk for developing a VTE in pregnancy.

## *Pathobiology*

### Normal Physiologic Changes

In pregnancy, there is a natural increase in the procoagulants fibrinogen, von Willebrand antigen, and factors VII, VIII, and X. Anticoagulant activity is decreased with lower total protein S levels and increased activated protein C (APC) resistance. The elevation of estrogen levels in pregnancy is a major contributor to the APC resistance [13]. Fibrinolytic activity is also inhibited from an increase in plasminogen activator inhibitor type 1 (PAI-1) and PAI-2 and decreased thrombin activatable

fibrinolytic inhibitor (TAFI) [14, 15]. These changes contribute to the natural increased risk for maternal thrombosis.

### Effect of Pregnancy on the Disease

The normal physiologic changes in pregnancy described above magnify the thrombosis risk of thrombophilia. In fact, pregnancy is often the precipitant to first identifying thrombophilia. When anticoagulant medication is needed for a patient with thrombophilia, the practitioner must consider physiologic changes in pregnancy and balance thrombosis with hemorrhage risk around delivery. Anticoagulant medication in pregnancy will be further discussed in Section "Thrombosis" of this chapter.

### Effect of Disease on the Pregnancy

Beyond increasing risk for a VTE in pregnancy, thrombophilias have been suspected to decrease placental efficiency and thereby increase risk for obstetric complications. These placenta-mediated complications include intrauterine growth restriction (IUGR), intrauterine fetal demise (IUFD)/stillborn, abruption, and early, severe, or recurrent preeclampsia. The data to support the association of thrombophilias with poor pregnancy outcomes is conflicting and often gathered from small cohorts or retrospective studies. Routine screening for thrombophilias is not currently recommended, and therefore this data is often not available. Women with poor pregnancy outcomes when tested are more likely to have a thrombophilia compared to women with a normal pregnancy [16, 17]. The specifics on which thrombophilia and which poor outcomes remain undefined. At this time, there appears to be a stronger association for FVL and for late (>10 weeks) pregnancy loss [18, 19] compared with other thrombophilia and poor pregnancy outcome associations. A large, prospective study is needed to confirm the suggested causality and furthermore the utility of anticoagulation for the prevention of poor pregnancy outcomes with thrombophilia.

Unlike the inherited thrombophilias discussed above, the antiphospholipid syndrome (APS) has been definitively associated with both thrombosis and poor obstetric outcomes. APS is an acquired thrombophilia characterized by laboratory features (see Table 6.2) and clinical events. Diagnosis requires at least one laboratory finding and one clinical event. These events include thrombosis, recurrent (three or more) miscarriages, late (>10 weeks) pregnancy loss, preeclampsia, IUGR, and placental abruption [20]. The pathogenesis of the obstetric outcomes in APS remains unclear but is unlikely due entirely to placental thrombosis. Several observational studies of placentas affected by APS reveal no

**Table 6.2** Inherited and acquired thrombophilias

| Type | Thrombosis risk in pregnancy | Diagnostic test |
|---|---|---|
| Inherited | | |
| Factor V Leiden mutation | High—homozygous<br>Lower—heterozygous | APC resistance assay not accurate in pregnancy so DNA analysis is required |
| Prothrombin gene mutation G20210A | High—homozygous<br>Lower—heterozygous | DNA analysis |
| Antithrombin III deficiency | High | Antithrombin III activity (<60 %) |
| Protein C deficiency | Lower | Protein C activity (<50 %) |
| Protein S deficiency | Lower | Protein S functional antigen assay (<55 %).<br>If abnormal follow-up with protein S free antigen, <30 % second trimester, <24 % third trimester |
| Acquired | | |
| Antiphospholipid antibody syndrome | High | Antiphospholipid antibodies, anticardiolipin antibodies, lupus anticoagulant, beta-2 glycoprotein (if abnormal repeat to confirm in 12 weeks) |
| Antithrombin III deficiency | High | Antithrombin III activity (<60 %) |

Sources: [8, 17]

**Table 6.3** Indications for thrombophilia evaluation

| |
|---|
| Unprovoked VTE at any age |
| Family hx of VTE or thrombophilia |
| Thrombosis at unusual site |
| Recurrent thrombosis |
| Recurrent IUGR |
| IUFD |
| Early severe or recurrent preeclampsia |
| Abruption |

Sources: [8, 17]

evidence of thrombosis, and other studies point to a complement-mediated inflammatory process [4].

