ACOI BOARD REVIEW
2014

CHERYL KOVALSKI, DO FACOI
ANEMIA

- Hemoglobin <13 grams
  or
- Hematocrit <39%
ANEMIA

MCV

RETICULOCYTE COUNT

Corrected retic ct :

>2%: blood loss or hemolysis

<2%: hypoproliferative process
ANEMIA

MICROCYTIC

Obtain and interpret iron studies

- Serum iron
- Total iron binding capacity (TIBC)
- Transferrin saturation
- Ferritin—correlates with total iron stores
  can be nml or inc if co-existent inflammation
IRON DEFICIENCY

- Most common nutritional problem in the world
- Absorbed in small bowel, enhanced by gastric acid
- Absorption inhibited by inflammation, phytates (bran) & tannins (tea)
CAUSES OF IRON DEFICIENCY

- Blood loss – most common etiology
- Decreased intake
- Increased utilization – EPO therapy, chronic hemolysis
- Malabsorption – gastrectomy, sprue
CAUSES OF IRON DEFICIENCY

- Other forms of iron loss:
  - Hemoglobinuria:
    - PNH, runners anemia
  - Pulmonary alveolar bleeding
CLINICAL MANIFESTATIONS OF IRON DEFICIENCY

- Impaired psychomotor development
- Fatigue, Irritability
- PICA
- Koilonychiae, Glossitis,
IRON DEFICIENCY LAB FINDINGS

- Low serum iron, increased TIBC
- % sat <20
MANAGEMENT OF IRON DEFICIENCY

- MUST LOOK FOR SOURCE OF BLEED:
  ie: GI, GU, Regular blood donor

- Replacement:

  1. Oral: Ferrous sulfate 325 mg TID until serum iron, % sat, and ferritin mid-range normal, 6-12 months
  2. IV
SIDEROBLASTIC ANEMIAS

DIVERSE GROUP OF DISORDERS OF RBC PRODUCTION CHARACTERIZED BY:

1. Defect involving incorporation of iron into heme molecule
2. Ringed sideroblasts in bone marrow
CLASSIFICATION OF SIDEROBLASTIC

- HEREDITARY
- ACQUIRED IDIOPATHIC – now considered one of the MDS categories
- REVERSIBLE – alcohol, INH, chloramphenicol
- LEAD POISONING – autonomic & motor neuropathy, abdominal pain
THERAPY OF SIDEROBLASTIC

- SUPPORTIVE
- PYRIDOXINE
- ALLO BMT
- EPO
THALASSESMIA

- Perhaps man’s most common genetic disorder
- Beta Thal – decreased synthesis of beta globin chain resulting in relative excess of alpha globin chains
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THALASSEMIA
THALASSEMIA

BIGGEST MISTAKE:
Treated with iron without benefit of iron studies
BETA THALASSEMIA: COMPLICATIONS

If transfusion dependent, best if managed in thalassemia center

- Pulmonary hypertension
- Thromboembolism
- Heart Disease
- Endocrinopathies
ALPHA THALASSEMIA

- SCREENING: in populations at high risk for Hb Bart’s or hydrops fetalis
- Hg H Disease: Regular medical follow-up
- Diagnosis of the very mild alpha thalassemias, carrier & trait is important only for counseling and avoiding misguided treatments like iron
- Diagnosed by Alpha Thal gene probe
NORMOCHROMIC NORMOCYTIC ANEMIA

ANEMIA OF CHRONIC DISEASE

Hypoproliferative anemia

- Decreased red cell survival
- Impaired EPO production
- Impaired marrow response to EPO
- Impaired mobilization of iron
ANEMIA OF CHRONIC DISEASE

- Chronic nonhematologic conditions:
  - Infectious
  - Malignant
  - Inflammatory
  - Traumatic
ANEMIA OF CHRONIC DISEASE: DIAGNOSIS

- Exclude other etiologies of anemia
- Confirm hypoproliferative anemia
- Low serum iron despite increased iron stores in bone marrow & macrophages
ANEMIA OF CHRONIC DISEASE: THERAPY

- Most are self-limiting and need no specific treatment
- Treat the underlying disorder
- Correct any coexistent deficiency
- Selected patients may benefit from EPO
MACROCYTIC ANEMIA

Characterized by abnormal nuclear maturation of red cell precursors

- B12 Deficiency
- Folic Acid Deficiency
- Chemotherapy
- MDS
- Monoclonal protein
B12 ABSORPTION

