Venous Thromboembolism and Thrombophilias in Pregnancy

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OUTLINE

* Hematologic Physiology in Pregnancy
* Venous Thromboembolism
* Inherited Thrombophilias
* Acquired Thrombophilia: Antiphospholipid Antibody Syndrome
* Summary of Clinical Recommendations
* References
What normally happens in clotting cascade?

Endothelial Disruption ("injury")

Platelet Activation ("platelet plug")

Clotting ("help arrives")

Cascade

Prothrombin > Thrombin; Fibrinogen > Fibrin

Fibrin Meshwork/Blood Clot
Platelet/coagulation factor activation

Lots of exciting biochemistry

CLOT!  CLOT!  CLOT!
Pregnancy is marked by increased clotting potential, decreased anticoagulant activity, and decreased fibrinolysis → adaptive mechanism to prevent excessive bleeding at delivery.

Thrombotic potential exacerbated by venous stasis in the lower extremities due to compression of the inferior vena cava and pelvic veins by the enlarging uterus, a hormone-mediated increase in venous capacitance, insulin resistance, and hyperlipidemia.

Venous thromboembolism complicates approximately 1 in 1600 births and is a leading cause of maternal morbidity in the United States.

Strong association between thrombophilias and venous thromboembolism, which makes detection of these mutations a logical target for prevention strategies.
Increased fibrinogen
* Increase in Factors II, VII, VIII, IX, X, and XII
* Increase in fibrinolytic inhibitors (PAI-1 and PAI-2)
* Decrease in Protein S activity
* Increase in resistance to activated Protein C
Pregnant women have a fourfold to fivefold increased risk of thromboembolism compared with nonpregnant women.
- Risk is twofold during the antepartum period.
- Risk is 14-fold in the postpartum period.

Approximately 80% of thromboembolic events in pregnancy are venous, with a prevalence of 0.5-2.0 per 1,000 pregnant women.
- 75% DVT, 20-25% PE.
- One half occur during pregnancy (equally distributed across trimesters), one half postpartum.

VTE accounts for 1.1 deaths per 100,000 deliveries, or 9% of all maternal deaths in the United States.

Leading cause of pregnancy-related maternal morbidity and mortality in the developed world.
DVT is more common in the left than the right leg
- Occurs in 15% of untreated DVTs, mortality rate of 15%
- Occurs in 4.5% of treated DVTs, mortality rate of 1%
- Death from PE occurs about every 1.1 to 1.5 per 100,000 pregnancies
RISK FACTORS

* Personal History of VTE (most important risk factor)
* Inherited or Acquired Thrombophilia (2nd most important)
* Family History of VTE
* Obesity
* Advanced Maternal Age
* Multiple Gestation
* Increased Parity
* Smoking
* Immobility – travel, bedrest
* Surgery or Trauma
* Nephrotic Syndrome
SIGNS AND SYMPTOMS

* DVT
  * Pain, erythema, and/or swelling in an extremity
  * Difference in calf circumference of 2cm or more

* PE
  * Chest pain
  * Shortness of breath
  * Tachycardia
  * Not detected clinically in 70-80% of cases
DIAGNOSIS

* DVT
  * Compression Ultrasonography – primary modality
  * Venography
  * D-Dimer Testing
* PE
  * V/Q Scan
  * CTPA
  * Pulmonary Angiography
RADIATION EXPOSURE OF DIAGNOSTIC TESTS (rads)

* Chest X Ray – 0.001
* Perfusion Scan – 0.018
* Ventilation Scan – 0.019
* Helical CT – 0.005
* Limited Venography – 0.050
* Pulmonary Angiography – 0.221
* Compression Ultrasound – None
* MRI - None
ANTENATAL COMPLICATIONS

* Pulmonary Embolus
* Post-thrombotic Syndrome
* Pulmonary Hypertension
* Death – maternal and/or fetal
TREATMENT

* Unfractionated Heparin
* Low Molecular Weight Heparin
* Warfarin (Coumadin)
* Inferior Vena Cava Filters
* Thrombolytic Agents
* Embolectomy
UNFRACTIONATED HEPARIN

