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- Education: 1977 graduate in Health Systems, Georgia Institute of Technology
- 1979 graduate of the Emory University PA Program
- 2006 graduate of the Career Masters in Physician Assistant at Emory
- Currently: Faculty member of the Emory PA Program, Advanced Didactic Co-Coordinator
- Awarded the Clinical Teacher of the Year Award by the graduating class of 1993, 2002 AAPA Paragon Teacher of the year award. 2007 SAAPA Presidents award, Course Director of the Behavioral Medicine and Professional issues courses for the Emory didactic PA students.

Heme Review

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Blood

- Blood has red cells (erythrocytes)
- White cells (leukocytes)
- Platelets (thrombocytes)

Blood Components

- Plasma 54%
- White cells and platelets 1%
- Red Cells 45%

White Blood Cells

- Fight infections
- Are increased in infections
- Move inside and outside of blood vessels
- Are made in the bone marrow

White Blood Cells

- WBC - White Blood Cells 4.5 - 11.0 K/uL
- Low = Leukopenia  High = Leukocytosis
- WBC Differential
  - Neutrophils - Segs  54 - 62%
  - Neutrophils - Bands  3 - 5%
  - Lymphocytes - Lymphs  25 - 33%
  - Monocytes - Monos  3 - 7%
  - Eosinophils - Eos  1 - 3%
  - Basophils - Basos  0 - 0.75%
  - Atypical Lymphs  0
Platelets
- Primary Hemostasis
- Help clotting cascade
- Made in the bone marrow

Red Blood Cells
- Carry oxygen from the lungs
- Carry carbon dioxide back to the lungs
- Normally live 120 days
- Contains the protein hemoglobin
- Made from iron, folic acid, vitamin B12
- Made in the bone marrow

Red Blood Cells
- Red cells look like doughnuts that are very flexible

Microscope View

Red Blood Cells - Shape
- Red cells travel through very narrow blood vessels

Red Blood Cells
- Red Cell Flow
Red Blood Cells

Oxygen

Hemoglobin, the main protein in red cells holds four oxygen molecules

Red Blood Cells - Adult Hemoglobin

Chromosome 16

Chromosome 11

Alpha  Alpha
Alpha  Alpha
Alpha  Alpha
Alpha  Alpha

Beta  Beta
Beta  Beta
Gamma  Gamma
Gamma  Gamma

97% = Hemoglobin A
1% = Hemoglobin F (Fetal)
2% = Hemoglobin A2

Red Blood Cells - Marrow

Red cells, white cells and platelets are made in the bone marrow

Red Blood Cells - Retics

- Reticulocytes, or Retics are young red cells just released from the bone marrow. The Retic count is the best indicator about how the marrow factory is doing.

Red Blood Cells - Recycled

- Red cells are recycled in the spleen and liver. The iron and protein are stored and bilirubin is released.

Red Blood Cells

Food with iron and vitamins is digested.

Red cells live 120 days in the circulation.

Red Blood Cells

Emory University Physician Assistant Program
**Hepcidin**

- Decreased levels increase iron absorption and release from cells – Erythropoetin, low iron
- Increased levels blocks absorption of Iron and cell release - inflammation IL6

**Erythropoietin**

- Made in the liver
- Erythropoietin is made by the kidney as a signal to the bone marrow to make more red cells

**The History**

- Weakness
- Tiredness - Fatigue
- Dyspnea
- Dizzy – non vertigo
- Palpitations
- New angina

**The History -2**

- History of melena, abdominal pain, Aspirin or non-steroidal anti-inflammatory agents (NSAIDs) use, past peptic ulcer disease, then consider GI bleeding, platelet dysfunction.
- In females the menstrual history quantifying the amount of bloodloss, or possible pregnancy should be obtained.
- History of pica or abnormal craving for ice, clay, starch...; dysphagia then consider iron deficiency.
- Poor diet, then consider iron or folate deficiency, and general malnutrition
- History of gastric surgery, distal paresthesias, gait problems - consider B12 deficiency
- History of alcohol abuse - consider folate deficiency or liver disease. If moonshine use or lead paint/pipe exposure, consider lead toxicity.

