Venous Thromboembolism (VTE)

Risk Factors VTE

- Personal history of thrombosis
- Inherited or acquired thrombophilia
- Obesity
- Hemoglobinopathies
- Hypertension
- Smoking
- Operative delivery

Pulmonary Embolism (PE)

Signs and symptoms of PE:

- Shortness of breath
- Chest pain
- Tachypnea
- Decreased oxygen saturation

PE Diagnostic testing: Computed tomographic (CT) angiography

Deep Vein Thrombosis (DVT)

- Left lower extremity is the most common site of a DVT.
- 2 most common signs and symptoms: pain and swelling of the extremity.
- Calf circumference difference ≥ 2 cm suggest DVT.
- Diagnostic test: compression ultrasound of the femoral and popliteal veins.

Acquired Thrombophilias

Antiphospholipid syndrome (APS)-The individual makes antibodies against phospholoipids resulting in VTE. It is associated with fetal loss, abruption, severe pre-eclampsia, and IUGR.

Diagnosis requires BOTH clinical and laboratory criteria.

Clinical criteria (at least one of the following)

- Thrombosis in any tissue or organ except superficial venous thrombosis.
- At least one fetal death at or beyond 10 weeks GA.
- At least one preterm birth ≤ 34 weeks GA due to pre-eclampsia or placental insufficiency.
- At least 3 consecutive SABs before 10 weeks GA.

Laboratory Criteria:

- Lupus anticoagulant activity detected.
- Anticardiolipin antibodies (IgG and IgM at moderate or high positive titers).
- Anti-β2-glycoprotein I antibodies (IgG and IgM at high positive titer).
- Repeat positive tests after 12 months to confirm persistence.

Patients who meet clinical and laboratory criteria should be diagnosed with APS and educated on S&S of VTE. Treatment is recommended.

APS Pregnancy monitoring and management

- Ultrasound for fetal growth at 24 weeks GA and q 4-6 weeks.
- Consult with MFM to assist with assessment and plan of care.
- Office visits q 2-3 weeks beginning at 24 weeks GA. Screen for S&S of pre-eclampsia.
- Uncomplicated APS: Delivery at 39 weeks GA.
- Earlier delivery for complicated APS (IUGR, pre-eclampsia, other).
- See Table 1 for treatment recommendations.
- Transition patients LMWH to UFH 7500 – 10,000 units SQ BID at 36 weeks GA for regional anesthesia.
- Due to postpartum risk of VTE, continue heparin therapy (UFH or LMWH) after delivery: 6 hours after vaginal delivery and 12-18 hours after cesarean delivery.
- Warfarin, LMWH, and UFH are safe during breastfeeding.
- Avoid estrogen containing contraceptives.
- APS patients with VTE history: coordinate long-term PPX with patient's primary care MD.
- Thrombophilic patients: Start warfarin 48-72 hours after delivery: 5 mg daily for 2 days. Continue therapeutic doses of UFH or LMWH for 5 days and until the INR is therapeutic (2.0-3.0) for 2 consecutive days.

Inherited Thrombophilia

Inherited thrombophilias have been associated with VTE and adverse pregnancy outcomes. Screening for thrombophilias is controversial and should only be used when the results will affect management decisions.

Recommendations for screening:

- **Women with a personal history of VTE.**
- **Women with a first-degree relative (parent or sibling) with a history of thrombophilia.**

Recommended screening tests: (Ideally, screening tests should be collected at least 6 weeks after a thrombotic event and while the patient is not pregnant or on anticoagulation or hormonal therapy).

- **Factor V Leiden mutation**
- **Prothrombin G20210A mutation**
- **Protein C deficiency**
- **Protein S deficiency**
- **Antithrombin deficiency**

See Table 1 for treatment recommendations.

Anticoagulation Therapy

- **Women with a history of thrombosis or those with an acquired or inherited thrombophilia are candidates for prophylactic or therapeutic anticoagulation therapy during pregnancy and the postpartum period see Table 1.**
- **Heparin compounds, unfractionated heparin (UFH) or low molecular weight heparin (LMWH) plus low-dose aspirin, are the preferred anticoagulants for use during pregnancy see Table 2.**
- **Warfarin is associated with harmful fetal effects and should not be used in pregnancy unless the woman has a mechanical heart which requires multidisciplinary care. Such woman should be referred to a maternal fetal medicine specialist for care.**
- **Data are conflicting as to whether there is a benefit of adding low-dose aspirin to heparin prophylaxis or therapy in the absence of anti-phospholipid syndrome. However, given the potential increase in the risk of vascular events during pregnancy (e.g. pre-eclampsia or placental dysfunction) for women with a prior VTE, at the University of Alabama at Birmingham (UAB) we typically recommend low-dose aspirin in addition to heparin.**
- **Acute thromboembolism, DVT or PE, should be treated with anticoagulation therapy using intravenous heparin or subcutaneous LMWH achieving therapeutic doses quickly to prevent clot extension see Table 3.**
- **Pneumatic compression devices are recommended in the intrapartum period until ambulatory in women with a known thrombophilia.**
- **Transition patients LMWH to UFH 7500 – 10,000 units SQ BID at 36 weeks GA for regional anesthesia.**
- **Due to postpartum risk of VTE, continue heparin therapy (UFH or LMWH) after delivery starting 6 hours after vaginal delivery and 12-18 hours after cesarean delivery.**
- **Warfarin, LMWH, and UFH are safe during breastfeeding.**

