Anemia

General Considerations for Anemia, regardless of causation.

- Is defined as a decreased oxygen carrying capacity for any reason.
- To diagnose, a panel will show you
  o CBC = Hemoglobin/Hematocrit
    ▪ Hemoglobin is a little higher in males (~45, instead of ~35)
    ▪ Hematocrit is about 1/3rd of hemoglobin
    ▪ 5:15:45 = Millions of RBCs: mg/dL Hgb: %Hgb = 5x3=15, 15x3=45, normal males
      ▪ A hematocrit less than 13 is anemia
  o MCV = mean cell volume
    ▪ Tells you what the volume of RBCs are; are they large or are they small?
    ▪ This allows categorization into microcyctic (small), macrocytic (large), and normocytic (normal sized) anemia, useful for you to keep them straight
  o Reticulocyte = Can the marrow respond to anemia?
    ▪ Reticulocytes are immature cells that contain nuclear content (RNA)
    ▪ Bone marrow revs up the production of RBCs and kicks out premature cells into circulation to accommodate the decreased oxygen carrying supply
    ▪ Is the blood loss begin accounted for by the bone marrow?
- 3 categories of anemia
  o Blood isn’t made = nutritional deficiencies
  o Blood is destroyed = hemolysis
  o Blood is lost = bleeding, trauma, menstruation
- Erythropoietin
  o Hormone released by the kidneys that induces proliferation of myeloblasts to RBCs
  o Increased erythropoietin = increased RBCs = oxygen carrying capacity. +
- Differentiation
  o If you turn yellow, get dark urine, and your bone marrow is fine, but your CBC is screwy, you likely have a hemolytic anemia
  o If you are pale, poor pallor, with small RBCs without a lot of color, you probably have a genetic abnormality or Iron deficiency: either Iron Deficiency, Alpha-Thal, or Beta-Thal
  o If your cells are huge, or there are 5+ lobes on a neutrophil, you have a megaloblastic anemia usually a result of folate or B12 deficiency
  o If there is no accommodation by the bone marrow, or there is an inappropriate overexpression of any one cell type, you probably have a myeloproliferative disorder resulting in anemia.
    ▪ Making too many WBCs (cancer) can cause the RBCs to be overcrowded
HEMOLYTIC ANEMIAS

All Hemolytic anemias demonstrate common features

- Shortened life span (<120 days) from increased hemolysis
- Elevated *erythropoietin* and increased *erythropoiesis* in marrow (reticulocytosis)
- Accumulation of products of hemoglobin catabolism (unconjugated bilirubin, LDH)
- Decreases in *haptoglobin*, which bind hemoglobin released for lysed cells

**Extravascular vs Intrvascular Anemias**

- **Intravascular**
  - Occurs outside of spleen, in the vasculature
  - Complement mediated or by physical trauma (as in sickle cell)
  - Key signs
    - Hemoglobinemia, Hemoglobinuria, Jaundice, Hemosiderinuria
    - Decreased Serum Haptoglobin

- **Extravascular**
  - Inside the spleen, as RBCs attempt to pass through splenic cords, they get stuck, and either lyse from physical forces or are eaten by macrophages
  - Decreased deformability (sickle cell, spherocytosis) increases the change of getting stuck
  - Key Signs
    - Severe Jaundice, Splenomegaly

**Hereditary Spherocytosis**

- **Causes**
  - Inherited disorder causes by intrinsic defects in the red cell membrane rendering the cell less deformable
  - Caused by mutations in the *cell membrane proteins*, particularly in *ankrin*, though *spectrin*, band 4.2, and other proteins can be affected.
    - Leads to reduced membrane stability, so forms a sphere
    - Osmotic changes force swelling in *spherical form*
    - Inability to pass through the vessels of *spleen* leads to hemolysis (leading to splenomegaly); *splenectomy is curative*

Smear

- Spherocytes are *round without central pallor*
- Spherocytes are not pathognomonic, as they are also found in autoimmune hemolytic anemia (WAHA, CAD).

- **Clinical Course**
  - Gallstones, pigmented type (from ↑hemolysis)
  - Hemolytic Crises are not uncommon, but are not associated with the disease
Pathology Heme/Onc Outline

Glucose-6-Phosphate Dehydrogenase Deficiency

- **Definition**
  - Deficiencies in the **Hexose Monophosphate shunt** or glutathione metabolism resulting from the lack of production of **NADPH** from 6GPD result in the inability to defend against free radicals resulting in hemolysis under oxidative stress.

- **Causes**
  - **Genetic Mutation** of which only two are significant; **X-Linked Recessive**
    - Oxidative stress can come from sulfa drugs (trimetoprim) anti-malarial drugs (primaquine or quinidine) or oxidative foods (fava beans)
    - Impart protection against malaria in the heterozygous state
  - **Oxidative Stress and Heinz Body**
    - Oxidative stress causes **denaturation of hemoglobin** forming **Heinz Bodies**
    - The spleen tries to rip these Heinz bodies out of RBCS resulting in **Bite Cells** look like they have a bite taken out of them and are products of

- **Findings**
  - Hemolysis is self-limiting and occurs only in old red blood cells
  - Young cells (those with RNA and DNA still present) can make more G6PD
    - Assessing for levels of G6PD after an acute attack will demonstrate NORMAL LEVELS (you kill the old RBCs without G6PD and test only the survivors)
  - Hemolysis still present
    - Increased unconjugated bilirubin, LDH, reticulocytosis
  - Heinz Bodies require a supravital stain (methylene blue) to see

Sickle Cell Disease

- **Cause**
  - Point mutation at the 6th position resulting in a valine substitution from glutamate, resulting in abnormal folding of **Beta Chain** (protective against malaria)
  - When deoxygenated, HbS molecules undergo aggregation and polymerization

- **Hemoglobin Electrophoresis**
  - Normal is HgA, about 98%, and 2% HgA2
  - HgS is an abnormal sickle cell hemoglobin
  - HgA + HgS = Heterozygous, HgS + HgS = ss, sickle cell disease
  - HbC is another point mutation at the 6th position to lysine, altering the severity of disease; HbS + HbC is not as bad as HbS+HbS

- **Symptoms**
  - **Vasocoocclusive Crisis**
    - Microinfarctions of joints cause pain, especially with exercise (hypoxia)
  - Effectively Asplenic
    - Autoinfarct their spleens by age 5, resulting from stagnation, thrombosis, and occlusion in the spleen, called **sequestration**
    - Decreases their ability to fight off capsulated bacteria
Aplastic Crisis
- **Parvovirus B19** = Fifth’s Disease = Slap-Cheek = Common Disease of Childhood. It shuts off RBC production in the bone marrow. No worries for normal people; but sickle erythrocytes don’t last for 120 days
- **Anticancer Drugs** = sickle cell patients are extra sensitive to bone marrow suppression, and may result in aplastic crisis
  - Pulmonary Hypertension is a new found cause of morbidity

- **Treatment**
  - **Folate** to improve production of RBCs
  - **Hydroxyurea** is a RNA reductase inhibitor that produces Hemoglobin F, a reversion to the unaffected fetal hemoglobin
  - **Bone Marrow Transplant** giving the stem cells without the genes.

**α-Thalassemia**

A chains of hemoglobin are coded by **two genes** each on 2 copies of the same allele. That means you have a total of 4 genes coding for α chain. All α chains are microcytic. Occurs by deletions.

<table>
<thead>
<tr>
<th>Cause</th>
<th>Types</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Deletion on chromosome 16</td>
<td>-/- α/α (black African). Both are often confused with iron deficiency</td>
<td>Silent carrier: -/- α/α (asymptomatic; no red cell abnormality)</td>
</tr>
<tr>
<td>Insufficient Hemoglobin A (normal hemoglobin) and toxic effect of unpaired hemoglobin chains result in anemia (2-betas + 0.5αs = 1.5beta toxicity)</td>
<td>α-Thalassemia trait: -/- α/α (asymptomatic; normal iron)</td>
<td>HbH disease: -/- -/α (severe; resembles β-thalassemia intermedia)</td>
</tr>
<tr>
<td></td>
<td>Lethal in utero without transfusions</td>
<td>Hydrops feta!lis: -/- -/-</td>
</tr>
</tbody>
</table>

- **Hemoglobin pairs**
  - α₁β₂ is normal adult
  - α₂γ₂ is normal fetal
  - Lack of α₂ = generation of **Hemoglobin Barts** (γ₄) or **Hemoglobin H** (β₄)

- **Labs / Smear**
  - **Microcytic Target Cells** on peripheral blood smear
  - **No change** in hemoglobin electrophoresis (until you get to HbH disease where the B₄ type or γ₄ type can be produced)
Beta-Thalassemia
- Point mutation in a splice site on one or two of the Beta chains on chromosome 11
- If one is deleted, there is a minor anemia (the other gene does an ok job)
- If both genes are deleted it is called Beta-Thal-Major
  o Results in ↑ Hgb-F (fetal hemoglobin = α₂γ₂) and ↑Hgb-A2 opposed to Hgb-A1
  Since α is still being produced, it has to bind with something, detectable on hemoglobin electrophoresis
  o Results in Microcytic target cells and severe hemolytic anemia