* Mechanism of Action
  * Stimulation of Antithrombin III activity
  * Direct Factor 10 inhibition
* Half Life of 1.5 hours
* Approximately 3% of pregnant women develop HIT
* Risk of osteopenia and vertebral fractures with long term use
* No risk of teratogenicity
* Protamine Sulfate – can reverse the effects of UFH
LOW MOLECULAR WEIGHT HEPARIN

* Mechanism of Action
  * Stimulation of Antithrombin III activity
  * Inhibition of Factor X
* Half Life is 4-7 hours
* Lower risk of HIT and osteopenia
* May consider monitoring with Factor Xa levels
  * Therapeutic 0.5 to 1.2 U/mL
  * Prophylactic 0.2 to 0.4 U/mL
**WARFARIN**

* Vitamin K antagonist – inhibits factors II, VII, IX, and X and decreases levels of protein C and S
* Crosses the placenta – can cause bleeding and teratogenicity
* May be recommended in patients with mechanical heart valves
* Warfarin Embryopathy
  * 4-5% of fetuses if exposure between 6 and 9 weeks gestation
  * Stippled epiphyses, nasal, and limb hypoplasia
* Have been used safely and effectively in pregnancy
* Placement typically suprarenal
* Indications for use are same as in nonpregnant:
  * Any contraindication to anticoagulant therapy
  * Serious complication of anticoagulation
  * Recurrence of PE in patients with adequate anticoagulation therapy
THROMBOLYTIC AGENTS

- Limited to life-threatening situations due to risk of substantial maternal bleeding
- Risk of placental abruption and fetal death is currently unknown
Treatment option when conservative measures fail

Indicated to prevent death in patients who are hemodynamically unstable despite anticoagulation and treatment with vasopressors

Associated with 20 to 40% incidence of fetal loss
INHERITED THROMBOPHILIAS
Genetic conditions that increase the risk of VTE and possibly some pregnancy complications

VTE is the leading cause of pregnancy-related maternal morbidity and mortality in the developed world

Up to 50% of women who have thrombotic events during pregnancy possess an underlying congenital or acquired thrombophilia
CLASSIFICATION

- Factor V Leiden
- Prothrombin G2021A
- Antithrombin III
- Protein C
- Protein S
- MTHFR/Homocysteinemia
Mutation arises from a G→A mutation in nucleotide 1691 of the factor V gene’s 10th exon, resulting in a substitution of a glutamine for an arginine at position 506

* Impairs the activated PC and PS complex inactivation of Factor Va
* Autosomal Dominant
* Most common cause of activated PC resistance
* Prevalence 5-10% in Europeans, 3% in African Americans, and rare in Asian and African populations
* Mutation in the promoter of the prothrombin gene leads to increase (1.5-2x) circulating levels of prothrombin and increased risk of VTE
* Autosomal Dominant
* Deficiency is the most thrombogenic of the inherited thrombophilias with a 70-80% lifetime risk of VTE
* Can result from numerous point mutations, deletions, and insertions
* Autosomal Dominant
* Cutoff for activity level is <60%
* Vitamin K dependent polypeptide synthesized primarily in the liver
* Activated PC combines with free PS to inhibit Factors V and VIII
* Deficiency can result from numerous mutations
* Autosomal Dominant
* Functional Assay cutoff of <50%
Vitamin K Dependent polypeptide synthesized primarily in the liver

Present in plasma in free (40%) and bound (60%) forms

Autosomal Dominant

Free PS Antigen <55% in non-pregnant should be detected at least twice

Pregnancy – decrease in pregnancy due to estrogen induced decreases in total PS and increases in complement 4b binding protein

* 2\textsuperscript{nd} Trimester: <30%

* 3\textsuperscript{rd} Trimester: <24%
Most common form of genetic hyperhomocysteinemia results from production of MTHFR with reduced enzymatic activity

Variants – C677T or A1298C

Isolated mutations are not associated with increased risk of VTE and should not be categorized as a thrombophilia
## Prevalence of Different Thrombophilias

