Diagnosis / Lab Findings

- During an acute episode may see
  - Peripheral smear – bite cells, Heinz bodies
  - Reticulocytosis
  - Increased indirect bilirubin

- G6PD will be normal or high during an acute crisis
  - Repeat several weeks after an episode to confirm deficiency

- **Blood normal between episodes**
Treatment

- No specific treatment
- Avoid oxidative stressors
  - Treat infections promptly
  - Avoid trigger drugs & fava beans
- Transfusions rarely indicated

"With some fava beans and a nice chianti."
Sickle Cell Anemia

- Autosomal recessive disorder in which abnormal Hgb (Hgb S) leads to chronic hemolysis
- Hgb S sickles under oxidative stress
  - Trouble traversing small blood vessels → occlusion
- In US, 1 in 400 AA births
  - 8% carry SS trait
Clinical Findings

- Issues arise in first year of life → Fetal Hgb falls
- Sickling increases with
  - Dehydration
  - Infection
  - Acidosis
  - Hypoxemia
- Limited life expectancy
  - 40-50 yrs
- Pallor
- Jaundice
- Splenomegaly
- Lower leg ulcers
- Retinopathy
- Gallstones
- Priapism
- AVN -> femoral head
- Infection
  - Strep pneumo
Acute Episodes

- Infarctive/pain crisis
  - Clusters of sickled cells **occlude microvasculature of organs**
  - Last hours to days
  - Severe skeletal pain, fever
  - Not associated with increased hemolysis
- Spontaneous or provoked
- Life threatening
Diagnosis / Lab Findings

- Dx confirmed by Hgb S on electrophoresis
- Chronic hemolytic anemia, with very low Hgb
  - average 7-10 g/dL
- Peripheral smear: sickled cells (5-50% of RBCs)
- Reticulocytosis
- Leukocytosis and thrombocytosis
- Indirect bilirubin high
Treatment

- Folic acid 1 mg daily
- Counsel patient: high altitude, hydration & treat infections promptly
- Vaccinate: pneumonia, flu & meningitis
- Transfuse **only if symptomatic**
  - Exchange transfusions
- Pain crises: fluids, $O_2$, narcotics, antibiotics
- Genetic counseling
- Hydroxyurea – increased HgbF to reduce sickling
- Stem cell transplant – curative, age <17, severe, unresponsive to hydrea, organ damage
Heme Malignancies

- Acute & chronic lymphocytic leukemia
- Acute & chronic myelogenous leukemia
- Lymphoma
- Multiple Myeloma
Acute Leukemias

- Characterized by unregulated production of immature cells (blasts), resulting in marrow replacement and hematopoietic failure.

- Classified by cell type
  - Myeloid or lymphoid

- Risk Factors
  - Family history, exposure to ionizing radiation, benzene, certain alkylating agents (chemo)
Acute Leukemia

**Acute Lymphocytic Leukemia (ALL)**
- 90% are children (peak = 3-7 yrs)
- 10% are adults
- **Remember: “ALL = almost ALL kids”**

**Acute Myelogenous Leukemia (AML)**
- 90% are adults, median age = 60 yrs
- 10% children

- **ALL > AML**
Clinical Findings

- Fast onset of symptoms (days to weeks)
- Fatigue
- Infections
- Lymphadenopathy
  - ALL > AML
- Bleeding and bruising
- Petechiae
- Swollen gums
- Mediastinal mass (ALL)

- Fever (abrupt onset with kids)
- Bone pain
- Weight loss
- Lethargy
- Dyspnea
- Meningitis
- Headache
- HSM
Diagnosis / Lab Findings

- **Hallmark** = pancytopenia & circulating blasts
  - Bone marrow with >20% blasts = diagnostic
- Severe anemia & thrombocytopenia
- WBC are usually high (blasts)
- Peripheral smear
  - Auer Rods (AML)
Treatment

- Chemotherapy to eradicate leukemic cells
- Prophylaxis for tumor lysis syndrome
  - Reduce uric acid levels with allopurinol & hydration
- Bone marrow transplant for poor responders

Prognosis

- 50% of children with ALL can be cured
- 70% of adults <60 years achieve remission
  - Cure in 30-40%
Chronic Lymphocytic Leukemia (CLL)

- Malignancy of B lymphocytes, characterized by immunosuppression, marrow failure and progressive organ infiltration

- Most common of all leukemias
  - Men > women
  - Incidence increases with age (~ 65 yrs)

- Insidious onset
  - Slow progression over years or decades
Clinical & Lab Findings

- Usually indolent course
  - 25% asymptomatic
- Lymphadenopathy
- Splenomegaly
- Recurrent infections
- Fatigue
- Night sweats

- CBC $\rightarrow$ lymphocytosis
  - WBC > 20,000
  - Anemia
  - Thrombocytopenia

- Peripheral smear
  - Smudge cells
  - Pathognomonic
Treatment

- Conservative → observation & supportive
- **Not curable**
- Criteria for treatment:
  - Recurrent infections
  - Significant cytopenias
  - Bulky lymphadenopathy
  - Significant symptoms
  - High risk disease
Chronic Myelogenous Leukemia (CML)