Table 6.2 lists inherited and acquired thrombophilias along with thrombosis risk category (high or lower) and the laboratory tests recommended for diagnosis of thrombophilia.

### *Diagnosis and Management*

The laboratory studies currently used to identify thrombophilias are listed in Table 6.2. Indications for thrombophilia evaluation are listed in Table 6.3. Testing is not recommended if the results will not change clinical management or if results would not be as reliable, such as around the time of acute thrombosis (factor may be consumed leading to falsely low levels), in pregnancy or on oral contraceptives (lowers protein S), or on anticoagulation therapy (protein C and S lowered by Coumadin, antithrombin by heparins).

When a woman with a known thrombophilia desires to or becomes pregnant, recommended anticoagulation management strategies are based on severity of thrombophilia risk, maternal history of VTE, and other VTE risk factors. Anticoagulation management in pregnancy including recommended strategies for thrombophilia in pregnancy is detailed in the Thrombosis section and in Table 6.5. Specified guidelines regarding fetal assessment and timing of delivery in pregnancies affected by thrombophilia are not currently available. The individual patient's history and risk assessment should be taken into account and may warrant frequent fetal assessment and delivery at 39 weeks in the absence of obstetric complications such as IUGR or preeclampsia. Pneumatic compression boots or elastic compression stockings should be considered in the peripartum until the patient is ambulatory. Women with thrombophilia should consider non-estrogen-containing contraception, especially with a higher-risk thrombophilia [21].

## Thrombosis

### *Background/Definition*

Pregnancy increases risk for thrombosis, including deep vein thrombosis (DVT), pulmonary embolism (PE), and cerebral vein thrombosis (CVT). A PE is an obstruction of the pulmonary artery or one of its branches. A DVT is defined as proximal or distal depending upon location of the thrombus. Distal vein thrombosis is confined to the deep calf veins. Proximal vein thrombosis is located in the popliteal, femoral, or iliac veins. In pregnancy, the incidence of DVT is three times higher than incidence of PE. DVT is left sided in close to 85 % of cases [2, 22]. Isolated pelvic DVTs are much more common in pregnancy, 11 % [2] versus 1 % in the nonpregnant [23]. CVT is a thrombosis in the cerebral vein or dural sinus. CVT is a rare occurrence in the general population, and 75 % of adult patients with CVT are female. Peripartum CVT affects 12 per 100,000 deliveries [24]. Thrombosis can occur at any time during gestation and into the postpartum. Very commonly, the event in pregnancy is the patient's first VTE, as the hypercoagulability associated with pregnancy acts as a stress test for VTE. Maternal and fetal well-being are

dependent on prompt diagnosis and management of acute thrombosis and when possible prevention of thrombotic events in pregnancy.

## *Epidemiology*

VTE is at least four times more common in the pregnant versus nonpregnant state [1, 25]. Some retrospective cohort studies [26, 27] when compared to age-/gender-/time-matched controls [28] suggest the risk may be up to ten times higher in pregnant patients compared with nonpregnant patients. The risk is further increased by the presence of additional risk factors which are listed in Table 6.1. Most DVTs occur antepartum, and the events are evenly distributed throughout gestation [22]. The day-to-day risk for VTE is greatest in the postpartum [25, 27]. PE may be more common postpartum [29].

## *Pathobiology*

### Normal Physiologic Changes and Effect of Pregnancy on the Disease

The natural pregnancy state is hypercoagulable and prothrombotic. The coagulation changes in pregnancy (see Section "Thrombophilia" of this chapter) promote clot formation and decrease clot dissolution. In addition to normal coagulation system changes, there are numerous vascular alterations in pregnancy which contribute to thrombosis risk through promotion of venous stasis and increased vascular damage. Causes of venous stasis in pregnancy include the large vein compression by the gravid uterus, the right iliac artery overlying and compressing the left iliac vein, hormonally mediated venous dilation, and immobilization. Vascular damage occurring from vascular compression at delivery and assisted or operative delivery also promotes thrombosis.