<table>
<thead>
<tr>
<th>Condition</th>
<th>General Population (%)</th>
<th>Patients w/ History of Thrombosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor V Leiden (Heterozygosity)</td>
<td>1-15</td>
<td>10-50</td>
</tr>
<tr>
<td>Prothrombin Gene (Heterozygosity)</td>
<td>2-5</td>
<td>6-18</td>
</tr>
<tr>
<td>ATIII Deficiency</td>
<td>0.02</td>
<td>1-3</td>
</tr>
<tr>
<td>Protein S Deficiency</td>
<td>0.1-1.3</td>
<td>1-5</td>
</tr>
<tr>
<td>Protein C Deficiency</td>
<td>0.2-0.4</td>
<td>3-5</td>
</tr>
<tr>
<td>Hyperhomocysteinemia</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>MTHFR (C677T Heterozygous)</td>
<td>5-14</td>
<td>--</td>
</tr>
</tbody>
</table>
ANTENATAL COMPLICATIONS

- VTE
- Adverse Pregnancy Outcomes – controversial
  - Pregnancy Loss
  - Placental Abruption
  - Preeclampsia
  - Fetal Growth Restriction

- **No consistent results that inherited thrombophilia is associated with adverse pregnancy outcomes**
# RISK OF VTE

<table>
<thead>
<tr>
<th>Factor V Leiden, Heterozygote</th>
<th>VTE Potential (RR)</th>
<th>Pregnancy: No History (%)</th>
<th>Pregnancy: Prior VTE (%)</th>
<th>Pregnancy: % of all VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-7</td>
<td>0.25-1.2</td>
<td>10</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>1.5-4</td>
<td>17</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Prothrombin Heterozygote</td>
<td>3-9</td>
<td>&lt;0.5</td>
<td>&gt;10</td>
<td>17</td>
</tr>
<tr>
<td>25</td>
<td>2-4</td>
<td>&gt;17</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>FVL/Prothrombin</td>
<td>84</td>
<td>4.5-5</td>
<td>&gt;20</td>
<td>1-3</td>
</tr>
<tr>
<td>Antithrombin III</td>
<td>50-100</td>
<td>0.4-7</td>
<td>40</td>
<td>1</td>
</tr>
<tr>
<td>Protein C</td>
<td>10-13</td>
<td>0.1-0.8</td>
<td>4-17</td>
<td>14</td>
</tr>
<tr>
<td>Protein S</td>
<td>2-10</td>
<td>0.1</td>
<td>0-22</td>
<td>3</td>
</tr>
</tbody>
</table>
EVALUATION/DIAGNOSTIC TESTING

* Insufficient evidence to support universal screening

* Screening:
  * Patients with history of VTE
  * VTE in current pregnancy
  * A first degree relative with a history of high risk thrombophilia
  * No screening recommended based on prior adverse pregnancy history
## TESTING CHARACTERISTICS

<table>
<thead>
<tr>
<th></th>
<th>Testing Method</th>
<th>Can Patients Be Tested During Pregnancy?</th>
<th>Is the test reliable during Acute Thrombosis?</th>
<th>Is the test reliable while on Anticoagulation?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor V Leiden</td>
<td>AP Resistance Assay DNA Analysis</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prothrombin Gene Mutation</td>
<td>DNA Analysis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein C</td>
<td>Protein C Activity (&lt;50%)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein S</td>
<td>Free Protein S Antigen (&lt;55%)</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATIII Deficiency</td>
<td>ATIII Activity (&lt;60%)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
ANTENATAL MANAGEMENT

* Treatment – Unfractionated Heparin or LMWH
  * Prophylactic Anticoagulation
  * Therapeutic Anticoagulation
  * Continued for a minimum of 6 weeks postpartum
ANTENATAL MANAGEMENT

- Early Ultrasound for accurate dating
- Detailed Ultrasound at 18-20 weeks gestation
- Fetal Growth Ultrasounds – every 4-6 weeks
- Fetal Surveillance – NSTs/BPPs starting at 32 weeks
- Daily fetal kick counts
- Delivery by EDC
ACQUIRED THROMBOPHILIA: ANTIPHOSPHOLIPID ANTIBODY SYNDROME
**BACKGROUND**

