SAFE MOTHERHOOD INITIATIVE
Venous Thromboembolism

Tuesday, July 29th
11:00am - 12:30pm
Dial-In: 1-800-320-9190 Access Code: 784829#
VTE Prophylaxis

• Venous thromboembolism (VTE) is a leading cause of maternal mortality and severe morbidity

• Maternal death from VTE is amenable to prevention

• Prophylaxis is the most readily implementable means of systematically reducing the maternal death rate

• Protocols in the UK has led to significant reduction in maternal death from VTE

• Strategies for preventing VTE require minimal resources and are easily implementable
Key Elements in VTE Prophylaxis Bundles

- Risk assessment tools
- Protocols for antenatal and postpartum prophylaxis
- Suggested dosing schedule
- Anesthesia recommendations
- Key references
  - International Guidelines
  - Key papers
Risk Assessment

All patients should be assessed for VTE risk multiple times in pregnancy including during:

- Presentation for prenatal care
- Hospitalization for an antepartum indication
- Delivery hospitalization (in-house postpartum)
- Discharge from a delivery hospitalization

Prophylaxis can be based on risk factors or can be empiric
Risk Assessment

• Thromboembolism prophylaxis is a Joint Commission quality measures

• The Joint Commission states that all patients should receive VTE prophylaxis OR have documentation why no VTE prophylaxis was given
  • Within a day of hospital admission
  • Within a day of surgery

The 2013 Joint Commission Specifications Manual for National Hospital Inpatient Safety
Risk Assessment Tools
Risk Assessment Tools

Sources:

- Risk assessment tools were based on recommendations from major society guidelines.
- Prenatal outpatient and postpartum discharge thromboprophylaxis are based primarily on American College of Chest Physicians and ACOG recommendations.
- Inpatient prophylaxis is based primarily on RCOG recommendations.
- Pharmacologic prophylaxis may be with unfractionated heparin (UFH) or low-molecular weight heparin (LMWH).

Chest, Feb 2012; 141
ACOG Practice Bulletin No 123, 2011
## Initial Assessment During Pregnancy

<table>
<thead>
<tr>
<th>Clinical history</th>
<th>Anticoagulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple VTE episodes&lt;br&gt;VTE with high-risk (HR) thrombophilia&lt;br&gt;VTE with acquired thrombophilia</td>
<td>Treatment dose&lt;br&gt;LMWH or UFH</td>
</tr>
<tr>
<td>Idiopathic VTE&lt;br&gt;VTE with pregnancy or oral contraceptive&lt;br&gt;VTE with low risk (LR) thrombophilia&lt;br&gt;Family history of VTE with HR thrombophilia&lt;br&gt;HR thrombophilia</td>
<td>Prophylactic&lt;br&gt;LMWH or UFH</td>
</tr>
<tr>
<td>1st VTE provoked&lt;br&gt;Family history of VTE with LR thrombophilia&lt;br&gt;LR thrombophilia (including acquired)</td>
<td>No treatment</td>
</tr>
</tbody>
</table>

*Chest, Feb 2012; 141, ACOG Practice Bulletin No 123, 2011*
Risk Assessment

High-risk thrombophilia

- Factor V Leiden or prothrombin gene mutation homozygous
- Antithrombin III deficiency
- Compound heterozygote disorders (FVL and prothrombin)

Low-risk thrombophilia

- Factor V Leiden or prothrombin gene mutation heterozygous
- Protein C or S deficiency

Acquired thrombophilia

- Antiphospholipid antibody syndrome

ACOG Practice Bulletin No 123, 2011
Prevalence and Risks of VTE with Thrombophilias