### Effect of Disease on the Pregnancy

VTE in pregnancy causes significant morbidity and mortality [30]. In the UK Confidential Inquiry on Maternal Mortality, the most common error leading to death from PE was failure to make the diagnosis; this occurred in over half of the 28 cases reviewed. Typical errors were to only consider infection as a cause of symptoms and failure to investigate because of mistaken belief that radiological testing is contraindicated in pregnancy. Two thirds of the deaths would potentially have been prevented with proper thromboprophylaxis [31]. The hospital mortality

**Table 6.4** Common VTE signs and symptoms in pregnancy

| VTE | Signs | Symptoms |
|---|---|---|
| PE | Tachycardia, tachypnea, hypoxia, abnormal heart and lung sounds, hypotension | Chest pain, dyspnea, hemoptysis, cough |
| DVT | Leg edema (especially unilateral), palpable cord, warmth, erythema, tenderness, skin changes | Swelling, pain, warmth |
| CVT | Abnormal neurologic exam, seizures, altered consciousness | Headache, stroke-like symptoms |

of untreated PE is 30 %, making prompt and accurate diagnosis critical [32]. The diagnosis of VTE in pregnancy affects labor and delivery plans due to the added risk of bleeding with anticoagulation. Complications from DVT which extend beyond the pregnancy include post-thrombotic syndrome (PTS). Up to half of patients with proximal DVT outside of pregnancy experience this condition of limb pain, edema, discoloration, and ulcers [21]. Long-term follow-up of women who experienced DVT in pregnancy finds that 40–80 % develop PTS and 65 % have objectively confirmed deep vein insufficiency [33, 34]. Women with a history of VTE are also more limited by their contraceptive choices as estrogen-containing contraceptives are generally contraindicated.

## *Diagnosis*

Common pregnancy complaints increase the challenge of VTE diagnosis. For example, symptoms of leg edema, dyspnea, or headache may be misinterpreted as due to normal pregnancy changes instead of as a clinical sign of a DVT, PE, or CVT, respectively. Furthermore, diagnosis may be delayed by physician and patient reluctance to perform a diagnostic study due to concern for fetal risk to radiation exposure. In the nonpregnant population, there are validated clinical assessment and diagnostic imaging procedures to guide the diagnosis of VTE [35]. These validated tools are not currently available for the pregnant patient. Guidance for VTE diagnosis in pregnancy is based on validated evidence from nonpregnant patients and information from small studies in pregnancy. Table 6.4 lists the most common signs and symptoms which can be associated with VTE in pregnancy.

### PE Diagnosis

In pregnancy, the laboratory studies of D-dimer and alveolar-arterial gradient are not useful for PE diagnosis. D-dimer is an estimate of blood coagulation and ongoing fibrinolysis and is elevated throughout pregnancy [36]. No diagnostic cohort studies are currently available using D-dimers in the diagnostic approach of suspected PE in

pregnancy. An abnormal arterial blood gas can be a clinical sign of PE. However, a normal alveolar-arterial gradient has been shown in 60 % of documented PEs [37]. Part of the initial work-up when a pregnant patient presents with signs and symptoms of a PE includes an electrocardiogram (EKG) and chest x-ray, although neither of these tests should be used to definitively rule in or rule out a PE [38]. In nonpregnant patients, the incidence of sinus tachycardia and evidence of right heart strain (i.e., RBBB) were found to be slightly increased in patients with PE. Chest x-rays may find possible alternative diagnoses such as pneumothorax, pulmonary edema, or pneumonia. If a pregnant patient presents with symptoms of both a DVT and PE, a reasonable first evaluation would be a compression ultrasonography (US) as the anticoagulation regimens for acute DVT and submassive PE are the same. This approach would limit fetal and maternal radiation exposure. However, a negative compression US for DVT alone should not be used to rule out the presence of a suspected PE due to low sensitivity. In one study, only thirty percent of patients with PE had a radiographically proven DVT at the time of presentation [39]. Therefore, a ventilation-perfusion (V/Q) scan or computed topography (CT) pulmonary angiography with US leg studies is recommended for PE diagnosis in pregnancy. There are advantages and disadvantages to either test, and prompt availability of the study varies by medical facility. The V/Q scan when compared to CT angiography has been studied more extensively in pregnancy, with a high (75 %) diagnostic value [40], and does not require contrast administration. V/Q scan results are interpreted through pretest probability; therefore, its negative predictive value is highest when results are normal or low probability [41]. In comparison to a V/Q scan, a CT angiography study when combined with a chest radiograph can offer an alternative diagnosis if no PE is present but also increases breast radiation exposure [42].