**The History -3**

- Family history of blood cell or bleeding disorder: consider Sickle Cell disease, G6PD, Thalassemia, Hemophilia, von Willebrand
- History of jaundice, transfusion, new medication, infection - consider hemolytic process
- History of weight loss, Cancer, HIV, rheumatoid arthritis, thyroid disease, renal disease - then consider secondary cause
- History of fever and chills, cough, dyspnea, then consider Infection.

**Physical Exam**
Sclera

Spoon Nails – Fe Def.

Glossitis and Chelosis – Fe and B12

Physical Exam

LAB- INITIAL SCREENING TESTS

CBC- Red Cell Measures
Red Cell Indices MCH, MCHC

- MCH - Mean Corpuscular Hemoglobin
  - 27 - 32 pg
  - Low = Hypochromic
  - High = Hyperchromic
- MCHC - Mean Corpuscular Hemoglobin Concentration
  - 30 - 36 gm/dl
  - Low = R/O Fe def.
  - High = Spherocytosis

Reticulocyte count

- Retic - Reticulocyte Count 0.5 - 1.5 %
  - Low in anemia = low marrow output
  - High = RBC loss

Corrected Retic Count

- Corrected Retic = Raw Retic
  - Percentage = Percentage X Pt's Hematocrit
- Corrected Retic = Raw Retic
  - Percentage = Percentage X Pt's Hemoglobin

- An example would be if the raw retic percentage reported on the CBC was 6% and the patient's hematocrit is 23 then:
  - The corrected retic percentage = 6% x 23/45 or 3%.
- The normal corrected reticulocyte percentage is 1 - 2%.
- With severe anemia and marked marrow response, other corrections may be necessary.

RBC Morphology

- Burr Cells
  - Uremia, Low K, artifact, Ca stomach, PUD
- Spur Cells
  - Post-splenectomy, Alcoholic liver disease
- Stomatocyte
  - Hereditary, Alcoholic liver disease
- Spherocyte
  - Hereditary, Immune hemolytic anemia, water dilution, post-transfusion
- Shistocyte - helmet
  - TTP, DIC, vasculitis, glomerulonephritis, heart valve, burns
- Elliptocyte - Ovalocyte
  - Hereditary, Thalassemia, Fe Def., Myelophthistic, megaloblastic anemias
- Sickle Cells
  - Sickle cell disease
- Target Cells
  - Thalassemia, iron Def., Lead Toxic
- Macrocyes
  - B12 of Folate Def.
- Parasites
  - Malaria, Babesiosis
**Diagnostic Pathway**

- >2 Increased Loss
- <2 Decreased Production
- Red Cell Indices MCV
  - >94 Macro
  - 80-94 Normo
  - <80 Micro
- Hemolysis:
  - Extracritic
  - Intracritic
- Coombs:
  - Positive
  - Negative
- Drug
- Warm Antibody
- Cold Antibody
- Coombs
- Membrane
- Hb
- Enzyme

**Microcytic**

- MICROCYTIC = "TICS"
  - T-Thalassemias
  - I-Iron Deficiency
  - C-Chronic Inflammation
  - S-Sideroblastic - lead, drug, or hereditary

**Microcytic Tests**

- TESTS TO ORDER:
  - Serum Iron
  - TIBC = Total Iron Binding Capacity = Transferrin binding sites for transporting iron
  - % Saturation = Transferrin saturation with Iron
  - Ferritin = Storage Iron
  - HBELP = Hemoglobin Electrophoresis
  - Lead level if exposed

