Anemia 3

Aplastic anemia (AA)

- Depletion of the myeloid stem cell
  - Extrinsic factor: Antigen cross reactivity — activated T-lymphocytes destroy stem cells
  - Intrinsic factors: inherited defect in telomerase — Thus expressing abnormal antigens on stem cells surface causing attraction of T-cells.
- Peripheral blood pancytopenia, with normochromic or macrocytic anemia
- Low reticulocytes
- Decreased hematopoietic cells in the BM

Fanconi anemia

- Rare inherited form of AA
- Defect in DNA repair proteins
- Develop AA & acute leukemia

Pure red cell aplasia

- Only erythroid cells are absent
- Congenital: diamond-blackfan anemia
- Aquired: autoimmune, parvovirus B19

Myelophthisic anemia

- Infiltation of BM causing physical damage to hematopoietic cells
- Causes
  - Cancer
  - Granulomatous disease: TB
  - Storage disease: Gaucher
- Immature granulocytes and erythroid precursors in the peripheral blood
- General symptoms, thrombocytopenia, neutropenia

Renal disease

- Low EPO from the kidney
  - Low RBC production
  - Low reticulocytes
- Abmornal platelets function
- Echinocytes (Burr cells)
- Doesn't correlate with kidney function

Liver disease

- Decrease syn. Of clotting factors & transferrin
- Bleeding from varices
- Acanthocytes (Spur cells)

Hypothyroidism

- Thyroid hormones stimulate erythropoiesis & EPO production
- Normocytic but can be macrocytic

Myelodysplastic syndrome

- Aquired, in old age
- Mutation of BM stem cells — Prolonged survival & defective maturation
- RBCs are macrocytes
- Anemia refractory to treatment

Hemolytic

- RBCs life span <120 days
- Hypoxia triggers EPO release
  - Erythroid hyperplasia in BM — Extramedullary hematopoiesis in severe cases
  - Peripheral blood reticulocytosis
  - Hg released from damaged RBCs — Hg bind to haptoglobin — Causing decrease in serum haptoglobin
- Site of hemolysis
  - Extravascular (in the spleen), causing: — Jaundice, pigmented gallbladder stones, splenomegaly
  - Intravascular (in the blood stream), causing — Sudden release of. Hg, hemoglobinemia, hemoglobinurea, hemosiderinurea, iron deficiency
- The cause of hemolysis
  - Extracorpuscular
  - Intracorpuscular

Thalassemia

- Inherited, decreased alpha or beta chain production
- Hg is below the normal
  - The deficiency in one of globin chains results in a relative increase in the other one, excessive unpaired chains will cause instability and hemolysis
- Autosomal recessive
- Patients are resistant to be infected by malaria falciparum
- Normal Hg types in adults
  - HgA
  - HgA2
  - HgF
- Genetics
  - Alpha chain (deletion)
    - Alpha is encoded by 2 genes on chromosome 16
    - Deletion of 1,2 genes — Silent carrier
    - Deletion of 4 genes — Hydrops fetalis
    - Deletion of 3 genes — Hg-H disease
      - Hg-H — Extra beta chains
      - Hg-Barts — Extra gamma chains

      Both have high affinity to oxygen
  - Beta chain (point mutation)
    - Beta is encoded by a single gene on chromosome 11
    - B/B+: slient carrier or mild anemia (Thal-minor) (trait)
    - B+/B+: thalassemia intermedia
    - B0/B0 or B0/B+: thalassemia major (Cooley anemia)

