Deep Venous Thrombosis in Pregnancy

Background
1. Definition
   - Thrombosis
     - Formation of blood clot within a vessel
   - DVT
     - Thrombus occurring in deep veins
     - Usually in lower extremity or pelvis
2. Overview of normal clotting
   - Injured endothelium exposes collagen and leads to:
     - Adherence
     - Activation of platelets

Pathophysiology
1. Pathology
   - Virchow's Triad - specific to pregnancy
     - Endothelial Damage
       - Delivery associated with injury at placental interface and to pelvic veins
     - Stasis
       - Hormones induce dilatation of veins
       - Enlarging uterus causes compression of veins
     - Hypercoagulable state
       - Increased levels of clotting factors seen in pregnancy
       - Resistance to protein C seen in late pregnancy
   - Inherited thrombophilic conditions
     - Factor V Leiden mutation
     - Prothrombin gene mutation
     - Protein S deficiency
     - Protein C deficiency or resistance
     - Dysfibrinogenemias
     - Hyperhomocysteinemia
     - Antithrombin III deficiency
     - MTHFR mutation
     - Sickle Cell Disease
     - Lipoprotein A elevation
     - Increased levels of clotting factors
   - Acquired thrombophilic conditions
     - Heart failure
     - Heparin Induced Thrombocytopenia
     - TTP
     - Antiphospholipid antibodies
     - Myeloproliferative disorders
     - Nephrotic Syndrome
     - Obesity
2. Incidence, prevalence
   - General population – 0.13%
   - Pregnant patients – 0.125%
Inherited thrombophilia – 5-33%
- Previous DVT – 2.4%
- More common postpartum than antepartum
- All trimesters carry same risk
- 90% of DVTs in pregnancy are left sided

3. Risk factors
- Inherited thrombophilias
- Malignancy
- Recent surgery
  - Including operative deliveries
- Trauma or major Injury
- Pregnancy
- Hormone replacement/OCP
- Immobilization
- Previous thromboembolic dz

4. Morbidity/ mortality
- According to data from CDC
  - PE is 2nd most common cause of pregnancy related deaths
  - Accounts for 20%

Diagnostics
1. History
- Classic symptoms
  - Pain and swelling of lower extremity
- Symptomatology may be insensitive in pregnancy
  - Due to presence of lower extremity edema near end of term
- Questions to Ask
  - Recent Surgery
  - Trauma
  - Family History
  - Prior DVT
  - Recent Activity Level
  - Past History of Cancer

2. Physical examination
- Classic findings
  - Palpable cord
  - Ipsilateral edema
  - Warmth
  - Discoloration
- Homan's sign
  - Pain upon dorsiflexion of ankle on affected side
  - May be helpful but fairly unreliable
- Physical exam
  - Neither sensitive nor specific for DVT
  - Less accurate in pregnant patients
- Diagnosis confirmed with studies

3. Diagnostic testing
- Use a combination of Wells score and D-dimer test to exclude DVT in low-to intermediate-risk outpatients with suggestive Sx
Laboratory evaluation
  - D-Dimer
    - Utility is controversial
    - Results should be interpreted in combination with clinical suspicion of DVT
    - D-Dimer increase can be normal in pregnancy

Diagnostic imaging
  - No guidelines suggesting different approach to Dx of DVT in pregnant vs. non-pregnant patients
  - Compression ultrasound
    - Most commonly used study to diagnose DVT
    - >95% sensitive and specific
      - If lack of vein compressibility is found
    - Performed in left lateral decubitus position in pregnant patients
    - If initially negative
      - Calf DVT not excluded
      - Repeat in 1-2 days
  - Contrast venography
    - Considered gold standard for diagnosis
    - No longer used as first line test, too invasive
    - Useful when other studies are not possible or non-diagnostic
  - Impedance plethysmography (IPG)
    - 1st non-invasive test used for Dx DVT
    - No longer used
      - Less accurate
      - Machines are no longer produced
  - MRI
    - Detects lower extremity and pelvic thromboses
    - Utility may be limited by cost & accessibility