- STOMACH: Acid, pepsin
  - Parietal cells
  - Intrinsic factor

- DUODENUM

- TERMINAL ILEUM
CAUSES OF B12 DEFICIENCY

- Dietary lack
- Inadequate proteolysis of B12
  - H2 Blockers, PPIs
- Deficiency of intrinsic factor
  - Gastrectomy, H2 Blockers
  - Pernicious Anemia
CAUSES OF B12 DEFICIENCY

- Metformin
- Pancreatic insufficiency
- Blind loop
- Diphyllobothrium latum
- Intestinal malabsorption
- Congenital disorders
- Nitrous Oxide inhalation
- Infections: HIV, H. pylori
SYMPTOMS OF B12 DEFICIENCY

- Brain and cranial nerves—dementia, personality changes, psychiatric disorders, disturbances in taste & smell, optic nerve abnormalities

- Peripheral neuropathy—paresthesias, sensory disturbances, diminished vibration and position sense
SYMPTOMS OF B12 DEFICIENCY

- Autonomic dysfunction
- Myelopathy affecting:
  - posterior columns: acroparesthesias, sensory disturbances, incoordination, ataxia, diminished vibration, position
  - lateral columns: weakness, spasticity
DIAGNOSIS

- Serum B12 level <300 is standard diagnostic test but may not accurately reflect true tissue levels
- Hyperlobated WBCs
B 12 DEFICIENCY

- Methylmalonic acid and homocysteine levels elevated
- Antibody testing to diagnose PA:
  - anti-parietal cell ab
  - anti-intrinsic factor ab
TREATMENT

- Oral - becoming the replacement mode of choice; includes SL
- IM or SQ
- Nasal, expensive
- Prophylactic for gastric or ileal resection
CAUSES OF FOLATE DEFICIENCY

- Dietary deficiency, can evolve in months
- Increased requirements
- Intestinal malabsorption
- Drugs that interfere with folate metabolism
DIAGNOSIS OF FOLATE DEFICIENCY

- **SERUM FOLATE**
  - May normalize after 1 meal
  - May be low normal with true folate deficiency

- **RBC FOLATE**
  - Normal or borderline in 60% pregnant pts
  - and 30% alcoholics with true folate deficiency
Folic acid 1 mg po daily is usually adequate

- Maintenance Rx: depends on underlying disorder

- Prophylactic Rx: Pregnancy, prematurity, hemolysis, dialysis
HEMOLYTIC ANEMIA

PREMATURE DESTRUCTION OF RBC’S

Occurs by 2 different mechanisms

- Extra vascular hemolysis: RBCs prematurely removed from circulation by liver or spleen
- Intravascular hemolysis: RBCs lyse in the circulation
HEMOLYTIC ANEMIA

2 MAIN CAUSES

- Intrinsic RBC defects (inherited)
- Extra-corpuscular causes (acquired)
HEMOLYTIC ANEMIA

HEREDITARY HEMOLYTIC DISORDERS

- RBC Enzyme Defects
- RBC Membrane Defects
- Hemoglobinopathies
- Thalassemias
HEMOLYTIC ANEMIAS

- ACQUIRED HEMOLYTIC DISORDERS
  - Immune Hemolytic Anemias
  - Splenomegaly
  - Microangiopathic Hemolytic Anemia
  - PNH
  - Direct toxic effect (malaria, clostridia)
  - Spur Cell Anemia
DIAGNOSIS OF HEMOLYTIC ANEMIA

- Corrected Retic ct >2%
- Elevated indirect bilirubin
- Elevated LDH
- Haptoglobin low or absent
- Urine hemosiderin: present in intravascular hemolysis only
- Urine hemoglobin: present in severe intravascular hemolysis—urine dipstick positive for blood but no RBCs seen on micro
AUTOIMMUNE HEMOLYTIC ANEMIA
DIAGNOSIS: Direct Antiglobulin Test-Coombs

- Useful in diagnosing immune hemolytic anemia where there is antibody coating a patient's red blood cells

- Done by mixing patients erythrocytes with antihuman globulin containing antibody to IgG and C3

- Test positive if agglutination occurs
DIAGNOSIS:
Indirect antiglobulin test

- Useful to detect antibodies present in patient’s serum
- Helpful in detecting alloantibodies induced by prior transfusion or by fetal transfer to mother
**Direct Antiglobulin Test**

1. Antibodies in serum
2. Reagent erythrocyte
3. In vivo antibody coating of erythrocytes
4. Anti-IgG AHG reagent added after erythrocytes are washed
5. AHG reagent causes IgG-coated erythrocytes to agglutinate

