Evaluation of Anemia
Laboratory Definition of Anemia

• **Hgb:**
  - Women: <12.0
  - Men: < 13.5

• **Hct:**
  - Women: < 36
  - Men: <41
Evaluating the Patient with Anemia

- Bleeding
  - BRBPR
  - Melena
  - Heavy Menses
  - Epistaxis
  - Urinary Losses
  - RP hematoma (recent femoral vein/artery manipulation?)
Tests Used to Evaluate Anemia

☐ My Standard Workup
  ■ CBC
  ■ Retic
  ■ LDH
  ■ Haptoglobin
  ■ SPEP
  ■ B12
  ■ Iron Studies w/ Ferritin

☐ Other tests based on situation
Tests Used to Evaluate Iron

- Serum Iron
  - Measures recent iron status
  - Reflects intake over the hours – days

- TIBC
  - Indirectly measures transferrin
  - Increased in iron deficiency as body attempts to scavenge more iron
  - Decreased with inflammation, low in “Anemia of Chronic Disease”
Tests Used to Evaluate Iron

- Ferritin
  - Measures STORAGE iron (mostly in liver and marrow)
  - In healthy individuals, very good test to assess true iron status
  - Increased in inflammation, often masking true iron deficiency
Tests Used to Evaluate Iron

- Soluble Transferrin Receptor
  - Controls level of free iron in blood
  - Increased in iron deficiency
  - Decreased in iron overload and malnutrition
  - Less effect of inflammation
  - Helpful in distinguishing iron deficiency (high) from “Anemia of Chronic Disease” (normal)
Tests Used to Evaluate Iron

- **Reticulated Hemoglobin**
  - Snapshot of iron status during reticulocyte maturation
  - Low in iron deficiency
  - Rises quickly in iron deficiency (2-4 days) so can be used to see if iron therapy is effective
Tests Used to Evaluate Anemia

- Reticulocyte Count

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Reference Range</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>RETIC COUNT</td>
<td>8.7</td>
<td>0.7–2.3</td>
<td>09/21/17-0455</td>
</tr>
<tr>
<td>RETIC PERCENT</td>
<td>0.7</td>
<td>2.0–3.0</td>
<td>09/21/17-0455</td>
</tr>
<tr>
<td>RED BLOOD CELL</td>
<td>1.99</td>
<td>4.0–5.80 x10^6/u</td>
<td>09/21/17-0455</td>
</tr>
<tr>
<td>RETIC, ABSOLUTE</td>
<td>72.9</td>
<td>28.9–104.4 x10^3/l</td>
<td>09/21/17-0455</td>
</tr>
<tr>
<td>IRF</td>
<td>0.34</td>
<td>0.02–0.15</td>
<td>09/21/17-0455</td>
</tr>
<tr>
<td>RETICULATED HGB</td>
<td>37.7</td>
<td>29.0–32.0 pg</td>
<td>09/21/17-0455</td>
</tr>
</tbody>
</table>

The IMMATURE RETICULOCYTE FRACTION (IRF) directly reflects the intensity of Erythropoietic stimulation. The absolute reticulocyte count (ABS RETIC) indicates the effectiveness of such stimulation in terms of bone marrow erythrocyte production.

The RET-He threshold for defining iron deficiency in adults is <29 pg.
Tests Used to Evaluate Anemia

- Reticulocyte Count
  - Measures young, immature RBCs (reticulocytes) identifiable by the presence of purple chromatin, first 1-2 days of life in peripheral blood of RBC
  - Presented as a PERCENTAGE
  - Overestimates actual number of retics in anemia
Tests Used to Evaluate Anemia

- Reticulocyte Count
  - Corrected Reticulocyte Count
    - Corrects Retics for level of anemia
    - Multiply Retic% x Hct/Normal Hct (45)
  - Reticulocyte Production Index
    - Further corrects Retic Count based on maturation rate
    - In severe anemia get very immature retics which retain chromatin longer
Tests Used to Evaluate Anemia