**Thalassemia Syndromes.**

- Hereditary – Alpha or Beta chain
- Decrease Hemoglobin A
- Hemoglobin ELP and normal Iron are diagnostic
- Supportive therapy or BMT
- Target Cells
- Increased Red cell count

**Iron deficiency**

- Low Serum iron, Low Ferritin, High TIBC
- Find out why – GI bleed, menses, diet
- Treat FeSO4 300mg tid

**Chronic Inflammation**

- Block of normal iron stores transport to bone marrow factory
- Normal Ferritin, serum iron and TIBC are low with a low saturation
- 30% Microcytic, 70% Normocytic
- High Sed rate or c-reactive protein
- Treat inflammation – RA, SLE, HIV...
**Sideroblastic**
- Ring sideroblasts in bone marrow
- Serum iron is increased and TIBC normal resulting in a high saturation. Serum ferritin is increased
- Basophilic stippling
- Lead toxicity is suspect

**Normocytic Anemia**
- Normocytic = "NORMAL SIZE"
  - N-Normal Pregnancy
  - O-Over hydration
  - R-Renal Disease
  - M-Myelophthistic
  - A-Acute Blood Loss
  - L-Liver Disease
  - S - Systemic Infection
  - I-Inflammatory Block
  - Z-Zero Production - Aplastic anemia
  - E-Endocrine: Hypothyroid, hypoadrenal, hypoandrogen

**Normocytic Tests**
- Blood Urea Nitrogen (BUN), Creatinine, AST, Alkaline Phosphatase, Bilirubin, Erythrocyte Sedimentation Rate (ESR) or C-Reactive protein, Urinalysis, and Thyroid profile
- Bone Marrow Biopsy

**Macrocytic Anemia**
- Macrocytic = "BIG FAT RED CELLS"
  - B12 Malabsorption
  - I-Inherited
  - G-Gastrointestinal disease or surgery
  - F-Folic Acid Deficiency
  - A-Alcoholism
  - T-Thiamine responsive
  - R-Reticulocytes miscounted as large RBCs
  - E-Endocrine - hypothyroid
  - D-Dietary
  - C-Chemotherapeutic Drugs
  - E-Erythro Leukemia
  - L-Liver Disease
  - S-Splenectomy

**Macrocytic Tests**
- The peripheral blood changes include:
  - Anemia with decreased reticulocyte count, - Increased MCV
  - Neutropenia with hypersegmented
  - Neutrophils
  - Thrombocytopenia with large platelets.
- LABS to order:
  - B12, Serum Folate, RBC Folate
  - If all normal, consider TSH, and a Bone Marrow Bx.

**B12 Cobalamin Deficiency**
- Physical signs include edema, pallor, jaundice, smooth tongue, decreased vibratory and position sensation
- PPIs, Metformin block B12
- Hypersegmented polys
- Low B12
- Pernicious anemia - anti- intrinsic factor antibodies Schilling's test
- Rx - cobalamin 1000 mcg I.M monthly
- Rx – Oral 100mcg daily
- Rx – Nasal Spray.
**Folate Deficiency**

- **Causes**: liver disease, diet vitamin B12 deficiency, and drugs such as methotrexate, ethanol, and dilantin.
- **Lab**: low serum and RBC Folate
- **Rx**: Folate 1mg po qD

**Hemolytic Anemia**

- **H-Hemoglobinopathy**: sickle cell disease
- **E-Hemoglobinuria**: Paroxysmal Nocturnal Hemoglobinuria
- **M-Enzyme Deficiency**:
  - M-Antibodies - Immune attack
  - M-Enzyme Deficiency
  - M-Medication - drug induced: aldomet, INH
- **A-Antibodies**: Immune attack
- **L-Liver disease**: D.I.C., artificial heart valves
- **O-Ovalocytosis**: and in Hereditary Eclipses
- **G-G6PD Glucose-6-Phosphate Dehydrogenase Deficiency**
  - G-Infection: malaria, babesiosis
  - G-Splenic destruction in hypersplenism
- **I-Immune attack**
- **T-Transfusion**