* Autoimmune disorder defined by the presence of characteristic clinical features and specified levels of circulating antiphospholipid antibodies
* Antiphospholipid antibodies are a diverse group of antibodies with specificity for binding to negatively charged phospholipids on cell surfaces
  * Antigenic determinant is Beta 2 glycoprotein I
  * Regulatory role in coagulation, fibrinolysis, and other physiologic systems
Antibodies are found in up to 5% of healthy controls
20 to 25% of SLE patients have APS
Anticardiolipin antibodies are found in 15% of women with recurrent miscarriage
Pathophysiology
- Thrombosis of placental vessels
- Interference with coagulation factors (reduced levels of annexin V)
- Inhibition of proliferation of trophoblasts
- Complement activation
Lupus Anticoagulant
- Presence is assessed indirectly
- Lupus anticoagulant sensitive activated partial thromboplastin time and dilute Russell’s viper venom time

Anticardiolipin
- IgG and IgM isotypes
- No clinical significance of IgA isotype

Anti-Beta 2 Glycoprotein I
- IgG and IgM isotypes
* History of three or more spontaneous unexplained first trimester losses < 10 weeks
* History of one or more unexplained fetal loss/death >10 weeks
* Early onset (<34 weeks) preeclampsia or fetal growth restriction, leading to indicated preterm birth
* SLE
* History of vascular thrombosis (DVT, PE, stroke)
One laboratory criteria and one clinical criteria

Laboratory Criteria – positive on two occasions at least 12 weeks apart
- Lupus Anticoagulant present in plasma
- Anticardiolipin Antibody (IgG or IgM) >40 GPL/MPL or >99th%
- Anti-Beta 2 Glycoprotein I (IgG or IgM) >99th%

Clinical Criteria
- Vascular Thrombosis – one or more clinical episodes of arterial, venous, or small vessel thrombosis, in any tissue or organ
- Pregnancy Morbidity
  - One or more unexplained deaths of normal fetus >10 weeks
  - One or more premature births of normal neonate <34 weeks due to severe preeclampsia or placental insufficiency
  - Three or more unexplained consecutive losses <10 weeks
* Venous and Arterial Thromboembolism
* Preeclampsia
* Autoimmune Thrombocytopenia
* Pregnancy Loss and Fetal Death
* Fetal Growth Restriction
* Preterm Birth
* Placental Abruption
* Other – autoimmune hemolytic anemia, livedo reticularis, chorea gravidarum, multi-infarct dementia
ANTENATAL MANAGEMENT

* Multidisciplinary management with Obstetrician, Maternal Fetal Medicine specialist, and/or Rheumatologist or Internal Medicine specialist

* Treatment
  * Low Dose Aspirin
  * Anticoagulation
    * Lovenox 40mg SQ BID
    * Heparin SQ BID (5,000 – 10,000U)
    * Continued for a minimum of 6 weeks postpartum
Early Ultrasound for accurate dating
* Detailed Ultrasound at 18-20 weeks gestation
* Fetal Growth Ultrasounds – every 4-6 weeks
* Fetal Surveillance – NSTs/BPPs starting at 32 weeks
* Daily fetal kick counts
* Delivery by EDC
SUMMARY OF CLINICAL RECOMMENDATIONS
WHO SHOULD BE TESTED FOR WHAT?

* Inherited Thrombophilia Evaluation
  * Personal history of venous thromboembolism that was associated with a non-recurrent risk factor
  * First degree relative with a history of high-risk thrombophilia
  * NOT recommended for recurrent fetal loss or placental abruption

* Acquired Thrombophilia Evaluation
  * Women with a prior unexplained arterial or venous thromboembolism, or a new arterial or venous thromboembolism during pregnancy
  * History of one fetal loss or three or more recurrent embryonic or fetal losses
  * Consider testing in patients with history of preterm severe preeclampsia or early onset placental insufficiency
  * Consider testing in patients with hemolytic anemia, autoimmune thrombocytopenia, amaurosis fugax, livedo reticularis, systemic lupus erythematosus, and a false positive rapid plasma reagin result
**ANTICOAGULATION REGIMENS**

* **Prophylactic LMWH**
  * Enoxaparin 40mg SQ QD

* **Therapeutic LMWH**
  * Enoxaparin 1mg/kg every 12 hours
  * May target anti-Xa level (0.6-1.0U/mL)

* **Prophylactic UFH**
  * UFH 5,000 – 10,000 units SQ BID
  * 5,000 1st Trimester; 7,500 2nd Trimester; 10,000 3rd Trimester

* **Therapeutic UFH**
  * UFH 10,000 units or more SQ 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
  * Vitamin K Antagonist for 4-6 weeks (target INR 2.0-3.0)
Any increased risk of venous thromboembolism in pregnancy is greatest before 20 weeks of gestation, and therefore, if antepartum prophylaxis is used, it should be initiated in the first trimester.