Reticulocyte Count

- **RETIC COUNTER**
  - **RETIC PERCENT**: 5.8
  - **H**
  - **0.7-2.3 %**
  - **10/01/17-0353**

- **RED BLOOD CELL**: 2.52
  - **L**
  - **3.90-5.10 x10 6/u**
  - **10/01/17-0353**

- **RETIC, ABSOLUTE**: 147.2
  - **H**
  - **28.9-104.4 x10 3/u**
  - **10/01/17-0353**

- **IRF**: 0.27
  - **H**
  - **0.02-0.15**
  - **10/01/17-0353**

*The IMMATURE RETICULOCYTE FRACTION (IRF) directly reflects the intensity of Erythropoietic stimulation. The absolute reticulocyte count (ABS RETIC) indicates the effectiveness of such stimulation in terms of bone marrow erythrocyte production.*

- **RETICULATED HGB**: 26.5
  - **L**
  - **29.0-32.0 pg**
  - **10/01/17-0353**

*The RET-He threshold for defining iron deficiency in adults is <29 pg.*
Tests Used to Evaluate Anemia

- Mean Cell Volume (MCV)
  - Usually about 80-100 fL
  - Macrocytic = >100
  - Microcytic = <80
Tests Used to Evaluate Anemia

- **Mean Cell Volume (MCV)**
  - Common Macrocytic Anemias
    - Alcohol Abuse
    - Elevated Retic Count (GI Bleed)
    - B12 deficiency
      - Confirmatory tests: MMA and HC
    - Folic Acid Deficiency
      - Confirmatory test: RBC-Folate
    - Hypothyroidism
    - Myelodysplasia
  - Medications (MTX, hydroxyurea, AZT)
Tests Used to Evaluate Anemia

- Mean Cell Volume (MCV)
  - Common Microcytic Anemias
    - Iron Deficiency
    - Thalassemia
      - Alpha – check with Alpha Thal. Mutation
      - Beta – check with Hgb. Electropheresis (after correcting iron deficiency)
  - Rare
    - Copper Deficiency
    - Lead Poisoning
Example Patient w/ Anemia


- 3 mos. ago
  - Hgb 9.6 (14-16.5)
  - MCV 86 (80-100)
  - Serum Iron 28 (35-150)
  - TIBC 213 (280-450)
  - Iron Sat (%) 13% (18-50)

- Started on PO OTC iron
Example Patient w/ Anemia

- 3 weeks ago
  - Hgb 9.5 (13-16)
  - MCV 84 (80-100)
  - Ser. Iron 85 (35-150)
  - TIBC 218 (280-450)

- Referred for Hematology Consult
- Other Tests?
Example Patient w/ Anemia

- Other Tests
  - Sol. Tran. Rec. 2 (2-2.5)
  - Ferritin 345 (30-300)
  - Retics (Absol.) 26k (29-104k)
  - Other “Std w/u” Neg

- Diagnosis?
Example Patient w/ Anemia

- Diagnosis
  - Anemia of Chronic Disease
- Patient referred for Colonoscopy (since overdue, always a good idea)
- Follow CBC over next 1-2 years, investigate further if needed
- Teaching Point = Feeling comfortable with “AOCD”
Example Patient w/ Anemia

- Female, 38yo, menstruating but not heavy, otherwise healthy.

- 2 mos. ago
  - Hgb: 8.7 (13-16)
  - MCV: 72 (80-100)
  - Serum Iron: 27 (35-150)
  - TIBC: 513 (280-450)
  - Iron Sat (%): 5% (18-50)

- Started on PO OTC iron
Example Patient w/ Anemia

☐ 2 weeks ago
  ■ Hgb 10.5 (13-16)
  ■ MCV 84 (80-100)
  ■ Ser. Iron 273 (35-150)

☐ PO OTC Iron stopped emergently

☐ Hemochromatosis Mutation, Neg

☐ Referred for Hematology Consult

☐ Other Tests?
Example Patient w/ Anemia

- Further Labs
  - Ferritin  27  (30-300)
  - Iron     53  (35-150)
  - TIBC     440 (280-450)

- Diagnosis?
Example Patient w/ Anemia

- Diagnosis
  - Correcting Iron Deficiency
  - Lab drawn hours after PO Iron and a Big Mac

- Teaching Point = Serum Iron is very unreliable in the diagnosis of Iron Def. Anemia since it only reflects recent iron intake
Example Patient w/ Anemia

- Male, 67yo, No bleeding. CAD w/stent. COPD.