Paroxysmal Nocturnal Hemoglobinuria
- It is the only acquired but intrinsic hemolytic anemia
- Due to a mutation in the PIG-A gene, responsible for the production of the GPI anchoring protein, required for defense against complement-mediated lysis
- Effects all cells from that one stem cell with the mutation
  o Sucrose in vitro causes the cells to lyse (Sucrose Lysis Test)
  o Acidosis in vitro activates complement, and induces lysis (Ham test)
    ▪ When patients sleep, there is a natural tendency to decrease respirations
    ▪ Decreased respirations = ↑CO₂ = ↑Acidosis = ↓pH = compliment activation
    ▪ Complement Activation is USUALLY inhibited by PIG-A, which is now broken
  o Results in Complement Mediated Lysis of RBC, WBCs, and Platelets
  o Results in a general pancytopenia

Autoimmune Hemolytic Anemia = Spherocytes
- Antibodies or complement on the cell surface. Determined by the Coombs test. Warm is IgG, Cold is IgM. The temperature is at what degrees the cell undergo lysis. Warm is body temperature (core problems), Cold is sub body temp (like fingers and nose)

  - Warm Antibody = IgG in the Spleen (warm autoimmune hemolytic anemia, WAHA)
    o IgG binds to RBCs at body temperature, binding to RH antigen
    o RBCs have their structural proteins stripped by the spleen identifying the Fc portion of IgG, leading to a decrease in membrane stability = spherocytes
    o You see spherocytes on peripheral smear, NOT Schistocytes, and it looks like inherited spherocytosis, differentiated by the Coombs Test
      ▪ Put RBCs in with an agglutinator, they clump at warm temperature
    o Associated with SLE or other autoimmune disease

  - Cold Agglutinin = IgM in the liver (cold agglutinin disease)
    o IgM binds to RBC surface antigens, recognized by Kupfer Cells in the Liver which leads to degradation
    o Clumping leads to an increased mean cell volume (since the “RBC” is so huge)
      ▪ Positive Coombs at cold temperature
    o Associated with mycoplasma (acute), lymphoid neoplasms (chronic)
**Microangiopathic Hemolytic Anemia** = Schistocytes

- Red blood cells have no intrinsic defects, but are literally clotheslined by fibrin deposition leading to the presence of Schistocytes, shredded lysed cells that have been popped. Associated with conditions such as DIC, Malignant HTN, TTP/HUS
- We did not discuss this topic in great detail, but after studying for Boards, I've included this write-up to help you differentiate the different clotting diseases
  - **Immune Thrombocytopenic Purpura**
    - This is an autoimmune disease caused by an antibody made in the spleen tagging platelets for destruction within the spleen. With destruction comes ↓Platelets and therefore an ↑Bleed Time but a normal PT and PTT
      - Antibody target is against glycoprotein IIb/IIIa
      - This will make more sense towards the end of the outline
    - If an **adult woman** gets it then it is likely a chronic disease
    - If a **child** gets it, then it is usually self-limiting
    - The bone marrow will show **hypermegakaryocytosis** showing that the marrow identifies the problem and is churning out platelets to accommodate
    - Treat with **corticosteroids** or **splenectomy**
  - **Thrombotic Thrombocytopenic Purpura** and **Hemolytic Uremic Syndrome**
    - Two diseases that are the same, but on opposite ends of spectrum
    - Patient presents with platelet clots all over his body without fibrin, called a hyaline clot. The platelets get used up making those erroneous clots, so when you measure it there are ↓platelets and therefore a ↑Bleeding Time
    - If the condition is an **adult woman** then there should be neuro symptoms
    - If the condition is a **child** than there should be renal symptoms
      - Caused by **Shigga Toxin** (Shigella and E Coli O157:H7)
  - **Disseminated Intravascular Coagulation**
    - This is a process in which blood loss leads to a paradoxical hypercoagulation of platelets in the blood, but not at sites of injury
    - This occurs after massive hemorrhage, amniotic fluid embolism, and septic shock
    - Just like TTP, you get ↓Platelets (because they are used up) and ↓Bleeding Time
NUTRITIONAL ANEMIAS

**Iron Deficiency**

- Most common cause of anemia in general population

**Causes**
- Decreased intake = no meat (vegans), is found in leafy veggies
- Decreased absorption = GI infection, cancer, etc.
- Increased Loss = bleed, fast or slow, i.e. menstruation, rectal, trauma

**Absorption**
- Absorbed via *transferritin* in the duodenum
- Stored via *Ferritin*
- Absorbed as a heme product (meat) and non-heme products (vegetables)
  - **If increased** prevents absorption and release of from macrophages saying “I’ve got enough.” Aberrant increase will lead to iron deficiency
  - **If decreased** it causes the absorption and release from macrophages saying “I need more.” Aberrant decrease will lead to hemochromatosis

**Symptoms**
- Asymptomatic if the loss is slow
- Symptoms include *tachycardia* and *fatigue* with little correlation between physical finding and actual anemia
- *Pununnel-Vision Syndrome*: Microcytic Anemia, Smooth Red Tongue, Esophageal Web
  - Rare, but all over the boards

**Labs**
- Peripheral Smear
  - Microcytic (small), Hypochromic (pale) cells from decreased maturation time and decreased Hemoglobin
  - Anisocytosis (varying size) and poikilocytosis (varying shape)
- **Decreased Serum Iron** and **Increased Total Iron Binding Capacity**
  - TIBC is a measure of transferrin
  - Serum Iron fluctuates with diet (eat a steak, in one hour, you may look normal)
  - The body tries to bring in more iron, so TIBC goes up
  - There is no alteration of Hemoglobin electrophoresis (Beta-Thal)
  - The TIBC is up, opposed to the TIBC being down in chronic anemia.
- Bone marrow aspirate is best way to confirm, though is invasive and expensive
- *Ferritin* levels provide ease of access from a blood sample (low in anemia)
  - Acute Phase reactant (it will go up if there is an acute inflammatory condition)

**USMLE Pearls**
- Female with ↑ menstrual Bleeding
- Occult colon bleeding in elderly male (cancer)
- Microcytic Hypochromic Anemia
- ↑TIBC, ↓Serum iron, ↑Ferritin

**Treatment**
- Identify reason for anemia (occult colorectal bleed, for example)
- Iron supplementation
  - Enteral = cheap, ferrous salt, daily supplementation, improved with Vit C
  - Parenteral = Iron Dextran, is expensive, and reserved for severe cases
  - Packed Cell Transfusion = Emergency situation (usually trauma related)
**Pathology Heme/Onc Outline**

**Anemia Of Chronic Disease**
Underproduction anemia. You are full of iron, but you can’t let it go from your macrophages, so it mimics an iron deficiency anemia. This is just a trick-you-up. When associated with inflammatory processes you may get a Microcytic, hypochromic anemia with decreased serum iron (oh gnoes, that’s iron deficiency!). The difference is in the TIBC, which is decreased in this disease (your body has enough, it just can’t release it) whereas it is increased in Iron deficiency.

**B12 Deficiency**
You need both folate and B12 in order to make DNA. If you cannot make DNA, the nucleus will never mature, and no divisions can take place. This is at the heart of Megaloblastic Anemia caused by either B12 or Folate Deficiency.

- Universal in animal products, becoming absorbed in our daily diets (included in milk, cheese, meats, eggs, etc), and stored for years (a decade), thus B12 deficiency is highly rare.
- **Normal Absorption of B12**
  - Pepsin causes release of B12 from proteins, allowing it to bind to haptocorrin
  - Intrinsic Factor and Haptocorrin (R-Factor) are released by parietal cells
  - Alkaline pH of the duodenum releases B12 from Haptocorrin, allowing B12 to bind to Intrinsic Factor where it is absorbed in terminal ileum

**Causes**
- **Strict Veganism** = no meat or dairy for decades results in depletion of B12 stores
- **Pernicious Anemia** = autoimmune disease destroying gastric mucosa while also secreting antibodies to B12, resulting in absence of Intrinsic Factor and prevention of binding, leading to decreased absorption of vitamin
- **Duodenal Resection** (terminal ileum), no chance to absorb even if properly digested
- **Others**, don’t bother with them

**Symptoms**
- Peripheral Neuropathies, Loss of Proprioception and Vibratory Sense, Dementia, Psychosis.
  - Dorsal and lateral myelin degrades leading to decrease in efficacy of DCMLS leading to loss of Proprioception and vibration, as well as motor function in severe disease

**Laboratory Findings**
- Peripheral Smear
  - **Macrocytic** (very large) RBCs and **Hypersegmented** Neutrophils
  - Nuclear/Cytoplasmic Asynchrony whereby the nucleus remains large, grainy, and immature, while the cytoplasm grows
- **Pancytopenia** – all blood cells are reduced
- **Marrow** is hypercellular and macrocytic

**Treatment**
- Neurological Symptoms are permanent
- Replace B12 for dumb vegans, Parenteral B12 for people who are really sick (PA)
Folate Deficiency

You can treat a B12 deficiency by throwing a lot of Folate at it. You will think they are cured until they develop permanent neurologic symptoms. You must identify the difference between Folate and B12. This is usually done on history (vegan, pernicious anemia = B12; alcohol = folate) but for the test, you have to know lab values.