- Myeloproliferative disorder in which results in unregulated production of granulocytes (WBC)
  - Slowly progressive, indolent course
  - Occurs in 3 phases
    - Chronic, accelerated, acute (blast crisis)
    - Inevitable transformation to acute disease

- Presents in young – middle aged adults (median 55)
Clinical & Lab Findings

- Fatigue
- Anorexia & weight loss
- Fevers
- Night sweats
- Abdominal fullness
  - Splenomegaly
- Leukocytosis
  - WBC >150K!
- Philadelphia chromosome (+)
- BCR-ABL gene mutation
- Anemia
- Thrombocytopenia
Treatment

- Tyrosine Kinase Inhibitors - long term remissions now possible
  - Imatinib (Gleevec)

- Allogeneic transplant is only known curative treatment

- Prognosis:
  - 5 year survival 80% (overall)
Non-Hodgkin’s Lymphoma

- Group of malignancies that arise from lymphocytes
  - 90% from B lymphocytes
  - Increased incidence in HIV+
  - Peaks between 20-40 yrs old, all ages affected

- Many different subtypes

- Can be indolent or high grade
  - Indolent often converts to aggressive disease
Clinical & Lab Findings

- Diffuse or isolated, painless lymphadenopathy
- Fever & night sweats
- Weight loss
- Pruritus
- Fatigue
- Extralymphatic sites
  - GI tract, skin, bone, bone marrow
  - Bulky nodes → SVC syndrome, jaundice, etc

- Lymph node biopsy required!
- Staging by PET/CT scans & bone marrow biopsy
- Serum LDH useful marker
Treatment

- Dependant upon subtype
  - Can include
    - Surgery
    - Chemotherapy (+/- biologic therapy)
    - Radiation
    - Bone marrow transplant for high risk or aggressive disease

- Prognosis
  - Median survival for indolent lymphomas 6-8 yrs
  - Less for aggressive varieties
Hodgkin Disease

- Group of cancers characterized by enlargement of lymphoid tissue, spleen and liver
  - Epstein-Barr virus (40-50% of cases)

- Typically arises in single area, and spreads contiguously

- Several subtypes → **nodular sclerosing** most common

- Ages 15-45 (**peaks in 20’s**), and again after age 50
  - Men > women in younger age group
Clinical & Lab Findings

- **Painless adenopathy**
  - Cervical, supraclavicular or mediastinal
  - alcohol
- **B symptoms**
  - Fever, night sweats, weight loss, pruritus, fatigue
- Rarely in extranodal sites

- Lymph node biopsy
  - **Reed-Sternberg cells** = confirm the diagnosis
- Staging with PET/CT scans and bone marrow biopsy
- Elevated sed rate
- CBC can be abnormal
Treatment

- Limited stage, low-risk disease
  - Radiation alone
- More advanced stage or more aggressive
  - Chemotherapy

- Prognosis is very good!
  - Chemo cures >50%, even with advanced stage
  - Low risk disease, 10 yr survival >80%
Multiple Myeloma

- Malignancy of plasma cells
  - Replacement of bone marrow → failure
  - Lytic lesions → bone destruction
    - Pathologic fractures
    - Hypercalcemia
  - Recurrent infections
  - More prone to blood clots due to hyperviscosity
  - Renal failure

- Median age: 65 yrs
Clinical & Lab Findings

- Fatigue
- Bone pain
  - Back, ribs
- Night sweats
- Anemia
- Elevated creatinine
- Elevated calcium
- Proteinuria
- Serum or urine protein electrophoresis
  - Monoclonal spike (abnormal protein)
  - IGG, IGA, light chain
- Bone marrow biopsy
- Skeletal survey
  - Lytic lesions
- Peripheral smear
  - Rouleaux formation
Rouleaux Formation
“stack of coins”
Diagnosis

- **Classic triad**
  - Monoclonal protein in serum or urine
  - Lytic lesions in bone
  - Plasmacytosis on bone marrow biopsy
    - atypical

- Important to distinguish myeloma from MGUS (monoclonal gammopathy of unknown significance)
Treatment

- Treatable, but not curable
- Chemotherapy, biologics, radiation for bone pain
  - Bisphosphonates

Prognosis
- Median survival with chemo – 3 yrs
- Some patients may be candidate for transplant
  - Not curable, but can offer a remission for a period of time
Coagulation Disorders

- Clotting factor disorders
- Thrombocytopenia
  - Idiopathic thrombocytopenic purpura (ITP)
  - Thrombotic thrombocytopenic purpura (TTP)
- Hypercoagulable states
Bleeding Disorders

- Due to issues with platelets or clotting factors
  - Congenital or acquired

- Congenital
  - Usually involve a single defect
    - Platelet function, coagulation, fibrinolytic system, vascular integrity

- Acquired
  - Usually a systemic issue
    - Liver, kidneys, collagen vascular system, immune system
  - Malignancy, infection, shock, obstetric complications, drugs (NSAIDs, ASA, heparin, anticoagulants), SLE, CLL
Clinical Features