**Indirect Antiglobulin Test**

1. Antibodies in serum
2. Reagent erythrocyte
3. In vivo antibody coating of erythrocytes
IMMUNE HEMOLYTIC ANEMIA

- 40–50% Idiopathic
- Induced by binding of antibody &/or complement to RBC membrane
- Caused by autoantibody directed against patients own RBCs or acquired alloantibody directed against transfused RBCs
- Coombs is only test that provides definitive evidence of immune hemolysis.
IMMUNE HEMOLYTIC ANEMIA

Warm-antibody Autoimmune Hemolytic Anemia

- Autoantibodies optimally reactive at 37°C
- IgG present on RBC surface
- May also have C3
- Most cases idiopathic
- Can be a complication of underlying disease
IMMUNE HEMOLYTIC ANEMIA

Warm Antibody Related Diseases

- Chronic lymphocytic leukemia
- Collagen vascular diseases
- Ulcerative colitis
- Congenital immunodeficiency
TREATMENT OF WARM-REACTIVE AIHA

- Prednisone 1 mg/kg/d
- Folic acid
- Splenectomy if refractory to prednisone
- Immunosuppressive drugs
- IVIg, Rituximab
- TRANSFUSE LEAST INCOMPATIBLE BLOOD
IMMUNE HEMOLYTIC ANEMIA

- Cold Antibody
  - Cold Agglutinin disease
    - idiopathic
    - chronic lymphocytic anemia
    - mycoplasma infection
    - infectious mononucleosis
  - Paroxysmal Cold Hemoglobinuria
TREATMENT OF COLD ANTIBODY AIHA

- Avoid cold exposure
- Folic acid therapy
- Treatment of underlying disorder
- Immunosuppressive agents
- Splenectomy of little value
- Rituximab
- Plasmapheresis
TREATMENT OF COLD ANTIBODY AIHA

- Transfusions of packed red blood cells:
  - Compatibility testing should be done at 37°C
  - Transfuse warm blood recommended but lacks proven efficacy
PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH)

- Acquired clonal stem cell disorder—in which a mutation of PIG-A gene causes defective production of GPI Anchor Protein
- Only a portion of RBCs affected
- Defective platelets & WBCS
- Increased sensitivity of RBCS to complement mediated hemolysis
PNH: CLINICAL PRESENTATION

- May remain undiagnosed for a long period of time

- History of unexplained, chronic hemolysis, hemoglobinuria, pancytopenia & thrombotic events

- Intravascular hemolysis

- Absent haptoglobin, increased LDH, hemoglobinuria, & hemosidinuria
PNH: CLINICAL PRESENTATION

- Can be found in the setting of another specified bone marrow disorder:
  - Aplastic Anemia
  - Refractory Anemia-MDS

- Can be subclinical (no hemolysis)
PNH: DIAGNOSIS

- Flow cytometry using antibodies directed against GPI-AP (glucosyl phosphatidylinositol-anchored proteins)
PNH: TREATMENT

- Folic acid
- Corticosteroids
- RBC Transfusions
- Iron (can precipitate hemolysis)
- Anticoagulation with warfarin
- Eculizumab (Solaris)
- Stem cell transplant
NONIMMUNE HEMOLYTIC ANEMIA

- Inherited nonimmune hemolytic anemia

RBC membrane disorders:

- Hereditary spherocytosis
- Hereditary elliptocytosis
- Hereditary stomatocytosis
- G6PD deficiency
HEREDITARY SPHEROCYTOSIS

- Molecular defect in one or more of the proteins in the red blood cell cytoskeleton causing the cell to contract into a sphere shape. It has a high osmotic fragility and more prone to physical degradation.

- Osmotic fragility test
HEREDITARY SPHEROCYTOSIS

- Mild to severe hemolytic anemia
- Spherocytes on peripheral smear
- Increased osmotic fragility
- Negative direct antiglobulin test
- Aplastic crisis with viral infection
- Splenectomy is treatment of choice in severe cases
HEREDITARY SPHEROCYTOSIS
G6PD DEFICIENCY

- MOST COMMON ENZYME DEFICIENCY WORLDWIDE.
- DIFFERENT GENE MUTATIONS CAUSE DIFFERENT LEVELS OF ENZYME DEFICIENCY AND DISEASE MANIFESTATIONS
G6PD DEFICIENCY

- G6PD helps protect hemoglobin from oxidation upon exposure to a drug or toxin that results in the generation of free radicals

