ANEMIAS

ABSOLUTE RETIC COUNT

Low <2% or <75,000 → **HYPOPROLIFERATIVE** Problem with RBC production

- **Microcytic** MCV<80
  - Iron deficiency
  - Thalassemias
  - Lead poisoning
  - Chronic Disease
- **Normocytic** MCV 80-100
  - AOCD
  - Renal Failure
  - Aplastic anemia
- **Macrocytic** MCV>100
  - Pernicious Anemia
  - B12-deficiency
  - Folate deficiency

High >2% or >100,000 → **HYPERPROLIFERATIVE** Good marrow response but ↑RBC loss

- **Hemorrhage** blood loss
- **Hemolysis** RBC destruction
  - **Hereditary**
    - G6PD deficiency
    - Sickle cell
    - Thalassemias
    - Hereditary Spirocytosis
  - **Acquired**
    - Autoimmune hemolytic anemia
    - DIC
    - TTP
    - HUS

Causes of hypoproliferative anemia

- acute blood loss or destruction
- nutritional
- bone marrow depression/failure
- defective RBC production
- destruction of marrow erythroid precursors
- replacement of normal bone marrow

IRON-DEFICIENCY ANEMIA

Epidemiology: pregnant woman, toddlers (9%) and adolescent girls (16%)
Etiology: blood loss
Clinical Presentation: pica and thrombocytosis
Diagnostic Mechanism: CBC. Ferritan. Iron studies.
Diagnostic Results: ↑RDW, ↓MCV, then ↓hgb ↓hct.
Ferritan <15.
↓serum iron, ↑TIBC, ↓transferin saturation
Treatment: treat underlying cause. Treatment of choice = oral iron replacement.

ANEMIA OF CHRONIC DISEASE

Epidemiology: affects people who have conditions that cause inflammation.
Etiology: ↑hepcidin → ↓iron absorption
Lab results: ↓serum iron, ↓TIBC, – or ↑ferritan
↓MCV ↓hgb ↓hct

Epidemiology:
Etiology:
Clinical Presentation:
Diagnostic Mechanism:
Diagnostic Results:
Treatment:

LEAD POISONING

Epidemiology: slightly higher in males. Incidence decreasing.
Etiology: workplace exposure. Unintentional ingestions.
Clinical Presentation: microcytic anemia and basophilic stipping of RBCs (gain granules)
Diagnostic Mechanism: direct measurement of blood lead.
Diagnostic Results: >10 = impaired development. >70 = severe poisoning. ↓MCV and ↓hgb. Basophilic Stipping.
Treatment: edetate calcium disodium (EDTA) IV. Oral chelator if minor.

MEGALOBLASTIC ANEMIAS

Defect in DNA synthesis.
- ↑MCV and immature nucleus

B12 DEFICIENCY ANEMIA

Etiology: ↓intake or absorption, diseases (crohns, etc)
Clinical Presentation: Neurological symptoms
Diagnostic Mechanism: anemia is presenting symptom
peripheral smear and CBC
Diagnostic Results: ↓B12, ↑homocysteine, ↑methylmonic acid | hypersegmented (>6) PMN
Treatment: IM B12 injections | treat underlying cause

FOLATE DEFICIENCY

malnutrition, malabsorption, drugs

daily oral folate

APLASTIC ANEMIA

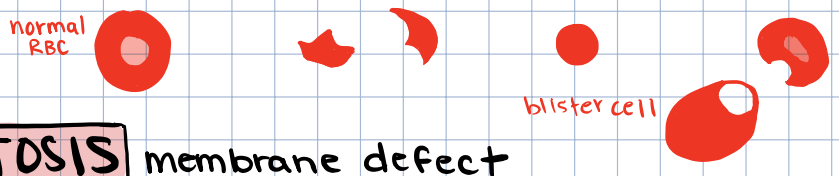
pancytopenia in the peripheral blood, with BMBx showing hypercellularity, arising from a deficiency of hematopoietic stem cells.