- Small reserves. Body stores depleted in weeks to months
  - Alcoholics lose their folate quickly, then EtOH prevents activation of Folate
  - Pregnant females demand increases and depletes rapidly
  - Treatment with Methotrexate for cancer (Folate antagonist)

- Peripheral Smear
  - Identical to B12 Deficiency
  - Identical to Chemotherapy
  - Whenever you inhibit DNA synthesis you get Megaloblastic anemic changes

- Labs
  - Homocysteine ONLY is high in Folate
    - Homocysteine and Methyl Malonyl are high in B12 deficiency
    - If Methyl Malonyl is in the urine, its NOT folate
  - MCV is high, and Folate levels are low

CHRONIC MYELOPROLIFERATIVE DISORDERS

Chronic means that these cells are generally differentiated and because they are leukemias they are in the blood. This organization is based on Dr. Kahn’s presentations. You will see another organization in the paragraph format. Chronic conditions can of any cell lineage – WBC, RBC, Platelet, and there is a chronic proliferative disorder of each. So, for these diseases think (1) in the blood, (2) differentiated, and (3) limited to one cell lineage.

Chronic Myelogenous Leukemia

- Cause
  - Philadelphia Chromosome is a 9:22 translocation with the creation of the BCR-ABL protein.
  - ABL, a tyrosine kinase of the nucleus, now expressed in cytoplasm, activates a growth factor cascade leading to proliferation

- Labs
  - 100% Cellular Marrow (usually 50/50 fat/cell)
  - Really high white count =Increased leukocytosis with a left shift

- Symptoms
  - Chronic Phase
    - Peripheral blood leukocytosis, left shift, basophilia
  - Accelerated Phase
    - Worsening Anemia, Thrombocytopenia, and increase in blasts
  - Blast Crisis
    - Acute leukemia (either a AML or ALL)

- Treatment
  - Gleevec (Imatinib) binds the ATP binding pocket on the CML enzyme, downregulating the ABL tyrosine kinase
Primary Myelofibrosis
Marrow rapidly progresses to the fibrotic state (just like the spent phase of other diseases)

Causes
- Megakaryocytes are the problem. They are large and dysplastic, secreting fibroblast growth factors leading to fibroblast proliferation

Lab
- Peripheral Smear
  - Teardrop cell, distorted RBC membrane; forced through fibrosis
  - Leukoerythroblastosis – presence of immature RBC and WBC in peripheral blood. Fibrotic distortion forces cells out prematurely
- Extramedullary Hematopoeisis = hepatosplenomegaly
- Rouleaux Formation on peripheral smear

Symptoms
- Anemia, splenomegaly, decreased Hct

Polycythemia Vera = Panmyelosis

- Cause
  - Progenitor cells have markedly decreased requirements for erythoropoitin
  - Greater than 90% have a JAK-STAT mutation, Valine for Phenylalanine, JAK-2

- Labs
  - Erythropoieten is decreased in PV, whereas in all other polycythemias, it is elevated
    - Sensors are working fine, trying to limit the polycythemia
    - In other diseases, there is no feedback, resulting from high epo levels
  - Panmyelosis (Erythrocytosis (Polycythemia), Thromobocytosis, and Granulocytosis)
    - Everything is up because the progenitors cells are so sensitive to epo
  - Early: Hypocellularity of the bone marrow, Hct of 60 or more
  - Late: Fibrosis of the marrow with extramedullary hematopoiesis in spleen/liver
    - This spent phase results in organomegaly of spleen and liver

- Symptoms
  - Almost exclusively related to the increased RBC and Hematocrit
  - Stagnation
    - pressure venous end blood cells, causing distention
    - Decreases flow leads to both clotting and hemorrhage
      - Includes epistaxis, cerebral hemorrhage, MI, DVT, ACS
  - Erythromelalgia – occlusion of small arteries in extremities (red arms and legs) from congestion in the extremities.

- Treatment
  - Simple Phlebotomy improves patient outcomes
  - Treatment with myelosuppressive or chemotherapeutic agents may result in AML
Essential Thrombocytosis = restricted to the platelet lines
- **Cause**
  - Increased proliferation and production confined to megakaryocytic elements
  - It is a diagnosis of exclusions since all chronic myeloproliferative disorders can be thrombocytotic
  - Exact pathogenesis remains unknown, but is similar to Polycythemia Vera (JAK2)
- **Symptoms**
  - Clots (no kidding) leading to DVTs, CVA, MI, Portal Vein thrombosis, though may also lead to bleeds
  - Burning of hands and feet caused by occlusion of small arterioles
  - **Indolent** - Symptoms come and go, long periods of nothing, then brief acute periods
- **Labs**
  - Bone marrow examination is useful for excluding other disorders
    - Cellularity is increased moderately
    - Increased megakaryocytes
  - Peripheral Smear important
    - Enlarged platelets (giant platelets) and leukocytosis

Chronic Lymphocytic Leukemia
- **Cause**
  - Clonal proliferation of mature B cells that express T Cell CD5 markers
- **Symptoms**
  - Occurs in older age ranges **65 years or older**
  - Usually indolent → they die with it, not because of it
  - There can be a disruption of the immune system
    - Autoantibodies = thrombocytopenia or hemolytic anemia
    - Hypogammaglobulinemia = infections
  - There can be richter transformation
    - Prolymphocytic Phase (less differentiation, poorer prognosis). **NO BLAST CRISIS**
    - **Richter phase** = most important, where they turn into diffuse B cell Lymphoma
- **Peripheral Smear**
  - Lymphocytosis, increased mature lymphocytes
  - Smudge cells = fragile cells broken by preparation
- **Labs**
  - Leukocytosis of predominantly lymphocytes, but it can be all white cells up
- **Treatment**
  - Rituxinab = monoclonal antibody against B cell marker CD20
  - Alkylating Agents or Purine Analogs, dealing with side effects

ACUTE LEUKEMIAS
These are proliferations that involve a block of differentiation. Cells normally grow up along their pathway, and then get stuck in one, nonfunctional step, which then proliferates, crowding out the good cells. These are acute, so are **not differentiated** and are leukemias, so are **in the blood**.
Acute Lymphocytic Leukemia

- Even though there are two types (B cell and T cells) they are morphologically indistinguishable as having blast cells in the peripheral smear

- Are able to penetrate sanctuary sites (brain / testes) to hide from chemo

- Peripheral Smear = normal leukemia blast information
  - Big cell with big nucleus, scant cytoplasm, small nucleoli
  - **No cytoplasmic granules** and **No Auer Rods**
  - Will be positive for Tdt and Calla immunology (markers of B cell immaturity)

- Symptoms
  - Most common in kids (white boys)
  - Malignant cells overtake the bone marrow, squashing the normal bone marrow, causing pancytopenia and bone pain.

- B cell vs T cell Difference
  - B cell is most common in young children
  - Adolescent males with mediastinal mass (thymic)

- Most patients achieve complete remission

Myelodysplastic Syndromes = “sick marrow”

- Causes
  - Maturation defect in the stem cell clone. Differentiation is NOT blocked at the blast phase, but differentiate poorly
  - Idiopathic or iatrogenic (alkylating agents to treat another cancer)

- Presentation
  - Usually in old patients
  - Hypercellular bone marrow, but cytopenias in peripheral blood
  - A result of ineffective hematopoiesis
  - The body knows there are too few cells, so it makes more in the marrow, but they don’t differentiate, so die early in the marrow

- Has a propensity to progress to AML

**USMLE Pearls Of Acute Leukemia**

- AML–Auer rods, most common acute leukemia in adults, myeloblasts
- M3 (Promyelocytic) Leukemia--t(15;17), RARα/PML, all-trans retinoic acid, DIC
- ALL--most common leukemia in children, sanctuary sites
- Myelodysplasia--chromosomal abnormalities, macrocytosis, older people, alkylating agents
- **Acute Myeloid Leukemia** *(this is also Acute Leukemia, but takes an entire page)*
  - **Classifications**
    - Two kinds
      - FAB (French American British) based on morphology
      - WHO (World Health Organization) based on cytogenic studies
    - FAB Classes (crap; don’t learn all Ms for the boards, just M3!)
      - M0 = minimally differentiated, so much you can’t tell from ALL
      - M1 = myeloid without maturation. You may see auer rods or granules
      - M2 = myeloid with maturation, most common, you can see the T(8:21)
      - M3 = Acute Promyelocytic Leukemia. UNIQUE
        - Predominance of Promyelocyte (red cytoplasmic granules)
        - Always caused by T(15:17) producing the RAR-PML fusion protein (Retinoic Acid Receptor –PML) fusion which can be treated with retinoic acid.
        - DIC is common complication and presenting symptom
      - M4 = Myelomonocytic Leukemia
        - Associated with chromosome 16 abnormalities
      - M5 = Monocytic
        - Associated with tissue infiltration (gums) and MLL gene
        - MLL mutates in previous therapy for other malignancies with alkylating agents.
      - M6 = Erythroleukemia
        - Dysplastic Erythroid precursors
      - M7 = Megakaryoblastic leukemia, from down syndrome
  - **Peripheral Smear**
    - Looks a lot like lymphoblast, but you have myeloblasts
    - Myeloblasts have a more granular cytoplasm with the presence of auer rods which form collections of granules.
      - Auer rod = abnormal, malignancy, AML, and poor prognosis
  - **Presentation**
    - Occurs in middle age *(40-60)* does not occur in kids (ALL does)
    - Abrupt onset with pancytopenia due to proliferation and crushing the good marrow cells leading to anemia, leukopenia, and thrombocytopenia
      - This causes fatigue, infection, and bleeding
LYMPHOMAS

Lymphomas are white Cell malignant neoplasms of that occur as a discrete tissue masses. Usually, you will see swollen but painless lymph nodes. There are two types of Lymphomas, the Hodgkins and the Non-Hodgkins Lymphomas, distinguished by the presences of the Reed-Sternberg Cells and their distribution (Non-Hodgkins can appear anywhere). There are 5 types of Hodgkin’s Lymphomas, with picky facts that are not terribly important (this page). Everything that follows in the LYMPHOMA section is actually a “Non-Hodgkins” Lymphoma. There are many different types; only the highest yield were included here. Some superfluous Non-Hodgkin’s Lymphomas were edited out from the original outline.