- 5 mos. ago
  - Hgb 11.8 (14-16.5)
  - MCV 83 (80-100)
  - Serum Iron 44 (35-150)
  - TIBC 440 (280-450)
  - Iron Sat (%) 10%(18-50)

- Started on PO OTC iron
Example Patient w/ Anemia

- 2 weeks ago
  - Hgb 9.8 (13-16)
  - MCV 90 (80-100)
  - Ser. Iron 31 (35-150)
  - TIBC 455 (280-450)

- Referred for Hematology Consult
- Other Tests?
Example Patient w/ Anemia

- Other Tests
  - Ferritin 15 (30-300)
  - Retics (Absol.) 124k (29-104k)
  - Haptoglobin normal
  - LDH normal
  - Other “Std w/u” Neg

- Rise in MCV due to Incr. Retics.
- Diagnosis?
Example Patient w/ Anemia

☐ Diagnosis
  ■ GI Blood Loss

☐ Patient referred for Colonoscopy and found to have bleeding AVMs

☐ Patient was unable to keep up with losses using PO iron
  ■ Treated with IV iron (Feraheme)

☐ Teaching Point = Iron Def. plus Incr. Retic is usually GI Blood Loss (occult)
Emergencies Not To Miss

- If Platelets are low consider TTP or HUS!
  - Must check smear for schistocytes (for sign of microangiopathic hemolytic anemia)
  - If renal failure, E. Coli O157:H7 exposure → HUS
  - Think of TTP frequently
    - Renal Failure / Insufficiency
    - Mental Status Changes
    - Abdominal Pain
    - Fever
Emergencies Not To Miss

- Are the other cell lines also low?
  - Consider APLASTIC ANEMIA!
  - Check medication list
    - NSAIDS (phenylbutazone), Sulfonamides, Acyclovir, Gancyclovir, chloramphenicol, anti-epileptics (phenytoin, carbamazepine, valproic acid), nifedipine
    - Check parvovirus B19 IgG, IgM
    - Consider hepatitis viruses, HIV
  - Consider AML, Lymphoma, Marrow Invasion
    - Blasts?
    - Increased Monos? Lymphs? Immature granulocytes?
    - Weight Loss?
    - Infections?
    - Tear Drop Cells?
Evaluating the Patient with Anemia

- Any jaundice, elevated bilirubin, suspicious for hemolysis?
  - Check for increased indirect bilirubin, increased LDH, decreased haptoglobin, increased reticulocyte count
  - Is Coombs test positive?
    - If yes, may be warm antibody hemolytic anemia; Consider drug as cause
Evaluation of Thrombophilia—Hypercoagulable Syndromes
Risk Factors for Thrombosis

- Hereditary thrombophilia
- Acquired thrombophilia
- Surgery trauma
- Estrogens
- Malignancy
- Immobility
- Atherosclerosis

Thrombosis
Recurrence Rate of DVT/VTE

- VTE due to major transient risk factor
  - Woman with VTE on hormones
    - Non-major transient risk factor
  - Woman with unprovoked VTE
    - DVT
    - PE
  - Man with unprovoked VTE
    - DVT
    - PE

<table>
<thead>
<tr>
<th>Cumulative VTE Recurrence Rate</th>
<th>1 year</th>
<th>5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Woman with VTE on hormones</td>
<td>1 %</td>
<td>3 %</td>
</tr>
<tr>
<td>Strong Thrombophilia</td>
<td>6 %*</td>
<td>15 %</td>
</tr>
<tr>
<td>Woman with unprovoked VTE</td>
<td>5 %</td>
<td>15 %</td>
</tr>
<tr>
<td>Man with unprovoked VTE</td>
<td>10 %</td>
<td>30 %</td>
</tr>
</tbody>
</table>


*[Douketis J et al. BMJ 2011;342:d813]*
Case Fatality Rate of Recurrent VTE and Bleeding

- 3.6% of recurrent VTE are fatal
- 10% of major bleeds are fatal

Thus:
If risk of recurrence $\geq 3x$ higher than risk of major bleed = long-term anticoagulation.