Table 1. Indications and Duration of Outpatient Anticoagulation Use in Pregnancy

Clinical Scenario	Antepartum Management	Postpartum Management
Personal VTE History		
Prior VTE associated with transient risk-factor that is no longer present (excludes a VTE during pregnancy or while on OCPs)	Surveillance without anticoagulation plus/minus low-dose aspirin*	6 weeks PPx LMWH or UFH
Prior single VTE without an associated risk-factor (includes a VTE during a pregnancy or while using an OCP use)	PPx LMWH or UFH Plus/minus low-dose aspirin*	6 weeks PPx LMWH or UFH
Two or more VTEs	Therapeutic LMWH or UFH Plus/minus low-dose aspirin*	6 weeks therapeutic LMWH, UFH, or warfarin
Medical Conditions		
Mechanical heart valve	See below (plus low-dose aspirin)	Return to pre-pregnancy regimen (will need a heparin bridge if transitioning to warfarin)
Atrial fibrillation (active)	Therapeutic LMWH or UFH Plus/minus low-dose aspirin*	6 weeks therapeutic LMWH, UFH, or warfarin
Mitral stenosis (risk of VTE 10-20%)[2]	Therapeutic LMWH or UFH Plus/minus low-dose aspirin*	6 weeks therapeutic LMWH, UFH, or warfarin
Antiphospholipid antibody syndrome without a history of a VTE	PPx LMWH or UFH plus low-dose aspirin	6 weeks PPx LMWH or UFH
Antiphospholipid antibody syndrome with a history of VTE	Therapeutic LMWH or UFH plus low-dose aspirin	6 weeks therapeutic LMWH, UFH, or warfarin
Inherited thrombophilias		
Thrombophilia carrier but no history of VTE		
Low-risk thrombophilia	Surveillance without anticoagulation Plus/minus low-dose aspirin*	Surveillance or 6 weeks PPx LMWH or UFH if additional risk factors exist (obesity, prolonged immobility)

Clinical Scenario	Antepartum Management	Postpartum Management
High-risk thrombophilia	PPx LMWH or UFH Plus/minus low-dose aspirin*	6 weeks PPx LMWH or UFH
Thrombophilia carrier without a personal history of a VTE but a first-degree relative with a h/o a VTE		
Low-risk thrombophilia	Surveillance without anticoagulation plus/minus low-dose aspirin*	6 weeks PPx LMWH or UFH
High-risk thrombophilia	PPx LMWH or UFH Plus/minus low-dose aspirin*	6 weeks PPx LMWH or UFH
Thrombophilia carrier with a history of a single VTE (not on long-term anticoagulation)		
Low-risk thrombophilia	PPx LMWH or UFH Plus/minus low-dose aspirin*	6 weeks PPx LMWH or UFH
High-Risk thrombophilia	Therapeutic LMWH or UFH Plus/minus low-dose aspirin*	6 weeks therapeutic LMWH, UFH, or warfarin
Thrombophilia carrier with a history of 2 prior VTEs	Therapeutic LMWH or UFH Plus/minus low-dose aspirin*	Therapeutic LMWH or UFH Plus/minus low-dose aspirin*

*Data are conflicting as to whether there is a benefit of adding low-dose aspirin to heparin prophylaxis or therapy in the absence of anti-phospholipid syndrome. However, given the potential increase in the risk of vascular events during pregnancy (e.g. pre-eclampsia or placental dysfunction) for women with a prior VTE, at UAB we typically recommend low-dose aspirin in addition to heparin. Based on the risk-benefit ratio in the US Preventive Service Task Force recommendations, there is no increase in the risk with low–dose aspirin and its addition to the regimen may lower the occurrence of pre-eclampsia and other conditions associated with placental dysfunction.

Table 2. Anticoagulant Regimen Definition

Anticoagulation Regimen	Definition
Prophylactic LMWH*	Enoxaparin, 40 mg SC once daily Dalteparin, 5,000 units SC once daily
Therapeutic LMWH†	Enoxaparin, 1 mg/kg every 12 hours Dalteparin, 200 units/kg once daily Target an anti-Xa level in the therapeutic range for twice daily regimens; slightly higher doses many be needed for once-daily regimen.
Prophylactic UFH	UFH, 5,000-10,000 units SC every 12 hours UFH, 5,000-7,500 units SC every 12 hours in the 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†	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; in some patients dosing every 8 hours may be necessary to achieve more sustained therapeutic concentrations.
Postpartum anticoagulation	Prophylactic LMWH/UFH for 6 weeks or warfarin for 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

Table 3. Anticoagulation Therapy for DVT or PE

Condition	Heparin	Enoxaparin
DVT or PE current pregnancy	IV heparin (aPTT 2-3 times control) for 5-10 days, followed by q 8-12 hour injections to prolong midinterval aPTT 1.5-2 x control for remainder of the pregnancy; anti-Factor Xa levels can alternatively be monitored every 4 hours. Warfarin can be used postpartum.	Enoxaparin 1 mg/kg (100 mg max) q 12 hours; monitor anti-Factor Xa levels at 4-6 hours post injection.