**Hodgkin Lymphomas**

- Spreads in a linear fashion, following the pattern of lymph nodes and contains distinctive Reed-Sternberg Cells. It is common in young adults and older adults. This is a typical biphasic age peak
  - Reed-Sternbeg Cells
    - Indicative of hodgkins lymphoma, possessing the “owl eye” cells that are enormous.
    - CD45 negative, CD15/CD30 positive
  - Symptoms of Hodgkin’s
    - Rubbery, Nontender, lymphadenopathy is a critical finding. Not all lymphadenopathy is lymphoma, but it definitely raises question
    - Fever, Night Sweats, and Weight Loss = “B Symptoms”
  - Staging
    - Anharbor system.
      - Stage 1: One site, One Lymph Node
      - Stage 2: Two sites on same side of the diaphragm
      - Stage 3: Any number of sites on both sides of the diaphragm
      - Stage 4: Extralymphoid site (spleen counts as lymphoid)

- 5 subtypes
  - Nodular Sclerosis
    - Fibrous bands divide tumor into nodules
    - Lacunar Cells have nucleus appears to be sitting in an empty space
  - Mixed Cellularity
    - Mononuclear Reed Sternberg cell with an eosinophilic background
    - Associated with EBV
  - Lymphocyte Rich
    - Rare, older patients, associated with EBV
    - Predominant cell is the reactive T cell with mixed cellularity without eosinophilia
  - Lymphocyte Depletion
    - Rarest, older males, associated with EBV and HIV
    - Worse outcome
  - Nodular Lymphocyte Predominant
    - Rare, younger males, but does not express the typical CD markers you’d expect
    - Diagnostic cell is the popcorn cell without the bilobed nuclei.
Burkitt’s Lymphomas - Large B cell Non-Hodgkin’s Lymphoma, Highest Yield Non-Hodgkins

- B cell malignancy associated with Epstein-Bar Virus infection which induces a Translocation 8;14 with c-MYC oncogene activation
- Look for Heterophile-Ab (positive Monospot) and Ballerina Skirt Cells (Downey Cells)
  - This virus also causes “Mono”
  - Incidence of cancerous disease is higher in Africa and immunocompromised
- “Starry Sky” pattern of deeply staining malignant lymphocytes (purple stuff) all over the place with scattered normal macrophages (white stuff)
  - With a huge mitotic rate (most aggressive B cell Lymphoma), some cells die
  - Macrophages come in and gobble up the dead or dying B Cells
- May result in tumor lysis syndrome after treatment
  - Treatment = ↑ cell turnover = ↑uric acid = renal failure

Follicular Lymphoma – Small B cell Non-Hodgkin’s Lymphoma – classic low grade Non-Hodgkins

- A very common adult disease. It is indolent but may transform into an aggressive tumor.
- Derived from germinal center B cells that you will see in disseminated lymph nodes
- Diagnostic cell = Buttock Cell on peripheral smear
- Translocation (14;18) with an overexpression of an anti-apoptotic BCL-2. There is an immunohistochemistry stain for BCL-2
  - BCL-2 is the signal that interrupts apoptosis, the “immortality gene”
  - Overexpression of BCL-2 prevents apoptosis, even of damaged genes

Mantle Cell and Marginal zone - Small B cell Non-Hodgkin’s Lymphom, Not Commonly Tested

- Translocation 11;14 = Cyclin D1 = Mantle;
- Translocation 11;18 = Autoimmune Maltomas (H. Pylori in stomach) = Marginal;
- Dr Ochipinti made a point to say that if you know this, you know Mantle and Marginal

Lymphoplasmacytic Lymphoma - Small B cell Non-Hodgkin’s Lymphoma

- May be classified as a plasma cell neoplasm because plasma cells are the terminal differentiated state of B cells, yet it is definitely Malignant B cells undergoing differentiation to plasma cells
- Associated with a clinical syndrome called Waldenstrom Macroglobulinemia
  - Secrete IgM, a very large immunoglobulin
  - Causes hyperviscosity syndrome leading to sluggish blood movement

OTHER B AND T CELL LEUKEMIA/LYMPHOMAS

These are the syndromes and diseases that do not fit neatly into categories given to us by the profs. If you want better organization, look at the Narrative Review for the heme section. There are no pictures, but organization and important points are stressed there. These diseases that follow are important. Don’t forget to skip to the end to do the bleeding disorders as well.
**Hairy Cell Leukemia**

**Cause**
- This is a rare indolent disease of middle aged white men. You will see more questions about it than there are patients.

**Labs and Smear**
- Positive TRAP test
- Mature B cell with filamentous projections on peripheral smear

**Treatment**
- Largely treatable with dichlorodeoxyadenosine \((\text{di-chloro-deoxy-adenosine}) = \text{DCDA}\)
  - Inhibits Adenosine Deaminase, causing toxic metabolites to accumulate, killing these cells (recall this was one mechanism of SCID in the immunology block)
- Cure rate of 95% (which is why it is so board friendly)

**Multiple Myeloma**

**Cause**
- Monoclonal expansion of terminally differentiated B cells (aka, plasma cells)
  - Plasma cells make immunoglobulin
  - Plasma cells crowd out all other cells in marrow or lymph
  - Predisposes to Fracture from weakened bones
  - Predisposes to deposition of protein (the immunoglobulin) in kidneys

**Symptoms**
- Bone Fractures – plasma cells crowd out the marrow, making the bones weak, leading to fractures, often axial skeleton
- Renal Failure – Bence Jones proteins (Ig light chain fragments) in urine
- Infection – monoclonal expansion means there is a lot of Immunoglobulin, but of the wrong kind to fight most infection. Since the other plasma cells are crowded out, only the bunk Immunoglobulin can be made, which actually ↓ immunity

**Labs**
- Bone marrow is hypercellular with plasma cells, “fried egg” appearance
- Ig electrophoresis demonstrates M-spike (monoclonal y-globulin expression)
- “Punched out” lytic lesions X-rays with spontaneous fractures is pathognomonic

**Differential**
- Waldenstrom’s Macroglobulinemia can present the exact same way, only without the punched out, lytic lesions
- If your reaction is Multiple Myeloma, but it just doesn’t sound quite right, look for Waldenstrom’s

**Mycosis Fungoides / Sezary Syndrome**

- T cell infiltration of the epidermis leading to a mushroom-like papular rash
  - Despite name, it has NOTHING TO DO with fungus
- When in the skin, its Mycosis Fungoides, found in the epidermis
- When in the blood, its leukemia, called Sezary Syndrome, poor prognosis
HEMOLYTIC DISORDERS (taken strictly from lecture)

- **Hemorrhage** = bleeding
  - **Causes**
    - **Trauma** = knife wound
    - **Aneurysm** = expansion of blood vessel leading to rupture
    - **Coagulation Abnormality** = don’t patch up the holes
  - **Internal vs External**
    - External you can see a
    - Internal you can’t see, and may be occult (GI, retroperitoneal)
      - Hematoma, Subdural, Pulmonary, Intracerebral, Intraventricular
  - **Types of Hemorrhage (body cavities)**
    - Hemothorax – bleeding into the thorax
    - Hemopericardium – bleeding into the pericardium
    - Hemoperitoneum – bleeding into the peritoneum
    - Hemarthrosis – bleeding into the joint (Hemophilia A and B)
  - **Types of Hemorrhage (appearance)**
    - Petechiae – small hemorrhage, lots of little dots
    - Purpura – larger than petechiae, smaller than ecchymosis
    - Ecchymosis – bruise/contusion, huge skin hemorrhage, petechiae coalescing

- **Hemostasis** – why you stop bleeding, and why you don’t throw clots everywhere
  - **Coagulation mechanisms**
    - Blood vessel constriction, platelets, coagulation system
    - Factors + Plasmin \(\rightarrow\) Fibrinogen \(\rightarrow\) Fibrin
  - **Anticoagulation mechanisms to control**
    - Fibrinolytic System (plasmin) protease inhibitors (antithrombin III and Protein C)
    - Antithrombin III \(\rightarrow\) Thrombin
    - Protein C \(\rightarrow\) Activated protein C \(\rightarrow\) factor VIII and factor V

- **Thrombosis** = formation of a clotted mass (thrombus) in the non-interrupted normal cardiovascular system; the inappropriate activation of the hemostatic process
  - **Damage to endothelial cell** \(\rightarrow\) is both thrombotic and antithrombotic
    - Atherosclerosis, Vasculitis, Hypercholesterolemia, Cigarette smoke, Homocysteinemia, MI
  - **Stasis and Turbulence of Blood** \(\rightarrow\) slowing down of blood
    - Decreased physical activity, vessel branching, venous valves
  - **Hypercoagulability** \(\rightarrow\) favor formation of fibrin
    - Trauma, Burn, Surgery, Oral Contraceptives, Inherent genetic disease (antithrombin III, Protein C or S deficiency, Factor V Leiden presence)
  - **Fates of thrombus**
    - Obstruction (infarction), Lyse (resolution), Embolus (breaks off and becomes an occlusive object somewhere else.)
Pathology Heme/Onc Outline