Differential Diagnosis
1. Key DDx
  - Cellulitis
  - Lymphangitis
  - Thrombophlebitis
  - Knee joint abnormality
2. Extensive DDx
  - Muscle strain or tear
  - Muscle hematoma
  - Injury to leg
  - Venous insufficiency
  - Baker's Cyst
  - Drug-induced edema
  - Lymphedema
**Therapeutics**

1. **Acute treatment**
   - Initial management is identical in pregnant vs. non-pregnant patients
   - **LMW Heparin**
     - Titrate to anti-factor Xa level of 1-2 IU/ml for once daily injections
     - Titrate to anti-factor Xa level of 0.5-1.2 IU/ml for twice daily injections
     - Use weight adjusted dosing
       - Dose may change as pregnancy progresses
     - Enoxaparin
       - 1 mg/kg BID, or
       - 1.5 mg/kg qD
   - **Unfractionated Heparin**
     - Titrate to PTT of 1.5-2.3
     - Use initial bolus of 5000 U
     - With subsequent continuous infusion of 30-35,000 U per 24 hour period
     - Pregnant patients require increased doses to reach therapeutic PTT
   - Immediate search for signs/symptoms of PE
     - Symptoms: dyspnea, chest pain, hemoptysis
     - Signs: tachypnea, tachycardia, fever

2. **Further management**
   - If start with IV treatment
     - Consider switch to subcutaneous injections
       - LMWH or UFH can be used
   - Warfarin contraindicated due to teratogenicity
   - Continue to monitor for Sx of PE
     - Imaging studies warranted if clinical suspicion
   - IVC Filter if standard treatment contraindicated

3. **Long-term care**
   - If using LMW Heparin
     - Switch to unfractionated 2 weeks prior to delivery
   - Unfractionated heparin stopped 24 hours before delivery
     - Protamine sulfate given if necessary to reverse PTT
   - Restart heparin 6 hours post-vaginal birth
     - 12 hours post-cesarean birth
   - 6 months of anticoagulation
     - Including at least 6 weeks postpartum
   - Most effective at preventing recurrence
   - Warfarin safe to use during lactation

**Follow-Up**

1. **Return to office**
   - Frequent lab studies
     - Until coagulation studies stabilize
     - May be harder to stabilize pregnant patients
   - Continue to monitor for Sx of PE
2. Admit to hospital
   o Patients are generally admitted to begin anticoagulation therapy
   o Thereafter hospital admission is not necessary
     - Unless complications such as hemorrhage or PE occur

Prognosis
1. Major adverse outcome is PE
   o Accounts for 20% of pregnancy related deaths
   o Second only to hemorrhage

Prevention
1. Pts with prior Hx of DVT due to transient risk factor
   o Close follow up is all that is required
   o If transient risk factor is pregnancy
     - Prophylaxis is needed
2. Pts with prior Hx of single DVT who are not currently on anticoagulation Tx
   o Antepartum and postpartum prophylaxis is indicated
   o 5000 U SC every 12 hours
     - Recommended for antepartum prophylaxis
3. Pts with prior Hx of single DVT and inherited thrombophilia
   o If not currently on anticoagulation Tx
     - Antepartum and postpartum prophylaxis is indicated
     - Pts with prior Hx of multiple DVTs or inherited thrombophilias
   o If currently on long term anticoagulation Tx
     - Prophylaxis should be continued
     - With long term anticoagulation undertaken postpartum
General recommendations
   o Left lateral decubitus position
     - Favorable to supine position
   o Compression stockings

References
Evidence-Based Inquiry
1. How can we best treat and monitor VTE during pregnancy?

PURLs
1. Is It DVT? Wells Score And D-dimer May Avert Costly Workup

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