**Hemolytic Signs**

1. Elevated reticulocyte count, with stable or falling hemoglobin.
2. Elevated indirect bilirubin -
3. Elevated serum lactate dehydrogenase (LDH)-
4. Decreased Haptoglobin levels - Haptoglobin binds hemoglobin released in the plasma from red cell breakdown.
5. Hemoglobinemia and hemoglobinuria
6. Erythroid hyperplasia in bone marrow
7. Abnormal Hemoglobin Electrophoresis

**Hemolytic Tests**

1. The direct antiglobulin (Coombs') test
   - Direct Coombs test looks for antibody on the red cells. The Indirect Coombs looks for antibody in the serum.
2. Hemoglobin electrophoresis
3. Heinz body stain
4. Osmotic fragility
5. Blood smear

**Hemoglobinopathy**

- **Sickle Cell Disease**: SS, SC, SD, SE, SOarab, S beta Thal
- **Newborn Screening or HbELP**
- **Daily Penicillin**: - birth -6yo
- **Hydroxyurea**: Prolongs life, prevents complications

**G6PD - Glucose - 6 - Phosphate Dehydrogenase Deficiency**

- **X linked genetic**
- **Precipitated by oxidant drugs**
- **Heinz body stain shows denatured Hb**
- **Avoid medications such as antimalarials, aspirin, sulfa drugs, and avoid eating fava beans.**
Parasites – Malaria - Babesiosis

Spherocytosis and Ovalocytosis

To Clot or Not Coagulopathies

Keep Blood in the Tubing

Clotting Process

Clotting system activated

- Intact and healthy endothelium
- Adequate platelets that work right
- Von Willebrand Factor (vWF)
- Clotting Factors

- Break in vessel wall – smooth muscle contracts
- Platelets with (vWF) stick to collagen and Activate
- More platelets are attracted
- Clotting Factors activate to form Fibrin
- Clot contracts

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Clot

- Red Cells, Platelets, and Fibrin

Platelets

- Made in the bone marrow
  - Thrombopoietin made in liver stimulates production
  - Fragments of megakaryocytes
  - No nucleus
  - 67% in circulation
  - 33% in spleen storage
  - Life 8 – 10 days

The Shape of Platelets

- Flowing Platelets
- Activated Platelets
- Aggregated - Active Platelets

Built in Clot Blockers and Busters

- Intrinsic Pathway – Inside the cut Endothelial Injury
  - Test = aPPT
  - XII to XII active
  - XI to XI active
  - IX to IX active
  - VIII to VIII active
  - Common Pathway
    - X to X active with V present
    - II Prothrombin to Thrombin
    - Fibrinogen to Fibrin
  - XIII to XIII active
  - Stabilizer to crosslink fibrin

- Extrinsic Pathway – Outside the cut in the plasma
  - Vitamin K - Liver dependent
  - Test = PT
  - VII to VII active
  - Common Pathway
    - X to X active
    - II Prothrombin to Thrombin
    - Fibrinogen to Fibrin

- Liver made Protein S
  - Protein C
  - Antithrombin III
  - Fibrin split products, D-Dimer
**Increased Clotting Presentation**
- Deep Vein Thromboplebitis (DVT)
- Calf swelling, pain
- Pulmonary Embolus (PE)
- Myocardial Infarction, Angina
- Stroke, or Transient Ischemic Attacks (TIA)
- High Risk – post operative, pregnancy, atrial fibrillation, congestive heart failure
- Elevated platelets (Over 900,000)

**Bleeding History**
- HX - History of melena, abdominal pain, Aspirin or non-steroidal anti-inflammatory agents (NSAIDs) use, past peptic ulcer disease, then consider GI bleeding, platelet dysfunction.
  - In females the menstrual history quantifying the amount of blood loss, or possible pregnancy should be obtained.
  - History of alcohol abuse - consider liver disease.
  - Family history of blood cell or bleeding disorder: consider Hemophilia, von Willebrand Disease