- Drugs associated with hemolysis: primaquine, sulfa, dapsone, nitrofurantoin

- Fava beans will cause acute hemolysis shortly after ingestion
G6PD DEFICIENCY

- Acute hemolysis lasts 2–4 days, self-limiting, rarely requiring transfusion
- Infections and diabetic ketoacidosis can trigger hemolysis
- “Bite” cells on peripheral smear and Heinz bodies (precipitated hemoglobin)
- Diagnosis made by level of G6PD, but may be normal in active hemolysis
HEINZ BODIES & BITE CELLS
HEMOGLOBINOPATHIES

- SICKLE CELL DISEASE—the bone marrow makes sickle shaped red blood cells due to qualitative defects of globulin chain synthesis
  - HbS > 50%
  - Multiple genotypes and phenotypes
  - Sickle Cell Trait is not a disease
A Normal red blood cells

- Normal red blood cell (RBC)
- RBCs flow freely within blood vessel

B Abnormal, sickled, red blood cells (sickle cells)

- Sickle cells blocking blood flow
- Sticky sickle cells
- Abnormal hemoglobin form strands that cause sickle shape
SICKLE CELL ANEMIA: COMPLICATIONS

- Painful episode—most common
- Acute chest syndrome
- Stroke (10% children)
- Osteonecrosis
- Proliferative retinopathy
- Venoocclusive complications
- Infectious complications
SICKLE CELL ANEMIA: COMPLICATIONS

- HEMOLYSIS
  - Gallstones
  - Aplastic crisis
  - Osteopenia
  - Anemia
  - Nutritional deficiencies
SICKLE CELL ANEMIA: TREATMENT

- General medical care
- Pain management:
  - AVOID MEPERIDINE!!
- Hydroxyurea
- Transfusion
- Stem cell transplant
APLASTIC ANEMIA

- Pure red cell aplasia
- Bicytopenia, pancytopenia
- Bone marrow failure
RED CELL APLASIA: CLASSIFICATION

- Congenital
  - Diamond Blackfan Syndrome

- Acquired
  - Idiopathic
  - Secondary
RED CELL APLASIA: CLASSIFICATION

Secondary
- Hematologic malignancies
- Solid tumors
- Immunologic disorders
- Infectious diseases
- Drugs
APLASTIC ANEMIA: DIAGNOSIS

- BONE MARROW BIOPSY: 4–5 cores showing cellularity of <30%
APLASTIC ANEMIA: TREATMENT

- Antithymocyte globulin (ATG) & Cyclosporin (CSA)
- Transplant: Cord blood
  - Stem cell
THROMBOCYTOPENIA

AND OTHER PLATELET DISORDERS
Etiologies of Thrombocytopenia

- Decreased Production
- Increased Consumption
- Destruction
- Dilution
- Sequestration
THROMBOCYTOPENIA IN HOSPITALIZED PATIENTS

- Sepsis
- Drugs: Heparin
  - H2 Antagonists
  - Antibiotics
- Dilutional
- DIC
HEPARIN INDUCED THROMBOCYTOPENIA

• A fall in platelet count to <150,000 five or more days after starting heparin
• With or without thrombotic complications
• Other causes have been excluded
• +/- positive serological test for HIT
RISK OF HIT

- Unfractionated heparin  2.6%
- Low molecular weight heparin  0.2%
- Fondaparinux  <0.2%
TREATMENT OF HIT

• STOP HEPARIN including LMW heparin
• Hirudin: Thrombin inhibitor
  Renal excretion
• Argatroban: Thrombin inhibitor
  Hepatic clearance
• Fondaparinux
• DO NOT USE WARFARIN ACUTELY!!- limb gangrene
DISSEMINATED INTRAVASCULAR COAGULATION

• Process initiated by infection, OB complications, tissue injury, burns, some malignancies

• Diagnosis made by concomitant decline in platelet count and fibrinogen level

• Bleeding more common than thrombosis
DIC TREATMENT

- Treat underlying disorder
- Platelet, cryoprecipitate and FFP transfusions if bleeding and very low levels of platelets or fibrinogen
- Heparin indicated if thrombotic complications
THROMBOTIC THROMBOCYTOPENIC PURPURA

- Due to auto antibodies against plasma protease ADAMTS13 that cleaves ultra large vWF multimers
- Congenital deficiency of ADAMTS13
Blood Flow