Postpartum treatment levels should be at least equal to antepartum treatment.
<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Antepartum Management</th>
<th>Postpartum Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk thrombophilia † without previous VTE</td>
<td>Surveillance without anticoagulation therapy</td>
<td>Surveillance without anticoagulation therapy or postpartum anticoagulation therapy if the patient has additional risks factors ‡</td>
</tr>
<tr>
<td>Low-risk thrombophilia with a family history (first-degree relative) of VTE</td>
<td>Surveillance without anticoagulation therapy</td>
<td>Postpartum anticoagulation therapy or intermediate-dose LMWH/UFH</td>
</tr>
<tr>
<td>Low-risk thrombophilia † with a single previous episode of VTE—Not receiving long-term anticoagulation therapy</td>
<td>Prophylactic or intermediate-dose LMWH/UFH or surveillance without anticoagulation therapy</td>
<td>Postpartum anticoagulation therapy or intermediate-dose LMWH/UFH</td>
</tr>
<tr>
<td>High-risk thrombophilia ‡ without previous VTE</td>
<td>Surveillance without anticoagulation therapy, or prophylactic LMWH or UFH</td>
<td>Postpartum anticoagulation therapy</td>
</tr>
<tr>
<td>High-risk thrombophilia ‡ with a single previous episode of VTE or an affected first-degree relative—Not receiving long-term anticoagulation therapy</td>
<td>Prophylactic, intermediate-dose, or adjusted-dose LMWH/UFH regimen</td>
<td>Postpartum anticoagulation therapy, or intermediate or adjusted-dose LMWH/UFH for 6 weeks (therapy level should be at least as high as antepartum treatment)</td>
</tr>
<tr>
<td>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</td>
<td>Surveillance without anticoagulation therapy</td>
<td>Postpartum anticoagulation therapy</td>
</tr>
<tr>
<td>No thrombophilia with previous single episode of VTE associated with transient risk factor that was pregnancy- or estrogen-related</td>
<td>Prophylactic-dose LMWH or UFH ‡</td>
<td>Postpartum anticoagulation therapy</td>
</tr>
<tr>
<td>No thrombophilia with previous single episode of VTE without an associated risk factor (idiopathic)—Not receiving long-term anticoagulation therapy</td>
<td>Prophylactic-dose LMWH or UFH ‡</td>
<td>Postpartum anticoagulation therapy</td>
</tr>
<tr>
<td>Thrombophilia or no thrombophilia with two or more episodes of VTE—Not receiving long-term anticoagulation therapy</td>
<td>Prophylactic or therapeutic-dose LMWH or UFH</td>
<td>Postpartum anticoagulation therapy or Therapeutic-dose LMWH/UFH for 6 weeks</td>
</tr>
<tr>
<td>Thrombophilia or no thrombophilia with two or more episodes of VTE—Receiving long-term anticoagulation therapy</td>
<td>Resumption of long-term anticoagulation therapy</td>
<td></td>
</tr>
</tbody>
</table>

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

1Low-risk thrombophilia: factor V Leiden heterozygous; prothrombin G20210A heterozygous; protein C or protein S deficiency.
2First-degree relative with a history of a thrombotic episode before age 50 years, or other major thrombotic risk factors (e.g., obesity or prolonged immobility).
3High-risk thrombophilia: antithrombin deficiency; double heterozygous for prothrombin G20210A mutation and factor V Leiden; factor V Leiden homozygous or prothrombin G20210A mutation homozygous.
4Surveillance without anticoagulation therapy is supported as an alternative approach by some experts.
# Table 3. Anticoagulation Regimen Definitions

<table>
<thead>
<tr>
<th>Anticoagulation Regimen</th>
<th>Definition</th>
</tr>
</thead>
</table>
| **Prophylactic LMWH**         | Enoxaparin, 40 mg SC once daily  
                                | Dalteparin, 5,000 units SC once daily  
                                | Tinzaparin, 4,500 units SC once daily |
| **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  
                                | 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. |
| **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**           | 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**              | Clinical vigilance and appropriate objective investigation of women with symptoms suspicious of deep vein thrombosis or pulmonary embolism |