Risk Factors for Venous Thrombosis

- Acquired
- Inherited
- Mixed/unknown
Risk Factors—Acquired

- Advancing age
- Prior Thrombosis
- Immobilization
- Major surgery
- Malignancy
- Estrogens
- Antiphospholipid antibody syndrome
- Myeloproliferative Disorders
- Heparin-induced thrombocytopenia (HIT)
- Prolonged air travel
Risk Factors—Inherited

- Antithrombin deficiency
- Protein C deficiency
- Protein S deficiency
- Factor V Leiden mutation (Factor V-Arg506Gln)
- Prothrombin gene mutation (G→A transition at position 20210)
- Dysfibrinogenemias (rare)
Risk Factors—Mixed/Unknown

- Hyperhomocysteinemia
- High levels of factor VIII
- Acquired Protein C resistance in the absence of Factor V Leiden
- High levels of Factor IX, XI
Genetic Thrombophilic Defects Influence the Risk of a First Episode of Thrombosis
## Risk of 1st VTE with Thrombophilias

<table>
<thead>
<tr>
<th>Thrombophilia</th>
<th>Relative risk increase for first VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>No thrombophilia</td>
<td>Reference group</td>
</tr>
<tr>
<td>II20210, hetero</td>
<td>3.8 (95% CI 3.0–4.9)</td>
</tr>
<tr>
<td>FVL, heterozygous</td>
<td>4.9 (95% CI 4.1–5.9)</td>
</tr>
<tr>
<td>II20210, homozygous</td>
<td>Insufficient data</td>
</tr>
<tr>
<td>FVL, homozygous</td>
<td>18 (95% CI 4.1–41)</td>
</tr>
<tr>
<td>Hetero II20210 PLUS hetero FVL</td>
<td>20 (95% CI 11.1–36.1)</td>
</tr>
<tr>
<td>Protein S deficiency</td>
<td>30.6 (95% CI 26.9–55.3)</td>
</tr>
<tr>
<td>Protein C deficiency</td>
<td>24.1 (95% CI 13.7–42.4)</td>
</tr>
<tr>
<td>Antithrombin deficiency</td>
<td>28.2 (95% CI 13.5–58.6)</td>
</tr>
</tbody>
</table>
Risk of **Recurrent** Venous Thromboembolism (VTE) in Thrombophilia Compared to VTE Without a Thrombophilic Defect

<table>
<thead>
<tr>
<th>Thrombophilic Defect</th>
<th>Rel. Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithrombin, protein C, or protein S deficiency</td>
<td>2.5</td>
</tr>
<tr>
<td>Factor V Leiden mutation</td>
<td>1.4</td>
</tr>
<tr>
<td>Prothrombin 20210A mutation</td>
<td>1.4</td>
</tr>
<tr>
<td>Elevated plasma Factor VIII</td>
<td>6.7 (above the 90th percentile)</td>
</tr>
<tr>
<td>Mild hyperhomocysteinemia</td>
<td>2.6 – 3.1</td>
</tr>
<tr>
<td>Antiphospholipid antibodies</td>
<td>2 – 9</td>
</tr>
</tbody>
</table>

Other Predictors for Recurrent VTE

- Idiopathic VTE
- Residual DVT
- Elevated D-dimer levels
- Age
- Sex
Antiphospholipid Syndrome
Antiphospholipid Antibody Testing

I) Antibody test (ELISA)
   - anticardiolipin
   - anti-β2-glycoprotein I
   - antiphosphatidylserine
   - antiphosphatidylincholine
   - antiphosphatidylethanolamine

II) Functional test
   - lupus anticoagulant (inhibitor)

Antiphospholipid Antibodies

- Up to 10% of pts with APLA syndrome only positive for anti-β₂-GP I

- B₂-GP-I Ab may be more specific for APLA syndrome
- Not yet recommended that anti-β₂-GP-I Ab test replaces ACA

- IgG and IgM recommended (for ACA and anti-β₂-GP-I Ab);
  - if neg: test for IgA.