GPIIb

VWF

Vessel Wall

ADAMTS13

Normal Hemostasis

No ADAMTS13

TTP

bloodjournal.hematologylibrary.org
TTP ETIOLOGY

• Primary, congenital deficiency of ADAMTS13, no disease association
• Primary, but triggered by a disease or disorder: vaccination, viral infections (Coxsackie B, Echo, Epstein-Barr), pregnancy
TTP ETIOLOGY

• Secondary: Drug associated (quinidine, ticlopidine), HIV, collagen vascular disease
• Chemotherapy-mitomycin
• Bone marrow transplant
TTP DIAGNOSIS

- Thrombocytopenia 100%
- Schistocytic Hemolytic Anemia 100%
- Neurological Events 65%
- Renal impairment 50%
- Fever 25%
TTP TREATMENT

- Mild (no symptoms): Prednisone 200 mg daily
- Deterioration: Plasma exchange
  Plasma infusions
HEMOLYTIC-UREMIC SYNDROME

- Distinct syndrome
  - Distinct pathogenesis-no deficiency of vWD cleaving metalloproteinase
  - Distinct etiology-E. coli gastroenteritis

E. Coli 0157:H7 is an emerging infectious disease caused by transfer of a gene from Shigella dysenteriae to a strain of enteropathogenic E. coli
TREATMENT OF HUS

• Supportive in children

• Plasma infusion/pheresis for severe HUS and in adults

• Eculizumab (Solaris)
THROMBOCYTOPENIA IN OUTPATIENTS

• ITP
• Hypersplenism
• Secondary: SLE, Lymphoproliferative Disorders
• Aplasia, Myelodysplasia
PRIMARY IMMUNE THROMBOCYTOPENIC PURPURA

- Thrombocytopenia with normal CBC & blood smear
- No congenital disorders, MDS or carcinomatosis
- No drugs
- No viral infection
- No SLE or other autoimmune disease
- No lymphoproliferative disease
ITP PATHOPHYSIOLOGY

- Platelet associated antibodies
- Rapid platelet destruction
- Suppression of thrombopoiesis
- Antibodies to megakaryocyte antigens
ITP DIAGNOSIS

- History & Physical
- CBC and peripheral smear exam
- HIV & HCV testing
- Bone marrow biopsy & PAIgG testing not necessary for classic presentation
ITP TREATMENT

• Treat if count < 30K
• Platelet < 50 K and significant mucous membrane bleeding or risk factors for bleed (PUD)
• Hospitalization for patients < 20K and significant mucous membrane bleeding &/or noncompliant
ITP TREATMENT

- Prednisone 1 mg/kg Q day
- Improvement usually in 3 days with maximum in 2 weeks
- Allows increased platelet production
- Reduces rate of platelet destruction
- Dexamethasone—good response rate but high relapse risk in 3 months
ITP TREATMENT

- IVIg
- Anti-D (WinRho)
- Splenectomy
- Vinca alkaloids
- Cyclophosphamide
- Rituximab
- Thrombopoietin agonists: N-plate, Promacta
PLATELET TRANSFUSION
PEARLS

• AVOID
• Current ARC recommendations:
  – Platelet count < 50K and bleeding
  – No bleeding, but platelet count < 5K, maybe
  – Dysfunctional platelets regardless of count and surgery required or patient bleeding
PLATELET TRANSFUSION
PEARLS

• Rule of thumb:
  – One unit single donor (pheresed) platelets
    = Six units random donor platelets

Good result would be an rise in the platelet count by 30,000 one hour after transfusion
INHERITED PLATELET DISORDERS

• Glanzmann’s thrombasthenia
• Bernard-Soulier
• Gray platelet syndrome
• Storage pool disease
INHERITED PLATELET DISORDERS

- Bleeding present at birth or can present later in life
- Manifestations include easy bruising, gingival bleeding, epistaxis, menorrhagia
- Bleeding time is prolonged in all these disorders
ACQUIRED PLATELET DISORDERS

• Result from medications, medical disorders, or hematologic disorders
HEMOSTASIS

PHYSIOLOGICAL BLOOD CLOTTING IN RESPONSE TO INJURY OR LEAK
DISORDERS OF HEMOSTASIS

• HEMOPHILIA

• VON WILLEBRAND DISEASE
HEMOPHILIA

• A DEFECT IN THE THROMBIN PROPAGATION PHASE OF COAGULATION
HEMOPHILIA A OR B
DIAGNOSIS

- BLEEDING TIME
  - Normal

- PT
  - Normal

- APTT
  - Prolonged

- FVIII:c or FIX:c
  - <1% = severe
  - 1-5% = moderate
  - 6-30% = mild

- vWF:Ag
  - Normal

- vWF:Rco
  - Normal
HEMOPHILIA

Bleeding as a function of clinical severity

Concentration of factor %

50-100: None

25-50: Bleeding after severe trauma

6-25: Severe bleeding after surgery
      slight bleeding after minor trauma

1-5: Severe bleeding after slight trauma

<1: Spontaneous bleeding mainly in joints or muscles
HEMOPHILIA: CLINICAL FEATURES