<table>
<thead>
<tr>
<th></th>
<th>Prev in Gen Pop %</th>
<th>Lifetime ↑ VTE Risk</th>
<th>% of all VTE</th>
<th>VTE Risk/Preg (No hx) %</th>
<th>VTE Risk/Preg (Prior VTE) %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low-risk thrombophilias</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FVL heterozygote</td>
<td>1-15</td>
<td>3-8</td>
<td>40</td>
<td>&lt; 0.3</td>
<td>10</td>
</tr>
<tr>
<td>PTG heterozygote</td>
<td>2-5</td>
<td>3</td>
<td>17</td>
<td>&lt; 0.5</td>
<td>&gt;10</td>
</tr>
<tr>
<td>Protein C activity (&lt;50%)</td>
<td>0.2-0.4</td>
<td>10-15</td>
<td>14</td>
<td>0.1-0.8</td>
<td>4-17</td>
</tr>
<tr>
<td>Protein S free Ag (&lt;55%)**</td>
<td>.03-0.1</td>
<td>2</td>
<td>3</td>
<td>0.1</td>
<td>0-22</td>
</tr>
<tr>
<td><strong>High-risk thrombophilias</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FVL homozygote</td>
<td>&lt; 1</td>
<td>2</td>
<td>2</td>
<td>1.5</td>
<td>17</td>
</tr>
<tr>
<td>PTG homozygote</td>
<td>&lt; 1</td>
<td>0.5</td>
<td>0.5</td>
<td>2.8</td>
<td>&gt; 17</td>
</tr>
<tr>
<td>FVL/PTG compound</td>
<td>0.01</td>
<td>1-3</td>
<td>4.7</td>
<td></td>
<td>&gt; 20</td>
</tr>
<tr>
<td>Antithrombin III def (&lt;60%)</td>
<td>0.02</td>
<td>25-50</td>
<td>1</td>
<td>3-7</td>
<td>40</td>
</tr>
</tbody>
</table>

** Should not be tested in pregnancy or high-estrogen states.
Initial Assessment During Pregnancy

**Provoked** VTE is defined as an event occurring in the setting of a temporary risk factor that increases risk such as:

- Orthopedic surgery
- Indwelling line
- Immobilization

**Unprovoked** VTE occurs in the absence of temporary risk factors.

*AN EXCEPTION:* VTE provoked by estrogen (OCP, prior pregnancy) should be treated as being at higher risk for recurrence and guidelines for “unprovoked VTE” should be followed for patients with this clinical history.
Antepartum Hospitalization

All patients → Mechanical prophylaxis

AND

All patients:

Should be given pharmacologic prophylaxis if risk factors are present (next slide)

OR

May be given pharmacologic prophylaxis empirically
Antepartum Hospitalization Risk-Factor Based Prophylaxis

Recommend heparin if at least 1 of the factors below is present:

- Already receiving LMWH or UFH as outpatient
- Pre-pregnancy Morbid Obesity (BMI > 40)
- Any history of VTE

OR 2 or more risk factors below are present:

- Age > 40 or < 15 years
- Pre-pregnancy obesity (BMI > 30)
- Bed rest
- Any thrombophilia
- Medical conditions
- Pregnancy complications

Prophylactic LMWH or UFH

Medical conditions
- Heart disease
- Lupus
- Renal disease
- Sickle cell
- Major infection
- Other major medical conditions

Pregnancy complications
- IUGR
- Preeclampsia
- Multiple gestation
- ART

RCOG, 2009 Green Top 37a
Delivery Hospitalization

All patients

Early mobilization
Avoid dehydration
Chemoprophylaxis based on risk factors

Women undergoing cesarean delivery should:

- Receive sequential compression devices perioperatively and postpartum
- Receive chemoprophylaxis (LMWH or UFH) either empirically OR based on risk factors
Delivery Hospitalization

Recommend heparin if at least 1 of the factors below is present

- Already receiving heparin as outpatient
- Pre-pregnancy class 3 obesity (BMI > 40)
- Any history of VTE
- Thrombophilia and family history of VTE

OR 2 or more risk factors below are present:

- 2 or more risk factors:
  - Cesarean delivery
  - Hemorrhage
  - Hysterectomy
  - General anesthesia
  - Postpartum infection
  - Age > 40 or < 15 years
  - Pre-pregnancy obesity (BMI > 30)
  - Bed rest
  - Any Thrombophilia
  - Medical or pregnancy complications

Prophylactic LMWH or UFH until discharge

RCOG, 2009 Green Top 37a
Assessment During Postpartum Discharge

Clinical history

- Multiple VTE episodes
- VTE with high-risk (HR) thrombophilia
- VTE with acquired thrombophilia