**Bleeding History**
- History of weight loss, Cancer, HIV, rheumatoid arthritis, thyroid disease, renal disease -then consider secondary cause.
  - History of fever and chills, cough, dyspnea, then consider Infection.
  - History of prolonged bleeding after dental extractions, epistaxis, gum bleeding, easy bruising, then consider low or dysfunctional platelets.
  - History of bleeding into joints, then consider hemophilia.
  - History of Lupus - Lupus anticoagulant

**Increased Bleeding Presentation**
- Bleeding gums
- Easy Bruising
- Prolonged Post-op Bleeding
- Prolonged Bleeding post dental work
- Petechiae or Purpura
- Increased Menstrual Bleeding
- Lab Finding of Low Platelets (under 50,000) or Abnormal PT, aPTT, abnormal platelet function
- G.I. Bleeding
- Elevated platelets (Over 900,000)
**Increased Clotting History**

- History of recurrent clots, PEs... consider protein S.C, or Antithrombin III deficient, Factor V Leiden, hyperhomocysteine, prothrombin 20210 mutation
- Pregnancy - Increased blood viscosity, fibrinogen and factor VIII. Post Partum - Hypercoaguable state
- Polycythemia vera - increased viscosity
- Prolonged travel or immobility

**Increased Clotting History**

- Smoking, Resent Surgery, Diabetes, Congestive Heart Failure, Cancer, Atrial Fibrillation are all high risk
- Autoimmune diseases such as systemic lupus erythematosis, and medications such as procainamide, chlorpromazine, and quinidine.
- Oral contraceptives - Estrogen

**Physical Exam**

- PHYSICAL EXAM
- GENERAL INSPECTION- clubbing in TB or lung cancer
- Skin- Hypothyroid, SLE, Bruises, lesions, petechiae or purpura.
- Weight - Loss in Cancer, HIV. Chronic disease
- VITAL SIGNS- Pulse: Tachycardia from increased cardiac output
- Respiration: Tachypnea from decreased oxygen transport
- BP: Orthostatic if volume depleted
- Temp: Fever in infections and drug or transfusion reactions,
- HEENT- Eye: Jaundice if hemolysis, pallor in palpebral conjunctiva

**Physical Exam 2**

- HEENT- Eye: Jaundice if hemolysis, pallor in palpebral conjunctiva
- LUNG- consider infection, lesion, rub
- CV - new murmer or CHF, Listen for Bruits
- ABDOMINAL- Liver/spleen size, masses, tenderness, surgical scars
- RECTAL- Stool guaiac,
- PELVIC/BREAST- Uterine abnormality, Pap smear, Breast nodule
- LYMPHNODES- consider lymphoma, leukemia, infection, connective tissue disease
- EXTR- Homan’s or calf tenderness/swelling

**Platelet Problems or Von Willebrand Disease (vWD)**

**Clotting Factor Disorders**

- Hemarthrosis
Vascular Wall Defects

Purpura

Tests to Order – Screen for Clotting ability

- CBC, WBC Differential, Cell Morphology
  - Platelet Count: 150,000 - 350,000 cu/mm. Bleeding can occur if < 50,000 or > 900,000 Clotting too much
  - Chem Profile (Hepatic profile, Indirect Bili in hemolysis, Renal)
  - PT - Prothrombin Time: +/+ 2 of control = 11 - 16 sec. Extrinsic system monitor for coumadin therapy. INR is International Normalization Ratio, 1 is normal, 2 - 3 for Coumadin Therapy, 2.5 - 3.5 if heart valve
  - aPTT - activated Partial Thromboplastin Time: 25 - 38 sec. Intrinsic system. Used to monitor Heparin therapy. (if abnormal do Factor analysis)