Etiology: Inherited. Autoimmune. 50% idiopathic (radiation, chemo, benzene exposure, EBV, chloramphenicol drug)
Clinical Presentation: Symptoms of anemia, low platelets (bleeding/bruising), and low neutrophil (infections)
Diagnostic Mechanism: rule out other causes of pancytopenia. Bone marrow biopsy → hypocellularity <25%.
Diagnostic Results: absolute neutrophil count <500. Platelet count < 50,000. Retic count <50,000.
Treatment: supportive (transfusion, EPs), definitive, and T-cell directed immunosuppression.
↳ SCT (if young and otherwise healthy) ↳ antithymocyte globulin (ATG) and cyclosporine

HEMOLYTIC ANEMIAS

decreased RBC lifespan

General clinical features: jaundice, ↑risk of gallstones, splenomegaly, aplastic crisis w/ parvovirus 19, and ↑folate requirement.
Laboratory evidence: evidence for ↑RBC production → ↑retic count
evidence for ↑RBC destruction → ↑LDH ↑bili ↓haptoglobin
morphologic evidence of RBC damage → schistocytes, spherocytes, bite cells



CONGENITAL

HEREDITARY SPHEROCYTOSIS

membrane defect

Epidemiology: most common defect leading to anemia. 1/5000 Europeans. Autosomal dominant.
Etiology: defect in proteins of the membrane skeletin (spectrin or ankyrin)
spherocyte formation due to progressive loss of membrane and surface area.
Clinical Presentation: increased hemolysis and abdominal pain with trivial illnesses.
Diagnostic Mechanism: peripheral smear. Flow cytometry using ESM (eosin 5'maleimide)
Diagnostic Results: Spherocytes → more prone to lysis. ↑free hgb
Treatment: folate supplementation. Splenectomy if refractory/symptomatic.

G6PD DEFICIENCY

enzymatic defect

Heinz bodies → bite or blister

Epidemiology: X-linked. In Africans, protein loses activity with age. Mediterranean - baseline low activity.
Etiology: hemoglobin loses protection from oxidative damage → denatured → precipitate as Heinz bodies.
Clinical Presentation: max anemia 7-10 days after exposure. ↑retics - body compensates

Diagnostic Mechanism: peripheral smear. Measurable blood test.

Diagnostic Results: bite or blister cells.

Treatment: supplement folate. Avoid oxidant agents (sulfa drugs, vit K, fava beans, mothballs, anti-mal)

IMMUNE-MEDIATED HEMOLYSIS

acquired hemolytic anemia

AUTOIMMUNE

	WARM ANTIBODIES	COLD ANTIBODIES
Epidemiology	NA	Idiopathic, infection, lymphoproliferative disease.
Etiology	IgG against RBCs at 37° → NO agglutination	IgM against RBCs at <32° → agglutination
Clinical Presentation	Splenomegaly, jaundice, ± anemia	Ischemia in extremities.
Diagnostic Mechanism	Coombs Test - IgG or C3 bound DIRECTLY to RBC Peripheral Smear	Coomb's Test Peripheral Smear
Diagnostic Results	+ coomb's - direct and indirect. +IgG. ± C3 Spherocytes ↑reticulocytes. ↑bili. ↑LDH.	+ coomb's test. Doesn't tell you cold vs. warm RBC agglutination (clumping)
Treatment	Mainstay = immunosuppression. corticosteroids ± rituximab RBC transfusion, if symptomatic.	Keep patient warm. Blood and IV fluids warmed. steroids + splenectomy → ineffective. Rituximab ✓

Spherocytes

Clumping

THALASSEMIAS

Heinz bodies

BETA

Epidemiology: most common in southern Europe. SE Asia, Africa, middle east. Mediterraneans. ← Transfusion-dependent

Etiology: mutations (β^0 - absent Bglobin synthesis. β^+ - decreased production.)