- Idiopathic VTE
- VTE with pregnancy or oral contraceptive
- VTE with low-risk (LR) thrombophilia
- Family history of VTE with HR thrombophilia
- HR thrombophilia (including acquired)
- VTE provoked*
- LR thrombophilia and family history of VTE*

* (two changes from initial assessment)

Anticoagulation

- 6 Weeks Treatment
  - LMWH/UFH

- 6 Weeks Prophylactic
  - LMWH/UFH

- No treatment

Chest, Feb 2012; 141 ACOG Practice Bulletin No 123, 2011
Anticoagulation - LMWH

• Advantages of LMWH compared to UFH
  • Fewer bleeding episodes
  • Lower risk of heparin induced thrombocytopenia (HIT)
  • Lower incidence of osteoporosis
  • More predictable pharmacokinetics
• Anti-Xa activity measurement not required for LMWH except for
  • Extremes of body weight
  • Renal impairment
• LMWH has longer half life than UFH
  • May be an advantage or a disadvantage

Contraindications to LMWH Therapy

- Hemophilia or other known bleeding disorder
- Active or threatened antenatal bleeding (e.g. placenta previa, placental abruption) based on clinical judgment of balancing risks/benefits
- Thrombocytopenia (platelet count <75 x10⁹)
- Recent stroke (hemorrhagic/ischemic)
- Severe renal disease (GFR <30ml/min)
- Severe liver disease (prolonged PT)
- Uncontrolled hypertension (BP >200mmHg systolic or >120mmHg diastolic)
- Unfractionated heparin should be used if there is a specific contraindication to LMWH
Screening for Heparin Induced Thrombocytopenia (HIT)

- For patients expected to be on either UFH or LMWH for greater than >7 days a complete blood count should be sent to assess for HIT 7-10 days after initiation of therapy.
- A platelet count of <150,000/microL or acute drop to <50% of baseline require further evaluation and immediate consultation with a hematologist or maternal-fetal medicine specialist.
- A preceding diagnosis of gestational thrombocytopenia or idiopathic thrombocytopenic purpura may confound screening for HIT, and consultation with a hematologist or maternal fetal medicine specialist may be required for patients with these conditions.
Prophylaxis and Spontaneous Labor

• For patients on LMWH prenatally, consideration should be made to switch to UFH at 35-36 weeks gestational age to facilitate administration of regional anesthesia.

• When patients are transitioned from LMWH to UFH, HIT should also be screened for with a CBC 7-10 after UFH is initiated.
### Protocols for Prophylaxis

<table>
<thead>
<tr>
<th>Agent</th>
<th>LMWH</th>
<th>Dalteparin</th>
<th>Tinzaparin</th>
<th>UFH Unfractionated heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Enoxaparin</td>
<td>Dalteparin</td>
<td>Tinzaparin</td>
<td>Gestational age-based</td>
</tr>
<tr>
<td>Weight based</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50kg</td>
<td>20mg daily</td>
<td>2500 units daily</td>
<td>3500 units daily</td>
<td>First trimester 5000-7500 units Twice daily</td>
</tr>
<tr>
<td>50-90kg</td>
<td>40mg daily</td>
<td>5000 units daily</td>
<td>4500 units daily</td>
<td>Second trimester 7500-10000 units Twice daily</td>
</tr>
<tr>
<td>91-130kg</td>
<td>60mg daily*</td>
<td>7500 units daily*</td>
<td>7000 units daily*</td>
<td>Third trimester 10000 units Twice daily</td>
</tr>
<tr>
<td>131-170kg</td>
<td>80mg daily*</td>
<td>10000 units daily*</td>
<td>9000 units daily</td>
<td></td>
</tr>
<tr>
<td>&gt;170kg</td>
<td>0.6mg/kg/day*</td>
<td>75 units/kg/day</td>
<td>75 units/kg/day</td>
<td></td>
</tr>
</tbody>
</table>

Hospitalized antepartum patients may receive 5000 units UFH twice daily for prophylaxis to facilitate regional anesthesia.