- If bleeding due to platelet problem
  - Skin and mucosa involved
    - Epistaxis, gum bleeding, petechiae, menorrhagia

- If bleeding due to clotting factor problem
  - Skin and muscles involved
    - Hemarthrosis
Lab Studies

- CBC → assess platelet count
- Peripheral smear
  - Platelet clumping
- Bleeding time → assess platelet function
  - Platelet function assay used more often now
- Protime (PT), partial thromboplastin time (PTT)
  - “Pitt’s Pet” → PTT (intrinsic), PT (extrinsic)
- Thrombin clotting time
  - Rate of conversion fibrinogen → fibrin in presence of thrombin
Thrombocytopenia

- Most common cause of abnormal bleeding
- Platelet count <150,000
  - Serious bleeding risk <20,000

- Due to
  - Decreased production
  - Increased destruction
  - Splenic sequestration
ITP – Idiopathic Thrombocytopenic Purpura

- **Autoimmune** mediated disorder causing platelet destruction
  - Acute – often in kids after **viral illness**
  - Chronic – often young **women** with autoimmune d/o
    - Can occur at any age, peak 20-50 yrs

- Both can have petechiae, purpura on skin & mucous membranes
- **No splenomegaly**
Lab Findings

- Acute ITP
  - Platelet count 10 – 20K
- Chronic ITP
  - Platelet count 25-75K
- Mild anemia
  - More severe if autoimmune hemolytic anemia (10%)
- Coagulation studies normal
Treatment

- Acute ITP – often resolves spontaneously
  - Steroids (avoid in kids)

- Chronic ITP- rarely resolves spontaneously
  - High-dose prednisone
  - Splenectomy
  - IVIG
  - Platelet transfusions prn

- Avoid platelet antagonists (aspirin)
TTP – Thrombotic Thrombocytopenic Purpura

- Rare, often fatal – 90% mortality if untreated
- Platelet consumption syndrome
  - ADAMTS-13 deficiency → autoantibodies
- Previously healthy individuals
  - Women > men
  - Ages 20-50
  - HIV
  - Precipitated by estrogen, pregnancy, drugs
Clinical & Lab Findings

- Purpura & petechiae
- Pallor
- Fever
- Abdominal pain
- **Abnormal neurological signs**
- Renal failure
- Severely low platelets (<20K)
  - Intravascular aggregation / thrombus
- Microangiopathic hemolytic anemia
  - Schistocytes
  - ↑ LDH, indirect bilirubin
  - Coombs test (-)
- Coagulation tests normal
Differential Diagnosis

- HUS – hemolytic uremic syndrome
  - Often in kids after infectious diarrhea, but can also see in pregnancy & estrogen
  - Low plts, anemia, renal failure, but NO neuro symptoms

- DIC – disseminated intravascular coagulation
  - Causes generalized hemorrhage → shock
    - Severe underlying illness (sepsis, cancer, transfusion rxn)
  - Evidence of coagulopathy (abnormal coags), low plts, hemolytic anemia
  - Thrombosis
TTP - Treatment

- Emergent plasmapheresis
  - Improves survival from 10% to around 80%
Clotting Factor Disorders

- Von Willebrand’s disease
  - **Most common congenital bleeding disorder**
  - vWF helps platelet adhesion & carrier for Factor VIII
  - 3 types: 75% have mildest form, Type 1
  - Men & women
  - Mucosal bleeding (nose, vaginal, GI), bruising, heavy post-op bleeding
- Labs
  - Prolonged bleeding time
  - Low vWF (might have low factor VIII as well)
- Treat with desmopressin (DDAVP) or Factor VIII concentrate
Hemophilia A

- “Classic” hemophilia, factor VIII deficiency
- Hereditary
  - X-linked, recessive
  - Excessively prolonged bleeding time
  - Spontaneous hemorrhages
    - Joints, GI, brain, soft tissue, epistaxis
- Labs: PTT prolonged, other coags normal
- Treatment
  - Infusion of factor VIII concentrates
  - Desmopressin for mild disease
Hypercoaguable States

- Causes
  - Congenital
    - Factor V Leiden, Protein C or S deficiency, anti-thrombin III deficiency, activated protein C resistance
  - Acquired
    - Malignancy, pregnancy, immobilization, intravascular devices, DIC, antiphospholipid syndrome, UC/Crohn’s, estrogens/OCPs
  - Heparin
    - Thrombocytopenia & thrombus
  - Lupus anticoagulant
Predisposing Factors

- Things to make you go *hmmmmmm*...
  - Family history of clot
  - Recurrent clot
  - Repeated clot despite adequate anticoagulation
  - Venous clot involving neck/arm/abdomen or arterial clot

- Clinical findings
  - Typical for venous or arterial thrombus

- Labs
  - PTT prolonged
  - Specific for suspected issue
Treatment

- Standard anticoagulation for thrombotic event
  - LMWH or warfarin
- No prophylaxis for at-risk person without history of clot
- Prolonged/life-long anticoagulation for at-risk person with history of clot
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