### DVT Diagnosis

The test of choice for diagnosis of DVT in pregnancy is serial compression US. The test is inexpensive and noninvasive and does not expose subjects to radiation [43, 44]. Pelvic DVTs are more common in pregnancy; therefore, the US protocol should include the iliac veins and inferior vena cava at the level of the liver. Magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) should be considered if a pelvic or iliac vein DVT is suspected and the US is negative. MRI does not require ionizing radiation and is generally considered to be safe in pregnancy, although fetal safety data is limited.

### CVT Diagnosis

The patient with cerebral vein thrombosis is ill and only rarely has focal findings. Diagnosis can be difficult—she will often otherwise appear to have aseptic meningitis, but the risks are much higher (i.e., seizure or bleeding). MRI/V will confirm the diagnosis in most cases. In cases where MRI is not readily available, a CT scan

may be considered for initial diagnosis, especially to evaluate for an alternative diagnosis such as cerebral infarcts or hemorrhages. However, the CT scan can appear normal in cases of CVT [24].

## *Management/Treatment*

### Treatment of Acute Thrombosis

Management of VTE in pregnancy is similar to the principles used in the nonpregnant patient, with the added complexity of avoiding harm to the fetus and maternal hemorrhage on anticoagulation. The suggested treatment plans are based predominantly on retrospective studies in pregnancy as no prospective trials have evaluated the efficacy and safety of different treatment modalities. Coumarins are not recommended for VTE treatment or prevention in pregnancy because they cross the placenta and can lead to fetal harm. Coumarins are associated with a distinctive embryopathy between 5 and 12 weeks' gestation, and after 12 weeks there is a 2–3 % risk of CNS abnormalities. Furthermore, coumarins increase the risk of fetal hemorrhage throughout the pregnancy. Heparins do not cross the placenta and therefore do not increase risk for teratogenicity or fetal hemorrhage. Both unfractionated heparin (UFH) and low-molecular-weight heparin (LMWH) are considered safe in pregnancy. The maternal risks associated with the heparins include heparin-induced thrombocytopenia and osteopenia leading to increased risk for vertebral fractures; these risks are higher with UFH than with LMWH [45]. The multidose vials used with UFH also pose a potential threat for contamination [46], and drawing up an individual dose may be more cumbersome for patient self-administration. Prior to starting anticoagulation, obtaining baseline complete blood count and renal and hepatic function is recommended.

Dosing requirements for UFH and LMWH increase with increasing gestation. A concern with UFH dosing is that there is no validated therapeutic range for the activated partial thromboplastin time (APTT) in pregnancy. The APTT can be affected by pregnancy due to the physiologic increase in coagulation factors and heparin-binding proteins [47]. Pregnancy concerns with LMWH dosing are related to variation in weight gained, changes to volume of distribution, and increases in plasma volume, creatinine clearance, and extracellular volume. When monitoring therapeutic level for LMWH, the target anti-Xa activity level is 0.6–1.0 IU/ml for twice a day dosing or 1.0–2.0 IU/ml for once daily administration (4–6 h after injection). The therapeutic target heparin anti-Xa level with UFH is 0.3–0.7 IU/ml [48]. For example, the typical therapeutic dose of the LMWH enoxaparin is 1 mg/kg every 12 h.

LMWH is currently the heparin of choice for treating acute thrombosis in pregnancy [48, 49]. If a patient has renal dysfunction, UFH may be the preferred anticoagulant. Also, the use of LMWH may affect a patient's eligibility for epidural anesthesia due to a longer half-life and concern for spinal hematoma. Administration

of therapeutic doses of LMWH is not recommended within 24 h of epidural placement or 12 h after epidural removal. Current guidelines recommend therapeutic anticoagulation until 6 weeks postpartum with a minimum duration of therapy of 3 months [48, 49].

Thrombolytics are reserved as a life-saving intervention in pregnancy for the treatment of VTE. There are no data on thrombolytics from randomized controlled trials in pregnancy, but a small number of case reports have shown therapeutic success with massive PE in pregnancy [50–52] remote from delivery when bleeding risk is prohibitive. Inferior vena cava (IVC) filters are recommended in pregnancy if there is a contraindication to or need for interruption of anticoagulation; an acute thrombosis occurs close to delivery, or recurrent VTE occurs despite adequate anticoagulation. Temporary filters can be placed in the suprarenal IVC as the risk of complications for suprarenal is likely similar to infrarenal [53]. Failure to retrieve temporary filters in pregnancy has been reported [54].