      Extra α-chains remain uncoupled, causing hemolysis of RBCs and precursors (ineffective erythropoiesis)
- Morphology
  - Hypochromic microcytic
  - Target cell
  - Basophilic stippling
  - Reticulocytosis
  - In thal major
    - In peripheral: Poikelocytosis, nucleated RBCs
    - In BM: ⬆️ normoblast, filling BM spaces & expanding into the bone, hemosiderosis
- Clinical symptoms
  - Traits are asymptomatic, normal life span, (premarital test is important)
  - Major: symptoms begin after age of 6 months, general sym., growth retardation, skeletal abnormalities, and both are ameliorated (improved) by regular blood transfusion
  - Intermedia and Hg-H disease: moderate anemia, don't require blood transfusion
  - Systemic hemochromatosis & related organ damage: in 2nd or 3rd decade of life
- Diagnosis — By gel eletrophoresis
  - In all beta thal: ⬆️ HgA2, HgF percentages
  - In beta thal major: HgA is absent or ⬇️
  - In HgH disease: HgH & Hg Barts bands appear
  - In alpha thal carrier & minor: NO abnormality is found — So we do genetic test

Sickle cell anemia

General info.

- Most common hemolytic anemia worldwide
- Resistant to malaria falciparum
- Autosomal recessive
- Glutamic acid ➡️ valine in beta chain
- Hg electrophoresis
  - Sickle cell disease (homozygous)
    - HgS is found, HgA is absent
  - Sickle cell carrier (heterozygous)(asymptomatic)
    - Both HgS & HgA are presented

Pathogenesis

- In deoxygentated case: HgS tents to polymerize in a longitudinal pattern
  - Causes distorting cell shape & creat sickle shape
- This change is reversible by reoxygenation
  - But with repeated sickling, the cell membrane is damaged and hemolysis occurs
- HgS polarization is inhibited in the presence of:
  - HgA
  - HgF in newborns
- When alpha thalassemia is presented too, the sickling is decreased
- Sickled RBCs take longer time to pass through capillaries
- They may adhere to the endothelial cells making a thrombus
- Sickled cells are removed by macrophages in spleen (extravascular hemolysis)

Clinical symptoms

- Chronic moderate severe hemolytic anemia
  - Manifesting after the age of 6 months
- Vaso-occlusive crisis
  - Results in organ infarction
- Hand-foot syndrome
- Acute chest syndrome
- Stroke
- Myocardial infarction
- Retinopathy
- Autosplenectomy
- Aplastic crisis
  - Infection by parvovirus B19
- Susceptibility for encapsulated bacteria

Diagnosis

- Blood smear
  - Adding hypoxic agent
- Hemoglobin electrophoresis
- DNA testing

Glucose-6-phosphate dehydrogenase (G6PD) deficiency

- X-linked inheritance
  - Males are more affected
- Intravascular hemolysis
- Triggers of hemolysis
  - Infection
  - Drugs
    - Sulfonamides
    - Nitrofurantoin
    - Vit K
    - Primaquine
    - Large dose of aspirin
  - Fava beans
- Characteristics
  - Heinz bodies (we need supravital stain to see them)
  - Bite cells
- Clinical symptoms
  - G6PD-A: ⬇️ G6PD, BM compensate by producing new RBCs.
  - G6PD- Mediterranean: qualitative defect of enzyme
    - More severe symptoms
  - Females can be affected if random inactivation affects the normal X-chromosome

Immune hemolytic anemia (IHA)

- The presence of auto-antibody against RBC membrane protein
- The antibodies are detected by Coombs test
  - Direct Coombs: — RBCs from the patient are incubated with antibodies that target normal human antibodies
  - Indirect Coombs — Patients serum is added to test RBCs that have certain surface proteins
- Types
  - Warm
    - High affinity IgG
    - In core circulation 37o
    - Removed by macrophages in the spleen (extravascular hemolysis)
    - Spherocytes
    - 60% are idiopathic, 25% with SLE, 15% by drugs (alpha-methyl dopa, penicillin)
    - Mostly: mild chronic anemia, splenomegaly
  - Cold
    - Low affinity IgM — Then RBCs bind also to C3b molecule
    - In peripheral areas 30o
    - When RBCs return to core circulation — IgM dissociates, but the C3b stays — Cells are indentified by splenic macrophages and removed
    - Raynaud phenomenon in small vessels
    - Transient: occur in recovery of infections by mycoplasma pneumonia & infectious mononucleosis — Mild, self limited
    - Chronic: in B-cell lymphoma or idiopathic