When is THROMBOPHILIA TESTING (HYPERCOAGULABLE WORK-UP) Indicated?

**PRACTICE POINTS:** Thrombophilia testing = Hypercoagulable work-up (estimated cost $1000.)
- Acquired: lupus inhibitor, antiphospholipid antibodies (IgG, IgM)=APLA, +/- high FVIII levels?
- Inherited: Factor V Leiden, Prothrombin mutation, Protein C, S and antithrombin deficiency

**WHEN IS THROMBOPHILIA TESTING INDICATED?**
1. When the results will influence the management of the patients or their family OR
2. Patients' preference for knowledge (after informed consent.)

**Unprovoked or Idiopathic:** indicates that no alternative explanation for clot AFTER appropriate history, physical and work up has been completed (depending on the clinical situation) – see examples of possible explanations/risk factors as listed below

**Recognized Causes of Arterial clot:**
- atherosclerosis (age, smoking, hypertension, hypercholesterolemia, diabetes, calcified aorta etc)
- cardioembolic (arrhythmia, left ventricular clot, structural cardiac disease)
- Other secondary causes (heparin induced thrombocytopenia, paroxysmal hemoglobinuria, vasculitis, OCP, etc)

**Recognized Causes of Venous clot:**
- Major provoked events: post operative state or trauma (within 4 weeks), immobilization (casting, hospitalization, bed ridden), active cancer/chemotherapy drugs (esp. estrogen containing contraception, HRT)
- Recurrent pregnancies lost: >3 first trimester losses or 1 or more stillbirth (spontaneous, normal anatomy, no chromosomal anomalies or infection)

**When is THROMBOPHILIA TESTING (HYPERCOAGULABLE WORK-UP) Indicated?**

**Has the patient had an arterial or venous clot?**
- NO
  - WAS THE CLOT UNPROVOKED*?
    - YES
      - TREAT THE UNDERLYING CAUSE
    - NO
      - ANY HISTORY OF UNEXPLAINED* RECURRENT LOST PREGNANCIES?

**Any family history of idiopathic* arterial/venous clot or both?**
- NO
  - WAS THE EVENT(S) ARTERIAL OR VENOUS OR BOTH?
    - Arterial Clot
      - 1. Test for acquired defects: lupus inhibitor & APLA
         2. If #1 positive need to repeat testing 12 weeks later
    - Venous Clot or both
      - Referral to Specialists (Neurology/cardiology/hematology) to consider anticoagulant vs antplatelet therapy
    - Arterial Clot
      - NO
      - Antiphospholipid syndrome (APS)
  - NO
    - Antiphospholipid syndrome (APS)
      - Referral to CCMB Hematology for counseling & decide if testing should change patient management or be done based on patients' preference

**Antiphospholipid syndrome (APS)**
- Referral to CCMB Hematology for counseling regarding ASA + peripartum heparin
- No thrombophilia testing

**Any history of unexplained* recurrent lost pregnancies?**
- YES
  - 1. Test for acquired defects: lupus inhibitor & APLA
     2. If #1 positive need to repeat testing 12 weeks later
- NO
  - WAS THE EVENT(S) ARTERIAL OR VENOUS OR BOTH?

**Is there consideration for estrogen therapy or pregnancy?**
- YES
  - Arterial Clot
    - Referral to CCMB Hematology for counseling & decide if testing should change patient management or be done based on patients' preference
- NO
  - Venous Clot or both or known thrombophilia
    - Referral to CCMB Hematology for counseling regarding ASA + peripartum heparin
    - No thrombophilia testing. Need to screen/optimize risk factors for arterial clot or venous clot
Rationale for Referral and Decisions Made for THROMBOPHILIA TESTING

Estrogen associated venous clot?

1. Test for acquired defects: lupus inhibitor & APLA
2. If #1 positive ➔ Must repeat testing 12 weeks later

Any high risk features?

1. Males OR
2. Females with 2 or more of the following:
   ● Hyperpigmentation,
   ● edema,
   ● redness,
   ● positive D-dimer,
   ● age >65,
   ● BMI >30

Antiphospholipid syndrome (APS)

1. 30% risk of recurrence clot if discontinued anticoagulation
2. Consider indefinite anticoagulation

Unprovoked venous clot?

1. Intermediate risk of 2nd recurrence (~10%)
2. Anticoagulate for 3 months and stop if estrogen can be safely discontinued. If not, consider referral for advice to balance the risk of clotting/bleeding/unwanted pregnancy, etc

Any high risk features?

1. Variable risk of recurrence clot if discontinued anticoagulation (5-20%)
2. Consider patient’s preference to decide regarding duration of anticoagulation (6 months versus indefinite)
3. Do inherited thrombophilia work up if the results will aid in patient’s decision making or due to patients’ preference

Problems “false reassurance” - still at increased risk compared to general population (~0.1% VTE per year)

Family history of Unprovoked* arterial/venous clot or both OR known thrombophilia? AND Consideration for estrogen therapy or pregnancy?

Consider testing for inherited thrombophilia to decide avoidance of OCP and/or peripartum thrombophylaxis

Absolute risk is dependent on the actual defect found
• FVL/prothrombin mutation: 0.4% VTE per year
• Protein C or S deficiency: 1% VTE per year
• Antithrombin deficiency: 4% VTE per year

If above defects found AND starting OCP – increase RR 2-4
• ~300 women need to avoid OCP in order to prevent 1 VTE (at cost of other complications (such as unwanted pregnancy/pregnancy associated VTE)
• *As such, thrombophilia is NOT an absolute contraindication for OCP but requires counselling

All pregnant women with a family history of unprovoked thrombosis or thrombophilia should be considered for postpartum prophylaxis for 6 weeks

End of Document