In cases of a CVT, a multidisciplinary team including neurology and neurosurgery is recommended. The initial goal of therapy is to stabilize the patient to prevent or reverse cerebral herniation. Treatment should include anticoagulation once there is confirmation of the diagnosis and no evidence of hemorrhage. In severe cases, intravenous mannitol, neurosurgical intervention, or thrombolysis may be required. The majority of patients with CVT have a good outcome [24].

## VTE Management Around Labor and Delivery and Postpartum

Issues to consider regarding VTE management at the time of labor and delivery include risk of bleeding, possibility of regional anesthesia [55], and the risk of recurrence of VTE. If a VTE occurs within 2 weeks of delivery, a retrievable IVC filter is preferable. Between 2 and 4 weeks of delivery, UFH is preferred. If it occurs

**Table 6.5** Antepartum indications for thromboprophylaxis

| Lower risk | Higher risk |
|---|---|
| Single prior VTE[a] without thrombophilia | Recent or recurrent thrombosis |
| Single prior VTE with the following thrombophilia: protein S deficiency, protein C deficiency, heterozygote for FVL or PGM | Single prior VTE with the following thrombophilia: homozygote for FVL or PGM, antiphospholipid antibodies |
| No prior VTE with the following thrombophilia: protein S deficiency, protein C deficiency, heterozygote for FVL or PGM | Antithrombin III deficiency |
| No prior VTE with obstetric complication and thrombophilia | Multiple thrombophilias/compound heterozygotes |
| Prolonged bed rest | Antiphospholipid antibody syndrome (low-dose aspirin (75–100 mg/day) also recommended) |
| | Single prior VTE with a first-degree relative with prior VTE or thrombophilia |

Source: (ACOG Practice Bulletin No. 123 2011, Bates 2012, RCOG 2009)
[a]Risk increased if single VTE idiopathic or pregnancy or estrogen related

**Table 6.6** Thromboembolism in pregnancy

| 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 | Surveillance without anticoagulation therapy | 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 LNWH/UFH for 6 weeks |

Source: Thromboembolism in Pregnancy. ACOG Practice Bulletin, Number 123, Table 2, September 2011

a month or more prior to delivery, then consider timing anticoagulant offset prior to induction of labor [56]. Following delivery, LMWH can typically be restarted within 4–6 h, once maternal bleeding risk has been minimized. If anticoagulation will be extended into the postpartum period, bridging from a heparin treatment to coumarin is a safe alternative, including with breastfeeding [48, 49].

## VTE Prophylaxis

All pregnant women should be assessed for VTE risk, and when appropriate prophylactic anticoagulation should begin early in the pregnancy. Table 6.5 lists the antepartum indications for thromboprophylaxis. The lower-risk group may consider

surveillance alone and withhold prophylactic anticoagulation but have a low threshold for treatment when added risk factors are present. In the postpartum, all women with one or more prior VTE should receive prophylaxis. Women without a prior history of VTE but with a high-risk thrombophilia should be considered for antepartum prophylaxis and receive postpartum thromboprophylaxis. Women with no history of VTE and with a lower-risk thrombophilia may undergo surveillance alone with anticoagulation added for additional risk factors (Table 6.6) [57]. Following a cesarean section, prophylaxis is indicated for women with risk factors beyond the surgery and pregnancy.

LMWH is the preferred preventive treatment. The dose and frequency of treatment is at the practitioner's discretion based on estimated risk level. For example, lower-risk patients can be treated with the LMWH enoxaparin 40 mg once a day and higher-risk patients twice a day. Postpartum thromboprophylaxis should be extended to 6 weeks or longer when indicated [48].

## Conclusions

The incidence of VTE is higher in pregnancy compared to age-/sex-/time-matched controls. Risk assessment and identification of pregnancy-specific factors are important to reduce mortality. Thrombophilias and family and obstetric history are strong risk factors for VTE. Diagnosis and treatment of VTE in pregnancy is challenging. Ongoing research is needed to guide practitioners in an evidence-based approach to prevention and management of thrombosis in pregnancy.

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