- "Testing for IgA Abs is NOT recommended"
Updated **Sapporo Criteria** for APS (2006):

- **Clinical criteria:**
  - Vascular thrombosis
  - Pregnancy morbidity

- **Laboratory criteria**:  
  - Anticardiolipin antibodies (IgG or IgM)  
    (medium or high titer: >40 GPL/MPL or >99th percentile)  
  - Anti-β₂-glycoprotein I antibodies (IgG or IgM) (>99th percentile)  
  - LA

*2 or more occasions, >12 wks apart.

Antiphospholipid Syndrome: Practical Points

- “APLA syndrome”: question the diagnosis
- ≥ moderately high titers of ACA (≥40 U/mL)
- Include anti-β₂-GP-I antibody testing
- Test outside the acute event
- Repeat APLA testing (3 months apart)
- Know the LA tests and their interpretation

- Role of IgA antibodies unclear.
Antiphospholipid Syndrome—Treatment

• Patients with thrombosis- anticoagulation
  – INR 2-3
  – 1990’s studies suggested INR 3-4, disproven
• Anticoagulation is long-term—risk of thrombosis is 50% at 2 years after discontinuation
• Women with recurrent fetal loss and APS require LMW heparin and low-dose heparin during their pregnancies
Thrombophilia: How Do You Decide Who to Test?
Whom to Consider Testing?

1. DVT/PE, intermediate risk recurrence
2. VTE in unusual locations, unprovoked
3. Arterial thrombosis, unexplained
4. Pregnancy loss(es), unexplained
5. VTE: Patient requests testing
6. Family members (if “strong thrombophilia” in index pt)
Who should test? When to test?

1. Only the professional knowledgeable about the 4Ps should test.
   * Patient selection
   * Pretest counseling
   * Proper lab test interpretation
   * Provision of education and advice
   

2. Do not test while patient is on an anticoagulant.
3. Do not test during acute thrombotic episode.
4. Do not test a hospitalized patient.
## Stratification of Potentially Thrombophilic Patients

<table>
<thead>
<tr>
<th>Clinical History</th>
<th>“Weakly”</th>
<th>“Strongly”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset &lt;50</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Recurrent thrombosis</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Positive family history</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>
What to test?

- Test for Factor V Leiden
  - Protein C Resistance Assay
- Genetic test for prothrombin gene mutation 20210A
- Functional assay of antithrombin
- Functional assay of protein C
- Functional assay of protein S
- Clotting test for lupus anticoagulant/ELISA for cardiolipin antibodies
- CBC, CD55/59 (PNH), JAK2
Whom NOT to test

Recommend *against* thrombophilia testing in pts with VTE associated with major transient risk factor.