- **Embolism**
  - Types
  - Air, fat, catheter, bullet, clot, DVT, Cardiac valvular clots
  - Problems caused by embolism
    - **Pulmonary Embolus** (forms in veins, goes to lungs)
      - Venous emboli enter the pulmonary arterial vasculature
    - **Stroke/MI**
      - Arterial emboli (valvular clot) breaks off into general arterial circulation
      - Can affect any organ (extremities) but major cases are stroke and MI
    - **Paradoxical**
      - Right to left shunt of heart allows venous embolus becoming arterial
  - **Greenfield filter**
    - Inserted into the vena cava that filters clots before they get to the heart

- **Infarction**
  - Insufficient blood supply to an organ causes first ischemia, then infarction
  - Causes
    - Thrombotic/Embolic Occlusion (duh)
    - Torsion – twisting of organs (testes/ovaries) strangles its own blood supply
    - Incarceration – abdominal muscles squeeze off the blood supply to an organ
    - Shock – hypoperfusion results in patent vessels that just aren’t filled
  - Results in
    - Necrosis tissue
      - Brain is Liquefactive, without scarring
      - Lung is hemorrhagic
      - Solid organs enlarge and die

- **Shock**
  - Causes
    - Cardiogenic (cant pump blood enough)
      - Pump failure, low cardiac output, hypotension causing impaired tissue perfusion and cellular hypoxia
    - Hypovolemic (blood loss or fluid loss)
      - Decreased blood volume, low cardiac output, leading to impaired tissue perfusion and cellular hypoxia
      - Caused by fluid loss (cholera), or hemorrhage (blood)
    - Septic, Neurogenic, Anaphylactic (massive vasodilation from infection)
      - Peripheral vasodilation and pooling of blood with a relative hypovolemia because of reduced venous return causing impaired tissue perfusion and cellular hypoxia
      - Causes by overwhelming infection, overdose of anesthesia, or bee sting
Edema

- Trans vs Exudate
  - Transudate
    - Non-inflammatory, mostly fluid, specific gravity < 1.012
  - Exudate
    - Inflammatory, rich in protein, specific gravity > 1.120

Causes of edema

- Increase of capillary hydrostatic pressure
  - Occlusion of vein, back up of blood, distends the blood vessel, forces fluid through capillaries
- Decrease capillary osmotic pressure
  - Decreased albumin prevents fluid absorption, favoring filtration
- Lymphatic Obstruction
  - Lymph takes away extra fluid that arteries filter and veins do not reabsorb. Without lymph, fluid accumulates

COAGULATION DISORDERS

Coagulation disorders come in three different forms, each with their own test to tip you off that they are broken. Unfortunately there are about 47 different molecules involved in clotting and anti-clotting, but the real important stuff can be talked about here.

- Primary Hemostasis
  - Comprised of the Platelets, von Willebrand Factor, and the Vessel Wall
    - **Von Willebrand Factor** tethers platelets to the vessel wall. It is endothelial derived and is used to start plugging the leak
    - **Glycoprotein 1B** acts as a receptor for vWF
    - **Glycoprotein 2b/3a** attach to each other, linking free platelets to the tethered platelet via either vWF or fibrinogen.

Tested with **Bleeding Time** and **Platelet Aggregation Test**

- Bleeding Time = stab patient (small hole), wait for them to stop bleeding. Normal is 9 minutes
- **PAT** = take patient’s platelets dissolved plasma, and add one piece of primary hemostasis to one vial, repeated for every factor. The platelets should clump and light transmission should go up (left). If it doesn’t, you’ve found the culprit
  - Drugs that interfere with primary hemostasis
    - Aspirin, NSAIDs, Clopidogel, GP2B/3A inhibitors (abciximab, tirofiban)
    - These are drugs that inhibit platelets causing interference with primary hemostasis, usually given when clotting has become pathological (old age, MI, Stroke, etc) for regular maintenance
  - Clinical Features
    - **Superficial Bleeding** = epistaxis, petechia, heavy menorrhea
    - Stark contrast to the deep bleeding of secondary hemostasis
**Secondary Hemostasis**

This is a large complicated structure of multiple factors. It is easier to first break it up into 3 different pathways, the *extrinsic*, the *common* and the *intrinsic*. Note that an “a” after the factor means “activated.”

You do not have to memorize this diagram for Tulane exams. You do for the Boards. Notice some key features, like Factor 5, Factor 8 and Factor 13 are cofactors and most other molecules must be activated. Both the intrinsic and extrinsic pathways feed into the same spot (factor 10)

- **Extrinsic pathway**
  - Called that because when we test it in vitro, we have to add something (the tissue factor)
  - Test for the extrinsic pathway with the **Prothrombin Time (PT)** normal = 13 sec
  - Drugs that effect this are **warfarin** which is aimed at altering the **INR** (normal is 1, therapeutic for patients at risk for clot diseases like a stroke is 2-3). The higher the INR the more likely bleeding is.
    - Note that Warfarin affects both intrinsic and extrinsic pathways by inhibiting synthesis of Factors 2,5,7,9, and 10
  - Pathway is activated after endothelial damage and release of Tissue Activator.

- **Intrinsic Pathway**
  - **Thrombin** is created by the common pathway, and activates the intrinsic pathway, leading to a feed-forward clotting effect
  - Test for the intrinsic pathway with **Partial Thromboplastin Time (PTT)**. Do this by adding phospholipid to accelerate (aPTT) the clotting.
  - Drugs that affect this are **Heparin**. The low molecular weight heparin is the same thing, but with decreased risk of massive bleed and osteoporosis. This is used in hospital in managing nasty clots (such as an MI without stenting or CABG availability). We want the aPTT to be 1.1-1.5 times normal
Pathology Heme/Onc Outline

- **Vitamin K dependent Factors**
  - There is an enzyme, **Vitamin K epoxide reductase** that causes **gamma carboxylation** of these factors to active them
  - Factors 2, 7, 9, 10 as well as **Protein C and Protein S** are all Vit K dependent
  - Warfarin inhibits this enzyme, Vitamin K is required for its activity

- **Von Willebrand Disease = Broken Primary and Secondary-Intrinsic Pathway**
  - **Cause**
    - The protein von Willebrand Factor is a very important molecule in aiding with coagulation. Not only does it **tether the platelets** in primary hemostasis, but it also **stabilizes factor 8**, required in the intrinsic pathway
  - **Labs**
    - **Increased Bleeding Time**, normal PT, **increased aPTT**
    - Primary Affected, Extrinsic not affected, Intrinsic affected
    - vWF antigen level increased or activity/co-factor decreased
  - **Treatment**
    - **DDAVP (desmopressin)** increases release of vWF stored in endothelial cell organelles (called **Weibel-Palade Bodies**).
    - **Cryoprecipitate** contains factor VIII and vWF
  - **Kahn’s USMLE Pearls**
    - Most common congenital coagulopathy
    - Autosomal Dominant
    - Prolonged Bleeding Time + aPTT
    - Treat with DDAVP

- **Hemophilia = broken intrinsic pathway**
  - Characterized by an absence of deficiency of certain factors, treatment is supplemental
    - Hemophilia A = factor 8, give factor 8
    - Hemophilia B = factor 9, give factor 9
  - **Labs**
    - Elevated PTT without any change in PT or in Bleeding time
    - Bleeding into joints and muscles
    - X-Linked recessive, so the vignette will have a **young boy**
    - Deep bleeding (joints, muscle, cerebral) = **hemarthrosis**
    - Prolonged aPTT without any other change

- **Multiple Factor Deficiency = Alcoholic Bleeder or Vitamin K Deficiency** (Warfarin Treatment)
  - Presentation = Gl bleeds or “hemophilia” in pts with cirrhosis (alcohol, hep C)
  - **Cause** = Liver failure (alcoholic cirrhosis) or inhibition of **gamma-carboxylation** (warfarin, Vit K deficiency) prevents synthesis of factors 2,5,7,9, and 10.
  - The liver is the only site of factor production.
  - **Labs** = Prolonged PT and prolonged aPTT
    - Factor 7 is the extrinsic pathway (PT) all others are intrinsic (aPTT)
  - Treatment = Fresh Frozen plasma, Erythrocyte replacement, Vitamin K
- **Anti-Coagulation**
  
  There are three systems that maintain an anti-coagulated state.

  - **Protein C/Protein S system**
    - Thrombin is a *coagulant* acting through the intrinsic pathway
    - Thrombin is also an *anticoagulant* acting through the thrombomodulin → Protein C + Protein S → inhibition of Factor 5 and 8
    - Errors in Protein C or its binding to Factor 5 and 8 increase risk of venous clotting (DVTs) such as in Factor V Leiden

  - **Plasminogen System**
    - Plasminogen is activated by Plasminogen Activator to Plasmin
    - Plasmin then cleaves fibrin to fibrin split products
    - This is why we give tPA (tissue plasminogen activator) to patients with occlusive strokes and heart attacks.