Tests – Bleeding too much

- Bleeding Time - (normal 3-8 minutes) is a measure of platelet function and an intact coagulation cascade.
- Thrombin Time, Reptilase Time
- Platelet Function Analysis (PFA)
- Platelet Aggregometry
- Von Willebrand Antigen Measurement
- Ristocetin Cofactor Activity (von Willebrand Activity)
- Factor VIII Activity
- Von Willebrand Multimer Analysis

Tests – Clotting too much

- Protein S, C, antithrombin III assay,
- Factor V Leiden assay
- Fasting homocysteine level
- Lupus anticoagulant
- Anticardiolipin antibodies
- Prothrombin 20210 mutation test
- Fibrinogen level
- HIT Assay

Tests – Is Clotting going on

- D-Dimer elevation
- Fibrin Split products
- Peripheral smear may show shistocytes (helmet cells)

Differential Diagnosis – Bleeding too much

- C - Cirrhosis/Liver Disease and Coumadin
- A - Aspirin and other drugs NSAIDs
- L - Leukemia, Lupus anticoagulant
- F - Factor Deficiency - Hemophilia
- D - Disseminated Intravascular Coagulation
- I - Idiopathic Thrombocytopenic Purpura
- P - Platelet Deficiency (TTP, HUS, DIC, Heparin- HIT) or Platelet Dysfunction (vWD)
- S - Scurvy, Vitamin C Deficiency
Von Willebrand Disease

- Most common inherited bleeding disorder
- Found in approximately 1% of the population
- Most individuals are asymptomatic unless a significant bleeding event occurs
- Blood Group O individuals have significantly lower vWF than other groups (30% lower)
- vWF stabilizes Factor VIII so any decrease in vWF will increase aPTT and platelet function analysis will be abnormal

Hemophilia

- US 13,320 cases of hemophilia A (VIII)
- and 3,640 cases of hemophilia B (IX).
- prolonged aPTT with a normal PT
- Bleeding into joints
- Treat with Recombinant Factor replacement (No plasma exposure)

Liver Disease

- The liver is THE site for coagulation factor synthesis (except Factor VIII)
- Liver failure leads to multifactorial coagulopathy
- Decreased coagulation factors
- Decreased anti-coagulation factors
- Decreased fibrinogen
- Decreased platelets
- Increased D-dimers (interfere with clot formation)
- Bleeding from liver failure is a major cause morbidity and mortality
- Give Vitamin K

Clotting too much

- Clotting too much - Pulmonary Embolus, Deep Vein Thrombophlebitis, Stroke, Myocardial Infarction

Virchow's Triad

- Stasis
- Clot
- Hyper-coagulable
- Vascular Injury
Differential Diagnosis - Hycoagulability

- The mnemonic is: 5 Ps HAD CAUSED CLOTS
- P - Pregnancy - Increased blood viscosity, fibrinogen and factor VIII, Post Partum - Hypercoaguable state
- P - Prothrombin 20210 mutation, Protein S, C, deficient - Inherited
- P - Polycythemia vera - Increased viscosity
- P - Paroxysmal Nocturnal Hemoglobinuria
- S - Smoking

Heparin-induced thrombocytopenia (HIT)

- Due to an antibody against heparin
- Occurs in 1-3% of adult patients receiving heparin for 1 week or more. Heparin binds to platelet factor 4 (PF4), forming a highly reactive antigenic complex on the surface of platelets
- An unexpected fall in platelet count occurring 4-14 days after heparin exposure
- Platelet count usually falls by 50%
- Mean platelet count 60,000 – 100,000/uL
- Platelets become activated and induce clotting
- Associated with thrombosis - 10-30% develop arterial or venous thromboses (usually DVTs or PEs)
- Of those forming a clot, 30% will die or require amputation
- Platelet counts should be monitored while patient is on heparin therapy
- HIT Assay

Drug Clot Busters tPA – reteplase, alteplase, tenecteplase

Intrinsic Pathway – Inside the cut Endothelial Injury
Test = aPTT
XII to XII active
XI to XI active
IX to IX active
VIII to VIII active

Extrinsic Pathway – outside the cut in the plasma – Tissue Thromboplastin
Test = PT
VII to VII active

Common Pathway
X to X active with V present
II Prothrombin to Thrombin
Fibrinogen to Fibrin

Plasminogen via tPA to Plasmin
Fibrin split products, D-Dimer

Who ya gonna Call?