Influence of anticoagulant on thrombophilia testing

<table>
<thead>
<tr>
<th>Test</th>
<th>Acute thrombosis</th>
<th>Unfractionated heparin</th>
<th>Low molecular weight heparin</th>
<th>Vitamin K antagonists</th>
<th>DOACs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor V Leiden genetic test</td>
<td>Reliable</td>
<td>Reliable</td>
<td>Reliable</td>
<td>Reliable</td>
<td>Reliable</td>
</tr>
<tr>
<td>APC resistance assay</td>
<td>Reliable&lt;sup&gt;a&lt;/sup&gt;</td>
<td>???&lt;sup&gt;a&lt;/sup&gt;</td>
<td>???&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Reliable&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Unreliable&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Prothrombin G20210A genetic test</td>
<td>Reliable</td>
<td>Reliable</td>
<td>Reliable</td>
<td>Relier</td>
<td>Reliable</td>
</tr>
<tr>
<td>Protein C activity</td>
<td>???&lt;sup&gt;f&lt;/sup&gt;</td>
<td>Reliable</td>
<td>Reliable</td>
<td>Low</td>
<td>Elevated&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Protein C antigen</td>
<td>???&lt;sup&gt;f&lt;/sup&gt;</td>
<td>Reliable</td>
<td>Reliable</td>
<td>Low</td>
<td>Elevated&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Protein S activity</td>
<td>May be low</td>
<td>Reliable</td>
<td>Reliable</td>
<td>Low</td>
<td>Elevated&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Protein S antigen</td>
<td>May be low</td>
<td>Reliable</td>
<td>Reliable</td>
<td>Low</td>
<td>Elevated&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Antithrombin activity</td>
<td>May be low</td>
<td>May be low</td>
<td>May be low</td>
<td>May be elevated&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Elevated&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Lupus anticoagulant</td>
<td>Accurate&lt;sup&gt;d&lt;/sup&gt;</td>
<td>??&lt;sup&gt;e&lt;/sup&gt;</td>
<td>???&lt;sup&gt;f&lt;/sup&gt;</td>
<td>False positive&lt;sup&gt;i&lt;/sup&gt;</td>
<td>Reliable</td>
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<tr>
<td>Anticardiolipin antibodies</td>
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<td>Reliable</td>
<td>Reliable</td>
<td>Reliable</td>
<td>Reliable</td>
</tr>
<tr>
<td>Anti-β&lt;sub&gt;2&lt;/sub&gt;-glycoprotein-I antibodies</td>
<td>Accurate&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Reliable</td>
<td>Reliable</td>
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<tr>
<td>Homocysteine</td>
<td>Reliable</td>
<td>Reliable</td>
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<td>Reliable</td>
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</tr>
</tbody>
</table>
Anticoagulation in Pregnancy Complications

“Whether anticoagulant therapy prevents recurrent miscarriage in women with inherited thrombophilia is controversial – inconsistent results from trials.”

[Middeldorp S. Hematology 2014; ASH Education Program:393-399]

ALIFE2

<table>
<thead>
<tr>
<th>Study information</th>
<th>Informatie voor patiënten</th>
<th>Participating hospitals</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAQ</td>
<td>Documents</td>
<td>Inclusions</td>
</tr>
</tbody>
</table>

Study information

ALIFE2 study: Anticoagulants for living fetuses in women with recurrent miscarriage and inherited thrombophilia

Objective

The primary objective of the ALIFE2 study is to evaluate the efficacy of low molecular weight heparin (LMWH) in women with recurrent miscarriage (RM) and inherited thrombophilia. Secondary objectives are to evaluate other possible effects of LMWH on adverse pregnancy outcome other than miscarriage (e.g. pre eclampsia, intrauterine growth restriction, HELLP syndrome, placental abruption, premature delivery, congenital malformations) as well as to evaluate the safety of LMWH in women with RM with inherited thrombophilia by registering complications such as haemorrhage.

[www.trialregister.nl, NTR3361]
Pregnancy Loss/Complications

• “Some asymptomatic women of fertile age”:
  • may choose ante- and postpartum VTE prophylaxis
  • may choose not to take hormonal contraceptives


• Benefit of testing and of LMWH treatment if thrombophilia found is unclear.
• Enroll patients into trials; or: non-evidence-based decision.
Contraceptive Options in Thrombophilia

- Estrogen combination pill
  - 3rd generation
  - 2nd generation

- Injectable progestins
  - Depot preparation
  - Rod

- Progestin pill (minipill)
- Progestin-releasing IUDs
- Non-hormonal methods

References:
## Management of Patients With Thrombophilia

<table>
<thead>
<tr>
<th>Risk Classification</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High Risk</strong></td>
<td>Indefinite Anticoagulation</td>
</tr>
<tr>
<td>2 or more spontaneous events</td>
<td></td>
</tr>
<tr>
<td>1 spontaneous life-threatening event (near-fatal pulmonary embolus, cerebral, mesenteric, portal vein thrombosis)</td>
<td></td>
</tr>
<tr>
<td>1 spontaneous event in association with antiphospholipid antibody syndrome, antithrombin deficiency, or more than 1 genetic defect</td>
<td></td>
</tr>
<tr>
<td><strong>Moderate Risk</strong></td>
<td>Vigorous prophylaxis in high-risk settings</td>
</tr>
<tr>
<td>1 event with a known provocative stimulus</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td></td>
</tr>
</tbody>
</table>
Thank you!!

Questions?