  - **Antithrombin System**
    - Antithrombin has two binding sites, one for thrombin and one for Factor 10.
    - It inhibits both thrombin and factor 10
    - Low Molecular Weight Heparin only inhibits factor 10 (thus the decreased risk of bleeding without the need to check aPTT levels constantly)

- **Factor V Leiden** = Inheritable Venous Hypercoagulation
  
  - Causes
    - Point mutation in the *Protein C binding site* on factor 5, decreasing affinity
    - Decreased inhibitory signal from protein C leads to increased clotting
  
  - Presentation + Labs
    - Younger patients (less than 50) with spontaneous DVTs
    - Often has a positive family history
    - Most common congenital etiology of venous hypercoagulability
  
  - Treatment
    - Warfarin (caution pregnancy, its teratogenic) for long term use
    - Heparin which enhances Antithrombin activity for treatment RIGHT NOW

- **Arterial Thrombosis**
  
  - Cause
    - Often NOT caused by congenital defect
    - Arteriosclerosis is leading cause; trauma, stagnation, and cancer possible
  
  - Labs/Findings
    - Stroke, MI, Peripheral Vascular Disease, Arterial Clotting
    - Decreased aPTT, PT, bleeding time
    - Hct/Hgb, Platelets may be elevated
  
  - Treatment
    - ASA daily, forever
    - Warfarin for at least the next 6 months
    - Greenfield Filter to catch and bust venous clots coming back to the heart.
<table>
<thead>
<tr>
<th>Type</th>
<th>Mechanism</th>
<th>Diagnostic</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm antibody hemolytic anemia</td>
<td>IgG autoantibodies to Rh bind RBCs and induce killing in spleen via Fc</td>
<td>Anemia, Spherocytosis, Splenomegaly</td>
<td>Extravascular</td>
</tr>
<tr>
<td>Cold Agglutinin disease</td>
<td>IgM autoantibodies to Rh bind RBCs and induce killing in Liver</td>
<td>Cold Agglutination Test (clumping of RBCs on peripheral smear) or a MCV super high (since one clump is read as a huge RBC)</td>
<td>Associated with Mycoplasma (acute) or low-grade lymphomas (chronic) Extravascular</td>
</tr>
<tr>
<td>Hereditary Spherocytosis</td>
<td>Red Cell membrane deficiency (ankrin, spectrin, Band 4.2, etc), causing a change in shape, spicule destruction</td>
<td>Autosomal Dominant Inheritance; anemia, spherocytosis on smear. Increased MCHC. Splenomegaly, Do not confuse with WAHA</td>
<td>Extravascular</td>
</tr>
<tr>
<td>Glucose-6-Phosphate Dehydrogenase Deficiency</td>
<td>Failure of HMP shunt to make NADPH required to regenerate Glutathione, leaving RBCs vulnerable to oxidative stress</td>
<td>Self-Limiting Hemolytic Anemia, reduced activity of erythrocyte G6PD, Heinz Bodies, and Bite cells. Do not assess G6PD levels after an attack</td>
<td>X-Linked Inheritance, heterozygous offers malarial resistance. Extravascular. May lead to avascular necrosis and priapism</td>
</tr>
<tr>
<td>Sickle-Cell Anemia</td>
<td>Point mutation in the 6th position of Beta-Chain results in a Valine for Glutamate substitution leading to aggregation under low oxygen tension states (exercise or high altitude)</td>
<td>Sickle cells on peripheral smear, vasoocclusive crises, hemoglobin electrophoresis, autosplenectomy, salmonella osteomyelitis, and strep pneumonia susceptibility (asplenism)</td>
<td>Heterozygosity offers malarial resistance. Extravascular. May lead to avascular necrosis and priapism</td>
</tr>
<tr>
<td>Paroxysmal Nocturnal Hemoglobinuria</td>
<td>Somatic mutation in PIG-A gene leads to all cells by that stem cell to have impaired synthesis of GPI anchoring protein</td>
<td>Flow-cytometry demonstrating CD59 negative erythrocytes. Acidity during sleep (hypoventilation) causes complement binding → hemolysis</td>
<td>Intravascular</td>
</tr>
<tr>
<td>MAHA</td>
<td>Fibrin deposition results in literal clotheslining of RBCs</td>
<td>Schistocytes on peripheral smear. Anemia brought on by excessive activity (marching, bongo playing)</td>
<td>Intravascular</td>
</tr>
<tr>
<td>β-Thalassemia</td>
<td>Point mutation in the Beta-chain gene leads to splice site mutation of Beta chains, as precipitate out and induce hemolytic anemia. α still produced, so gamma sometimes produced instead. Chromosome 11.</td>
<td>Microcytic Target cells with altered Hemoglobin electrophoresis towards production of Fetal and A2 Hemoglobin, splenomegaly, distortion of head and facial bones.</td>
<td>Called Mediterranean Anemia or Cooley Anemia</td>
</tr>
<tr>
<td>α-Thalassemia</td>
<td>Deletion of one, two, or three of the α genes on chromosome 16. Leads to incomplete formation of hemoglobin, beta precipitates out, leads to hemolysis. Deletion of all 4 alpha genes is incompatible with life</td>
<td>Microcytic Target cells without alteration of Hemoglobin electrophoresis (though γ4 and β2 can be present). No clinical manifestations with only one mutation</td>
<td>Require minimum of 2 for “trait”, 3 for Hemoglobin H (β4) and hydrops fetalis if all 4.</td>
</tr>
<tr>
<td>Iron Deficiency Anemia</td>
<td>You don’t have enough Iron to make good hemoglobin as in heme occult blood (old man) or menorrhoea (woman)</td>
<td>Hypochromic Microcytic Anemia, Decreased serum iron increased TIBC</td>
<td>Hypochromic Microcytic (Pale and small)</td>
</tr>
<tr>
<td>Anemia of Chronic Disease</td>
<td>Associated with inflammation, it induces the macrophages to retain iron. Your body has the iron, but you just can’t use it.</td>
<td>Hypochromic Microcytic Anemia, Decreased serum iron levels Decreased TIBC</td>
<td>Normochromic Normocytic Anemia</td>
</tr>
<tr>
<td>Pernicious Anemia / Vitamin B12 Deficiency</td>
<td>Autoimmune gastritis and anti-Intrinsic Factor antibodies prevents absorption of B12; absence of B12 = delayed or absent division</td>
<td>Homocysteine and Methylene malonyl Macrocytic RBCs Hypersegmented Neutrophils, Hypercellular Marrow</td>
<td>Megaloblastic Anemia (large) with neurologic symptoms (subacute combined degeneration)</td>
</tr>
<tr>
<td>Folate Deficiency</td>
<td>Either insufficient intake (alcoholics) or increased demand (pregnancy) or by being antagonized by drugs (methotrexate)</td>
<td>Homocysteine Only Elevated Macrocytic RBCs Hypersegmented Neutrophils, Hypercellular Marrow</td>
<td>Megaloblastic Anemia in Mom, spinal tube defects in developing fetus</td>
</tr>
</tbody>
</table>
### NEOPLASMS OF BLOOD AND LYMPH