Clot Busters
tPA (tissue Plasminogen Activator)
**Heparin**

Intrinsic Pathway – Inside the cut Endothelial Injury

- XII to XII active
- XI to XI active
- IX to IX active
- VIII to VIII active

Extrinsic Pathway – outside the cut in the plasma – Tissue Thromboplastin

- XII to XII active
- XI to XI active
- IX to IX active
- VIII to VIII active

Common Pathway

- X to X active with V present
- II Prothrombin to Thrombin
- Fibrinogen to Fibrin

Protamine reverses Heparin

LMW Heparin
- dalteparin – (Fragmin)
- tinzaparin – (Innohep, Logparin)
- enoxaparin – (Lovenox, Oxenax)

Factor Xa Inhibitor
- fondaparinux – (Arrixtra) direct blocker, non Heparin

LMW Heparin
- Danaparoid
- Orgaran

Antithrombin III

**Thrombin Inhibitors**

Intrinsic Pathway – Inside the cut Endothelial Injury

- XII to XII active
- XI to XI active
- IX to IX active
- VIII to VIII active

Extrinsic Pathway – outside the cut in the plasma

- XII to XII active
- XI to XI active
- IX to IX active
- VIII to VIII active

Common Pathway

- X to X active with V present
- II Prothrombin to Thrombin
- Fibrinogen to Fibrin

Antithrombin III

LMW Heparin
- Danaparoid
- Orgaran

**Coumadin**

Intrinsic Pathway – Inside the cut Endothelial Injury

- XII to XII active
- XI to XI active
- IX to IX active
- VIII to VIII active

Extrinsic Pathway – outside the cut in the plasma

- XII to XII active
- XI to XI active
- IX to IX active
- VIII to VIII active

Common Pathway

- X to X active with V present
- II Prothrombin to Thrombin
- Fibrinogen to Fibrin

Reverse with Vitamin K

Coumadin blocks the liver – Vitamin K dependent factors

Vitamin K - Liver dependant

Test = PT

VII to VII active + III Tissue factor

**New Oral Factor Xa inhibitors**

Intrinsic Pathway – Inside the cut Endothelial Injury

- XII to XII active
- XI to XI active
- IX to IX active
- VIII to VIII active

Extrinsic Pathway – outside the cut in the plasma

- XII to XII active
- XI to XI active
- IX to IX active
- VIII to VIII active

Common Pathway

- X to X active with V present
- II Prothrombin to Thrombin
- Fibrinogen to Fibrin

May replace Coumadin with fewer side effects. All 3 are in extensive clinical trials now

Apixaban
- Dabigatran
- Rivaroxaban

May replace Coumadin with fewer side effects now. All 3 are in extensive clinical trials now

LMWH blocks the liver – Vitamin K dependent factors

**Platelet Activation Blockers**

- Collagen
- Thrombin, TXA2
- Arachidonic acid
- TXA2 and ADP released
- Endothelium

- Aspirin, NSAIDS
- Cyclooxygenase COX
- ADP receptor
- TP receptor
- Unstable Plaque (Plax)
- Leukotrienes (Persantine and Aggrenox - ASA combo)
- Increased CAMP inhibits adhesion
- Inhibits vWF
- abciximab (ReoPro), tirofiban (Aggrastat), and eptifibatide (Integrelin)