• Muco-cutaneous bleed
• Hemarthrosis
• Muscle bleeds
• Intra-cranial bleed
• Post-dental bleed
• Post-surgical bleed
HEMOPHILIA TREATMENT

• Factor replacement
• DDAVP
• All patients should be cared for life long in a bleeding disorder clinic
ACQUIRED HEMOPHILIA
CHARACTERISTICS

• AGE: MOST >50

• BLEEDING PATTERN: More severe soft tissue bleed; hemarthrosis less common

• INHIBITOR

• UNDERLYING DISORDER: usually none, but can be seen post partum, autoimmune disease, malignancy, drug reaction
ACQUIRED HEMOPHILIA

• Major bleeding requiring transfusion: >75%
• Death due to bleeding: >15%
• Immediate Rx with appropriate activated factor products
• Long term: Attempt suppression of inhibitor
VON WILLEBRAND DISEASE

• Inherited bleeding disorder presenting with: muco-cutaneous bleeding:
  • nosebleeds, bleeding with dental work, heavy menses
• Autosomal Dominant
• Bleeding usually mild to moderate
VON WILLEBRAND DISEASE

• DIAGNOSIS:
  - FVIII LEVEL
  - VWF ANTIGEN
  - RISTOCETIN COFACTOR
  - PFA
  - RIPA
  - VWF MULTIMERS
VWD: TREATMENT

- DDAVP
- Factor VIII concentrates that contain vWF
- ANTIFIBRINOLYTICS (Amicar, thrombin w/gelfoam)
- Severe types should be cared for life long at a bleeding disorder center
THROMBOSIS

PATHOLOGICAL BLOOD CLOTTING
HYPERCOAGUABLE STATES

• ACQUIRED:
  Advancing age
  Prior thrombosis
  Immobilization
  Major surgery
  Malignancy
  Estrogens
  Antiphospholipid antibody syndrome
  Myeloproliferative disorders
  IBD
  HIT
  Prolonged air travel
HYPERCOAGUABLE STATES

• INHERITED
  Antithrombin III deficiency
  Protein C deficiency
  Protein S deficiency
  Factor V leiden
  Prothrombin gene mutation
  Dysfibrinogenemias
HYPERCOAGULABLE STATES

• MIXED/UNKNOWN
  Increased Factor VIII
  APC resistance in the absence of FVL
  Increased Factor IX
  Increased Factor XI
  Elevated homocysteine level no longer considered thrombogenic
HYPERCOAGUABLE STATES

Strongly Thrombophylic Clinical History
Age of onset <50
  Recurrent thrombosis
Positive family history of thrombosis, MI or CVA at young age
HYPERCOAGUALABLE WORKUP

- Prothrombin gene mutation
- Factor V Leiden
- Activated Protein C resistance
- Antithrombin III
- Protein C activity
- Protein S assay, total & free
- Lupus anticoagulant
- Anticardiolipin antibody
TREATMENT OF DVT/PE

• HEPARIN
  Unfractionated or LMW for 5 days

• WARFARIN
  Start day 1
  INR 2-3
  Treat 3-6 months
DURATION OF ANTICOAGULANT THERAPY

• First event with reversible or time limited risk factor:
  
  3-6 months, INR 2-3

• Unprovoked VTE, first or second event:
  
  6 months, INR 2-3, then consider indefinite anticoagulation, INR 2-3, weighing recurrence vs. bleeding risk
DURATION OF ANTICOAGULANT THERAPY

SPECIAL SITUATIONS: Consider indefinite anticoagulation after first event in the following cases:

- Cancer—until resolved (consider LMWH)
- Antiphospholipid antibody syndrome
- Antithrombin III deficiency
- Protein C or S deficiencies
- Multiple genetic defects
DURATION OF ANTICOAGULATION

Criteria for long term oral anticoagulation:
• No resolution of triggering risk factor
• Sites and severity of thrombosis
• Identification of a prothrombotic defect
• Family thrombotic history
• Bleeding risk
• Patient preference (life style, occupation) with understanding of risks vs. benefits