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute Lymphocytic Leukemia</strong></td>
<td>Most Common Cancer of Childhood, though most kids actually go into remission/are cured. This is acute (not differentiated) and lymphocytic (lymphocytes) form of leukemia (in the blood). There is a hypercellularity of the bone marrow with a pancytopenia in the blood → Anemia and infection. Presents with bone pain, frequent nose bleeds, and multiple undifferentiated blast cells on peripheral smear.</td>
</tr>
<tr>
<td><strong>Acute Myeloid Leukemia</strong></td>
<td>Cancer of middle age that generally responds poorly to therapy. This is acute (undifferentiated) myeloid (RBCs) leukemia (in the blood). Multiple subtypes; M3 = the 15:17 translocation is treatable with Vitamin A (leads to differentiation). Auer rods are pathognomonic for AML on peripheral smear.</td>
</tr>
<tr>
<td><strong>Chronic Myelogenous Leukemia</strong></td>
<td>Cancer of 20-something males and the elderly, controlled well with Imatinib/Gleevec. This is chronic (differentiated) myeloid (RBC) leukemia (in the blood). Caused by the 9:22 Translocation forming the Philadelphia Chromosome producing the Protein BCR-ABL, which is a tyrosine kinase, upregulating cell proliferation, inhibited by Imatinib by binding the ATP-pocket. Patients will present with Leukocytosis with left shift, hypercellular marrow, and thrombocytopenia. Even with treatment, there may be a reversion to AML, called a Blast Crisis, Carrying a dismal prognosis.</td>
</tr>
<tr>
<td><strong>Chronic Lymphoblastic Leukemia</strong></td>
<td>Most common cancer of the elderly, this is the lowest yield leukemia. This is chronic (differentiated), lymphoblastic (Lymphocytes), Leukemia (in the blood). Proliferation of B cells expression a T Cell Marker (CD5) with Smudge Cells in the peripheral smear.</td>
</tr>
<tr>
<td><strong>Polycythemia Vera</strong></td>
<td>A disease of middle aged, obese, hypertensive males. Caused by a JAK-STAT mutation leading to a hypersensitivity to erythropoietin. Findings are Panmyelosis (↑RBCs, ↑WBCs, ↑Platelets) despite a ↓Epo. Progresses to a spent phase where the bone marrow becomes fibrotic with extramedullary hematopoiesis.</td>
</tr>
<tr>
<td><strong>Primary Myelofibrosis</strong></td>
<td>A disease of fibroblasts, which are erroneously activated to lay down collagen, leading to marrow fibrosis. ↑of growth factors (PDGF or TGF-β) leads to a decreased “normal” and “working” area of bone marrow. RBCs are “squeezed” through the fibrosis, forming tear-drop cells on peripheral smear. Bone marrow looks like the spent phase of PV.</td>
</tr>
<tr>
<td><strong>Multiple Myeloma</strong></td>
<td>A disease of plasma cells, the final determinants of B cells. There is a monoclonal expansion of plasma cells, so they are all alike, and their IgM is all alike. M spike on electrophoresis, Benece-Jones Proteins in the urine, and Punched Out lytic bone lesions. The bone marrow has a fried egg appearance.</td>
</tr>
<tr>
<td><strong>Waldenstrom</strong></td>
<td>When the vignette gives you the reaction of Multiple Myeloma, but it’s not quite there, pick Waldenstrom.</td>
</tr>
<tr>
<td><strong>Hairy Cell Leukemia</strong></td>
<td>A disease of lymphocytes, in particular a T cell proliferative disorder. Classic image is a lymphocyte with fibrous cytoplasmic projections (so it looks “hairy”). Positive TRAPP test, a dry tap on marrow biopsy, and treatment with 2-CI-DNA are pathognomonic.</td>
</tr>
<tr>
<td></td>
<td>Non-Hodgkins Lymphomas.</td>
</tr>
<tr>
<td><strong>Burkitt’s</strong></td>
<td>Associated with Epstein-Barr Virus, and an 8:14 Translocation with overexpression of c-myc oncogene. EBV infects B cells, look for Heterophile-Positive (Monospot positive) and Ballerina Skirt Cells on smear. The classic histologic picture is a stary-sky appearance (like the painting, “starry-sky”). Rapidly growing tumor associated with Africa (endemic, worse) and the U.S. (nonendemic, better).</td>
</tr>
<tr>
<td><strong>Follicular</strong></td>
<td>Caused by a 14:18 Translocation it causes overexpression of anti-apototic gene BCL-2. Histologic slide shows the buttock cell, immunohistochemistry tags BCL-2.</td>
</tr>
<tr>
<td><strong>Mantle</strong></td>
<td>11:14 translocation, overexpression of Cyclin D1, low yield.</td>
</tr>
<tr>
<td><strong>Marginal</strong></td>
<td>11:18 translocation, associated with autoimmune maltonas, h pylori induced, low yield.</td>
</tr>
<tr>
<td><strong>Diffuse Large B</strong></td>
<td>B cell tumors occurring in immunocompromised states (post-transplant, HIV).</td>
</tr>
<tr>
<td></td>
<td>Hodgkins Lymphoma.</td>
</tr>
<tr>
<td><strong>Generalities</strong></td>
<td>This is the more benign form of leukemia that spreads contiguously (through lymph nodes), Owl-Eye Reed Sternberg Cells, and presents with Fever, weight Loss, and Night Sweats (i.e. B symptoms). There are 5 subtypes.</td>
</tr>
<tr>
<td><strong>Nodular Sclerosis</strong></td>
<td>Fibrous Bands divide tumor into nodules forming Lacunar cells.</td>
</tr>
<tr>
<td><strong>Mixed Cellularity</strong></td>
<td>Reed-Sternberg + Eosinophilia.</td>
</tr>
<tr>
<td><strong>Lymphocyte Rich</strong></td>
<td>Rare, seen in older patients, there are a lot of lymphocytes, low yield.</td>
</tr>
<tr>
<td><strong>Lymphocyte Poor</strong></td>
<td>Still rarer, older males, HIV, EBV, worst prognosis, lowest yield.</td>
</tr>
<tr>
<td><strong>Nodular Lymphocyte Predominant</strong></td>
<td>Popcorn Reed-Sternberg Cells.</td>
</tr>
</tbody>
</table>
### BLEEDING DISEASES

<table>
<thead>
<tr>
<th>Disease</th>
<th>Disease of the...</th>
<th>Bleeding Time</th>
<th>Platelets</th>
<th>PT</th>
<th>PTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITP</td>
<td>Platelets (autoimmune destruction)</td>
<td>↑</td>
<td>↓</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>TTP/HUS</td>
<td>Platelets (they clot everywhere)</td>
<td>↑</td>
<td>↓</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hemophilia A</td>
<td>Intrinsic Pathway (Factor 8)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>↑</td>
</tr>
<tr>
<td>Hemophilia B</td>
<td>Intrinsic Pathway (Factor 9)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>↑</td>
</tr>
<tr>
<td>Vitamin K Deficiency</td>
<td>Factors 2,5,7,9,10</td>
<td>-</td>
<td>-</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Von Willebrand’s</td>
<td>Platelets and Intrinsic Pathway (Factor 8)</td>
<td>↑</td>
<td>-</td>
<td>-</td>
<td>↑</td>
</tr>
<tr>
<td>DIC</td>
<td>Everything</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

↑Increased, ↓Decreased, - unchanged, Bleeding Time: Platelets, PT:Extrinsic, PTT:Intrinsic

### CLOTTING DISEASES

<table>
<thead>
<tr>
<th>Disease</th>
<th>Character</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor V Leiden</td>
<td>Mutation in Factor V that makes it immune to activated Protein C</td>
</tr>
<tr>
<td></td>
<td>The “always on” signal causes ↑risk for venous clotting and embolism</td>
</tr>
<tr>
<td></td>
<td>↑DVTs, Pulmonary Embolism, requires Coumadin treatment (INR 2-3)</td>
</tr>
<tr>
<td>Antithrombin 20210A</td>
<td>Second most common congenital etiology of venous Hypercoagulability. There is a mutation of the untranslated region of Prothrombin gene, ↑levels of Prothrombin = ↑levels of thrombin, and more clotting.</td>
</tr>
<tr>
<td>Protein C or Protein S</td>
<td>Protein S makes Protein C work better. Protein C inactivates Factor V.</td>
</tr>
<tr>
<td>Deficiency</td>
<td>If there is a break in Protein S or in Protein C, factor V will stay</td>
</tr>
<tr>
<td></td>
<td>Presenting just like in Factor V Leiden.</td>
</tr>
</tbody>
</table>

### COMPARING TYPES OF CLOTS

<table>
<thead>
<tr>
<th>Arterial</th>
<th>Venous</th>
<th>Postmortem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lines of Zahn</td>
<td>No Lines of Zahn</td>
<td>No Lines of Zahn</td>
</tr>
<tr>
<td>High Blood Flow</td>
<td>Low Blood Flow</td>
<td>No Blood Flow</td>
</tr>
<tr>
<td>Found in Myocardial Infarction and Stroke</td>
<td>Found in Deep Leg Thrombosis venous status, Pulmonary embolus</td>
<td>Found after death</td>
</tr>
<tr>
<td>Thrombi on Endothelium</td>
<td>Thrombi on Endothelium</td>
<td>Thrombi not on endothelium</td>
</tr>
<tr>
<td>Bright Red</td>
<td>Dark Red</td>
<td>Dark Red</td>
</tr>
<tr>
<td>Risk in Hypertension, Hypercholesterol, Atherosclerosis, Obesity</td>
<td>Risk in CHF, Postoperative Patients, Bed-Ridden patients, Factor V Leiden</td>
<td>“Risk” only in Death</td>
</tr>
</tbody>
</table>

Reorganization of information taken from information in BRS Pathology, Edition 3

### COMPARING TYPES OF SHOCK

<table>
<thead>
<tr>
<th>Type</th>
<th>Character</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypovolemic</td>
<td>Hemorrhage, Nausea/Vomitting, or even uncontrolled diuresis can cause a loss of fluid</td>
</tr>
<tr>
<td></td>
<td>↓Intravascular fluid volume = ↓Venous Return = ↓Cardiac Output = Hypotension and infarction</td>
</tr>
<tr>
<td>Cardiogenic</td>
<td>Commonly caused by heart failure (either left or right), acutely from MI or chronically from HTN</td>
</tr>
<tr>
<td></td>
<td>If the pump is broke, cardiac output falls, hypotension results</td>
</tr>
<tr>
<td>Septic</td>
<td>Gram Negative systemic sepsisemia causes a massive vasodilation (IL-1, IL-6, TNF, Lipopolysaccharide)</td>
</tr>
<tr>
<td></td>
<td>Staph Aureus also posses the superantigens associated with toxic-shock syndrome</td>
</tr>
<tr>
<td></td>
<td>Strep Pyogenes also posses the superantigen associated with scarlet fever</td>
</tr>
<tr>
<td></td>
<td>Regardless of pump status, the “tank is too big” and there is not enough fluid to fill it</td>
</tr>
<tr>
<td>Neurogenic</td>
<td>Caused by either trauma (ex. spinal dissection) or drugs (ex. anesthesia)</td>
</tr>
<tr>
<td></td>
<td>Loss of sympathetics causes vasodilation and creating a “tank that is too big,” similar to septic shock</td>
</tr>
</tbody>
</table>

Reorganization of information taken from information in BRS Pathology, Edition 3
### Comparing Types of Emboli