*Abbreviations: aPTT, activated partial thromboplastin time; INR, international normalized ratio; LMWH, low molecular weight heparin; SC, subcutaneously; UFH, unfractionated heparin.*  
*Although at extremes of body weight, modification of dose may be required.*  
*Also referred to as weight adjusted, full treatment dose.*
Consideration should be given to substituting a comparable dose of UFH at 36 weeks of gestation

Anesthesia
* Discontinue Heparin 24 hours prior to planned induction of labor or cesarean delivery
* No regional anesthesia within 12 hours after last dose of prophylactic LMWH or 24 hours after last dose of therapeutic LMWH

Postpartum
* Vaginal Delivery – restart UFH/LMWH 4-6 hrs after
* Cesarean Delivery – restart UFH/LMWH 6-12 hrs after
* If transitioning to Warfarin, continue UFH/LMWH for 5 days and until the INR is therapeutic (2.0-3.0)
* Breastfeeding is safe while on anticoagulation
* Avoid estrogen containing contraceptives
Consensus Bundle on Venous Thromboembolism

National Partnership for Maternal Safety
Prophylaxis recommendations from medical and surgical specialties as well as guidelines from the Royal College of OBGYN differ substantially from recommendations from ACOG and ACCP.

Despite increasing use of mechanical prophylaxis during cesarean birth, data have demonstrated that obstetric VTE increased 72% during hospitalizations for childbirth between 1998 and 2009 and remained relatively constant proportionately as a cause of maternal mortality.
* Readiness
  * Establishment of risk-assessment strategies for patients throughout pregnancy
  * Four Timepoints: First prenatal visit, during all antepartum admissions, immediately postpartum, on discharge home

* Recognition
  * Maternal risk should be recognized and screening performed

* Response
  * Prophylaxis for at-risk patients

* Reporting and Systems Learning
  * Recommendations for quality assurance and surveillance
* Clinical recommendations for thromboprophylaxis with low molecular weight heparin:
  * If score ≥ 4 antenatally, consider thromboprophylaxis from the first trimester
  * If score ≥ 3 antenatally, consider thromboprophylaxis from 28 weeks
  * If score ≥ 2 postnatally, consider thromboprophylaxis for at least 10 days
  * If admitted to hospital antenatally consider thromboprophylaxis
  * If prolonged admission (≥3 days) or readmission to hospital within the puerperium consider thromboprophylaxis
4 Points:
* Previous venous thromboembolism (except for a single event related to surgery)
* Ovarian hyperstimulation syndrome (first trimester only)
3 Points:
- Previous venous thromboembolism provoked by major surgery
- Known high-risk thrombophilia
- Any surgical procedure in pregnancy or puerperium except immediate repair of the perineum
- Hyperemesis
- Medical Comorbidities (cancer, heart failure, active SLE, inflammatory polyarthritis or IBD, nephrotic syndrome, type 1 DM w/ nephropathy, sickle cell disease, current IV drug use)
2 Points:
- Cesarean in labor
- Obesity (BMI >40 kg/m²)
1 Point
* Family history of unprovoked or estrogen related VTE in first degree relative
* Known low-risk thrombophilia (No VTE)
* Age >35 years
* Obesity (BMI >30 kg/m²)
* Parity ≥3
* Smoker
* Gross varicose veins
* Preeclampsia in current pregnancy
* ART
* Multiple pregnancy
* Elective cesarean
* Prolonged labor (>24 hours)
* Postpartum hemorrhage (>1L or blood transfusion)
* Preterm birth <37 weeks in current pregnancy
* Stillbirth in current pregnancy
* Current systemic infection
* Immobility, dehydration
* In contrast to clinical practice in the US, where pharmacologic prophylaxis is provided to only the highest risk women, guidelines in the UK support broad, risk-factor based assessments for both antepartum and postpartum patients

* Evidence that implementation of this approach (2004) may have substantially decreased mortality from thromboembolism
  * 1.94 deaths per 100,000 births from 2003-2005
  * 0.79 deaths per 100,000 births from 2006-2008
REFERENCES