Arachidonic acid

Collagen

Aspirin, NSAIDS

Endothelium

Von Willborn Factor VWF

Ticagrelor

Prasugrel

Clopidogrel

(Plavix)

Dipyridamole (Persantine and Aggrenox – ASA combo)

Acetylsalicylic acid (ASA)

Endothelium

Increased CAMP inhibits adhesion

Ticlopidine (Persantine and Aggrenox – ASA combo)

abciximab (ReoPro), tirofiban (Aggrastat), and eptifibatide (Integrelin)

Arachidonic acid

Collagen

Aspirin, NSAIDS

Endothelium

Von Willborn Factor VWF

Ticagrelor

Prasugrel

Clopidogrel

(Plavix)

Dipyridamole (Persantine and Aggrenox – ASA combo)

Acetylsalicylic acid (ASA)

Endothelium
### Anti-Clotting Therapy

- **To block Platelets** (MI and Stroke prevention)
- Antiplatelet agents – aspirin or clopidogrel, or aspirin + dipyridamole
- **Stop Clotting and Clot prevention** - (DVT, PE, MI, AFib, Genetic....)
- Heparin (Reversed with Protamine)
- LMW Heparin and factor Xa blockers
- Coumadin (Reversed with vitamin K)
- Thrombin inhibitors
- **To Bust Clots** (PE, MI, Thrombotic Stroke)

### Lymphadenopathy

- **L** - Lymphoma, Leukemia
- **Y** - Yersinia Pestis (Plague)
- **M** - Mononucleosis or CMV
- **P** - Parasite - Toxoplasmosis
- **H** - Hodgkins Disease or HIV infection
- **N** - Neoplasm or metastasis
- **D** - Obvious local infection or inflammation
- Other systemic infections: Hepatitis B, Rubella, Tularemia, Cat scratch
- **D-Drug** - Procainamide (Pronestyl), Phenytoin (Dilantin)
- **E-Endocrine** - Addison's, Hypothyroid
- **S-Syphilis**: -SLE/Rheumatoid arthritis
- -Serum sickness
- -Sarcoid

### Mononucleosis

**Mono - continued**

- **Hodgkins Disease**
- **Hodgkins – Reed Sternberg cells**
Multiple Myeloma

- Symptoms and Signs: Itching, Bone pain, weakness, anemia, lytic bone lesions, increased protein, M-Spike, Bence Jones protein in urine

Primary - Polycythemia vera

- Sx: Pruritis HA, Dizziness, vertigo, visual disturbance, tinnitus
- PE: Rubor, BP increased, splenomegaly or hepatomegally
- Lab: HCT >55 Increased platelets and WBC count
- RX: Phlebotomy, Hydroxyurea

Secondary Polycythemia

- Increase erythropoietin due to hypoxia (COPD, smokers, high altitude), tumors of kidney, ovary, liver, brain, drugs: steroids, androgen, dehydration, burns
- PE: No hepatosplenomegaly unless tumor

Leukemia and Lymphoma

- ALL: Acute Lymphocytic Leukemia (Usually in Children)
- AML: Acute Myelogenous Leukemia
- CLL: Chronic Lymphocytic Leukemia
- CML: Chronic Myelogenous Leukemia
- Lymphomas, Hodgkins

- HX: Fatigue, anorexia, wt loss, fever, bone pain, headaches, lymphadenopathy, non-healing infections, thrush, bleeding
- PE: Pallor, gingival hyperplasia, Candida infections, lymphadenopathy, hepatosplenomegaly, lung infiltrates, bleeding, bruising
- Lab: CBC, WBC Differential, Chem 18, Bone Marrow Biopsy
- Philadelphia Chromosome seen in CML
- Auer bodies or rods in AML
- Lymph node BX: Reed-Sternberg cells in Hodgkins Disease
- CT - MRI chest and abdomen
- CXR - Chest infiltration, pneumonias
- RX: Chemotherapy, Bone Marrow Transplant