<table>
<thead>
<tr>
<th>Type</th>
<th>Character</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>Commonly a result of deep vein thrombosis resulting in venous embolism to the lungs. Saddle Embolus is a large thrombosis that sits on the pulmonary artery split (is fatal). Pulmonary Infarction, V/Q Mismatch, and Hemorrhagic Infarction are common (See Pulmonary).</td>
</tr>
<tr>
<td>Arterial</td>
<td>Arterial thrombi may occlude flow of blood regardless of embolus status (attached or free). Arterial thrombi are commonly from the mitral valve (pyogenic or not). They usually stop somewhere in the arterial circulation: carotid bifurcation, mesentery, renal artery</td>
</tr>
<tr>
<td>Paradoxical</td>
<td>With the presence of a R→L shunt (see cardio), venous clots can embolize to the systemic circulation</td>
</tr>
<tr>
<td>Fat</td>
<td>Caused by a fracture of long bones or CPR, fat is released into the arterial circulation. Often presents with a shower embolus pattern: multiple small infarcts throughout the affected organ, often the lungs, brain, and skin (petechia)</td>
</tr>
<tr>
<td>Air</td>
<td>This isiatrogenic (IV administration of air) or caused by deep-sea diving (“the Bends”). If the amount of air exceeds the partial pressure allowed for solution, the effect is the same as a clot</td>
</tr>
<tr>
<td>Amniotic Fluid</td>
<td>A condition caused by the introduction of amniotic fluid to the arterial and venous system during delivery. They activate coagulation, resulting in disseminated intravascular coagulation (DIC) and maternal death</td>
</tr>
<tr>
<td>Pyogenic</td>
<td>If there is an infection, usually bacterial, especially of the mitral valve, the friable lesions can break. The infection will disseminate throughout the arterial circulation, resulting in abscess formation and liquifactive necrosis wherever it lands</td>
</tr>
</tbody>
</table>

Reorganization of information taken from information in BRS Pathology, Edition 3

### Pathognomonic Cell Type

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smudge Cell</td>
<td>Chronic Lymphoblastic Leukemia</td>
</tr>
<tr>
<td>Hairy Cell</td>
<td>Hairy Cell Leukemia</td>
</tr>
<tr>
<td>Tear-Drop Erythrocyte</td>
<td>Primary Myelofibrosis</td>
</tr>
<tr>
<td>Bite Cell or Heinz Bodies</td>
<td>G6PD Deficiency</td>
</tr>
<tr>
<td>Ballerina Skirt or Down Cell</td>
<td>Epstein-Barr, Burkitt’s Lymphoma</td>
</tr>
<tr>
<td>Buttock Cell</td>
<td>Follicular Non Hodgkin’s Lymphoma</td>
</tr>
<tr>
<td>Auer Rods</td>
<td>Acute Myelogenous Leukemia</td>
</tr>
<tr>
<td>“Owl Eye” in Lymph = Reed-Sternburg Cells</td>
<td>Hodgkins Lymphoma</td>
</tr>
<tr>
<td>Starry Sky Histology</td>
<td>Burrkit’s</td>
</tr>
<tr>
<td>Cereiform T Cells</td>
<td>Sezary Syndrome</td>
</tr>
<tr>
<td>Flower Pedal Nucleus</td>
<td>HLTV-1 T cell Leukemia</td>
</tr>
<tr>
<td>Howell-Jolly Bodies</td>
<td>Sickle Cell Anemia</td>
</tr>
<tr>
<td>Bence-Jones Protein</td>
<td>Multiple Myeloma</td>
</tr>
<tr>
<td>Spherocytes</td>
<td>Hereditary Spherocytosis or Autoimmune Hemolytic Anemia</td>
</tr>
<tr>
<td>Schistiocytes</td>
<td>Microangiopathic Hemolytic Anemia (TTP/HUS/DIC)</td>
</tr>
<tr>
<td>Target Cells</td>
<td>Thalassemias (any symptomatic, alpha or beta)</td>
</tr>
<tr>
<td>Basophilic Stippling</td>
<td>Lead poisoning (we didn’t do this in this block)</td>
</tr>
<tr>
<td>Ring Sideroblasts</td>
<td>Sideroblastic Anemia</td>
</tr>
</tbody>
</table>

### Translocation to Disease (in order of importance)

<table>
<thead>
<tr>
<th>Translocation</th>
<th>Disease</th>
<th>Protein/Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:22</td>
<td>Chronic Myelogenous Leukemia</td>
<td>BCR-ABL protein</td>
</tr>
<tr>
<td>15:17</td>
<td>Acute Myeloid Leukemia, M3</td>
<td>Retinoic Acid Receptor - PML</td>
</tr>
<tr>
<td>8:14</td>
<td>Burkitt’s Lymphoma</td>
<td>c-MYC</td>
</tr>
<tr>
<td>14:18</td>
<td>Follicular Non Hodgkin’s Lymphoma</td>
<td>BCL-2</td>
</tr>
<tr>
<td>11:18</td>
<td>Marginal Non Hodgkins</td>
<td>H. Pylori Maltoma</td>
</tr>
<tr>
<td>11:14</td>
<td>Mantle Non Hodgkins (lowest yield)</td>
<td>Cyclin D</td>
</tr>
</tbody>
</table>

I made this myself!

---

Owl Club Review Sheets
DIFFERENTIAL BETWEEN B12 AND FOLATE DEFICIENCY

<table>
<thead>
<tr>
<th>B12 Deficiency</th>
<th>Folate Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homocystine and Methyl Malonyl Elevated</td>
<td>Homocystine only elevated</td>
</tr>
<tr>
<td>Long Term Vegans/Pernicious Anemia</td>
<td>Alcoholics</td>
</tr>
<tr>
<td>Neurological Symptoms</td>
<td>No Neuro Symptoms</td>
</tr>
<tr>
<td>Megaloblastic Anemia</td>
<td>Megaloblastic Anemia</td>
</tr>
<tr>
<td>Hypersegmented Neutrophils</td>
<td>Hypersegmented Neutrophils</td>
</tr>
</tbody>
</table>

These are factoids for your Path Block, but you should look at Biochem for your Shelf/Boards to know why.

DIFFERENTIAL BETWEEN ANEMIAS

<table>
<thead>
<tr>
<th></th>
<th>Iron Deficiency</th>
<th>Anemia of Chronic Disease</th>
<th>Thalassemia</th>
<th>Sideroblastic Anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Iron</td>
<td>↓</td>
<td>↓</td>
<td>Normal</td>
<td>↑</td>
</tr>
<tr>
<td>TIBC</td>
<td>↑</td>
<td>↓</td>
<td>Normal</td>
<td>↓</td>
</tr>
<tr>
<td>% Saturation</td>
<td>↓</td>
<td>↑</td>
<td>Normal</td>
<td>↑</td>
</tr>
<tr>
<td>Serum Ferritin</td>
<td>↓</td>
<td>↑</td>
<td>Normal</td>
<td>↑</td>
</tr>
</tbody>
</table>

HODGKINS VS NON-HODGKINS

<table>
<thead>
<tr>
<th>Reed-Sternberg Cell</th>
<th>Hodgkin</th>
<th>NonHodgkin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spread</td>
<td>Present, CD 45 negative but CD30+ and CD15+</td>
<td>No Reed-Sternberg Cells</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Linear and Continuous, often do not get into blood. Uses the Anharbor Staging System</td>
<td>Starts in Lymph tissue but often becomes a leukemia through hematogenous spread</td>
</tr>
<tr>
<td>Distribution</td>
<td>Lots of B Symptoms: Fever, Night Sweats, Weight Loss</td>
<td>Little to no B Symptoms</td>
</tr>
<tr>
<td>Treatment</td>
<td>Radiation, decent prognosis based on staging Can induce Papillary Carcinoma of the Thyroid</td>
<td>Often ineffective without surgical resection. Because it’s a leukemia, prognosis is poor</td>
</tr>
</tbody>
</table>

HISTOLOGY OF BLOOD CELLS

<table>
<thead>
<tr>
<th>Red Blood Cell Line (Myeloid Stem Cells)</th>
<th>White Blood Cell Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocyte</td>
<td>B Cell</td>
</tr>
<tr>
<td></td>
<td>CD Markers are usually the high numbers (CD 15 +)</td>
</tr>
<tr>
<td></td>
<td>Make Antibodies</td>
</tr>
<tr>
<td>Neutrophil</td>
<td>T Cell</td>
</tr>
<tr>
<td>Multi-Lobed Nucleus, Acute Inflammation</td>
<td>CD Markers are usually the low numbers (CD 3,4,8)</td>
</tr>
<tr>
<td>Contain Hydrolytic Enzymes</td>
<td></td>
</tr>
<tr>
<td>Hypersegmented in B12/Folate Deficiency</td>
<td></td>
</tr>
<tr>
<td>Eosinophil</td>
<td>NK Cell</td>
</tr>
<tr>
<td>Bilobed Nucleus, Eosinophilic Granules</td>
<td>Tumor Surveillance cell, CD56 positive</td>
</tr>
<tr>
<td>Basophil</td>
<td></td>
</tr>
<tr>
<td>Bilobed Nucleus, Dense Basophilic Granules</td>
<td></td>
</tr>
<tr>
<td>Macrophage</td>
<td>Phagocytosis of bacteria, IFN-y, has MHC II</td>
</tr>
<tr>
<td>Platelets</td>
<td>Small cytoplasmic fragment of a Megakaryocyte, causes clots to form</td>
</tr>
</tbody>
</table>

First Aid 2009 Page 326 has a good deal of information about the histology of Heme/Onc. While it is not essential information to know in this block, it will make handling cancers (which cells are absent, which are present) much easier if you review the fundamentals of the cells.