*=may be given in two divided doses

Adapted from ACOG Practice Bulletin 123, ACCP Recommendations, RCOG Green Top Guideline 37a
## Protocols for Therapeutic Dosing

<table>
<thead>
<tr>
<th></th>
<th>LMWH Enoxaparin</th>
<th>Dalteparin</th>
<th>Tinzaparin</th>
<th>Unfractionated heparin</th>
<th>Warfarin (postpartum)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing:</strong> Antepartum or Postpartum</td>
<td>1mg/kg twice daily</td>
<td>200 units/kg/day</td>
<td>175 units/kg/day</td>
<td>10000 units or more twice daily adjusted to mid interval target aPTT (1.5-2.5)</td>
<td>INR 2.0-3.0 (postpartum only)</td>
</tr>
</tbody>
</table>

Adapted from ACOG Practice Bulletin 123

**Protocols for Therapeutic Dosing**
# Timing of Neuroaxial Anesthesia

<table>
<thead>
<tr>
<th>Antepartum/Intrapartum</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UFH prophylaxis</strong> (\leq 10,000\text{IU/day})</td>
<td>No contraindications to timing of heparin dose and performance of neuraxial blockade</td>
</tr>
<tr>
<td><strong>UFH therapeutic</strong></td>
<td>Wait (6) hours post last dose prior to neuraxial blockade</td>
</tr>
<tr>
<td><strong>LMWH prophylaxis</strong></td>
<td>Wait (12) hours post last dose prior to neuraxial blockade</td>
</tr>
<tr>
<td><strong>LMWH therapeutic</strong></td>
<td>Wait (24) hours post last dose prior to neuraxial blockade</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Postpartum</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UFH prophylaxis</strong> (\leq 10,000\text{IU/day})</td>
<td>Wait (\geq 1) hour after epidural catheter removal or spinal needle placement</td>
</tr>
<tr>
<td><strong>UFH therapeutic</strong></td>
<td>Wait (\geq 1) hour after epidural catheter removal or spinal needle placement</td>
</tr>
<tr>
<td><strong>LMWH prophylaxis</strong></td>
<td>Wait (\geq 4) hours after epidural catheter removal or spinal needle placement</td>
</tr>
<tr>
<td><strong>LMWH therapeutic</strong></td>
<td>Avoid therapeutic dosing with epidural catheter in situ. Wait at least (24) hours after catheter removal or spinal needle placement</td>
</tr>
</tbody>
</table>

Sources: FDA Drug Safety Communication Nov, 2013; NYP protocol
Post-Cesarean Prophylaxis

• Unfractionated heparin (UFH)
  • The patient should receive the first dose of UFH on meeting criteria for PACU discharge, but no sooner than one hour after epidural catheter removal
  • Standard order 5000 units SC every 12 hours
  • If an epidural catheter remains in situ for pain control, it should not be removed until 3 hours after last dose of UFH
  • Intraoperative UFH (infrequent) should be given no sooner than 30 minutes after spinal or epidural
Post-Cesarean Prophylaxis

- Low-molecular-weight heparin (LMWH)
  - The patient should receive the first dose of LMWH no sooner than 6 hours postoperatively regardless of anesthesia technique
  - If an epidural catheter remains in situ for pain control, it should not be removed until 12 hours after last dose of LMWH
  - If the epidural catheter is to be removed prior to a dose of LMWH, the LMWH may not be given until 4 hours after removal

Sources:  FDA Drug Safety Communication Nov, 2013; NYP protocol
Therapeutic Postpartum Prophylaxis

- For patients who have *therapeutic LMWH* postpartum anticoagulation planned:
  - LMWH should be deferred until at least 24 hours after spinal needle placement or epidural catheter removal
  - Prophylactic UFH dosing should be considered during the 24 hours postpartum after regional anesthesia for these patients
  - For patients with major risk factors for hemorrhage precluding therapeutic LMWH (recent postpartum hemorrhage, wound hematoma, coagulopathy) prophylactic UFH and/or SCDs should be considered
Conclusion

• All patients require VTE risk assessment at multiple time points in pregnancy and postpartum

• All patients undergoing cesarean delivery require mechanical prophylaxis, early ambulation, and adequate hydration

• Women with additional risk factors for VTE after delivery will benefit from pharmacologic prophylaxis

• Empiric pharmacologic prophylaxis for all women undergoing cesarean delivery and for all antepartum hospital admissions is a reasonable clinical strategy