Clinical Presentation: anemia, splenomegaly, bony deformities, iron overload (bronze skin and liver failure) ← due to transfusion and ↑RBC

Diagnostic Mechanism: hemoglobin electrophoresis.

Diagnostic Results: α_4 tetramers. Absent (or deficient) normal hgbA. Microcytic. ↑RBC.

Treatment: turn off erythropoietan. Gene therapy. Get iron out of body.

ALPHA

Epidemiology: SE Asia and West Africa.

	$\alpha\alpha/\alpha-$	Asians: $\alpha\alpha/--$ OR $\alpha-/\alpha-$	African Americans (5-7%): $\alpha-/--$ HgH
		← cis deletion ← trans deletion	
Etiology:	one alpha gene deletion		By tetramers → Heinz bodies
Clinical Presentation:	Silent. Not anemic.	Mild anemia.	Variable. Splenomegaly
Diagnostic Mechanism:	Hgb electrophoresis normal	Hgb electrophoresis normal	Peripheral Smear
Diagnostic Results:	Minimal microcytosis	Microcytosis with MCV ~ 70	Bite cells ↓Hgb ↓MCV ↑RDW
Treatment:	not treated	Not treated	

HYDROS FETALIS: $--/--$. No alpha chains form.

- Predominant chain synthesized is γ_4 tetramers = Hemoglobin Barts.
- Interuterine death.

Treatment: in utero by exchange transfusions or in utero bone marrow transplantation.

SICKLE CELL DISEASE

Epidemiology: 1/12 AAs carry trait. 1/500 have disease. 1/1000-5000 hispanic-Americans. Middle east, Mediterranean, India.

Etiology: missence mutation in 6th AA in Bchain forms HbS.
Hypoxia and acidosis → HbS polymerizes and cells sickle. Eventually become irreversibly sickled → obstruct vessel.
SS = sickle cell anemia. SC = more mild. Sβ-thal = β° indistinguishable from SS. Sβ⁺ = more mild.

Clinical Presentation: hematologic → anemia, leukocytosis, thrombocytosis.
- by adulthood, functionally asplenic (howell-Jolly bodies and infections)
- thromboses → increased risk for venous clots

Sickle cell crises → splenic sequestration - massive splenomegaly and hypovolemic shock
aplastic crisis - parvovirus19 leads to marrow suppression
painful (episode) crisis - painful episodes of acute vascular occlusion

acute chest syndrome → hypoxemia, new infiltrate, new fever, chest pain, dspnea.
- most freqvent cause of death.

pulmonary hypertension

stroke → median age = 5. Due to disordered blood vessels.

Diagnostic Mechanism: hemoglobin electrophoresis

Diagnostic Results:

Treatment: hydroxyurea - increases HbF decreasing HbS. AE - bone marrow suppression. Not used if preg.
exchange transfusion - Stroke
Simple transfusion - acute chest or pre-operative.
antibiotics and oxygen for acute chest

THROMBOCYTOPENIA

too few platelets

Underproduction

- **marrow failure**: myelodysplasia, aplastic anemia, vit deficiency
- **marrow infiltration**: tumor, granulomatous, fibrosis, leukemias, lymphomas
- **marrow toxins**: drugs, radiation, infection, alcohol

Peripheral Destruction

- **Non-Immune**: DIC, TTP
  Schistocytes
- **Immune**: Antibody-mediated

Splenic Sequestration

DISSEMINATED INTRAVASCULAR COAGULATION

Schistocytes

Epidemiology: NA

Etiology: abnormal activation of coagulation, consumption of clotting factors, destruction of platelets and activation of fibrinolysis. Triggered by ↑TF in wrong place.

Clinical Presentation: oozing, bruising, sepsis

Diagnostic Mechanism: PT and aPTT. CBC. Peripheral Smear.

Diagnostic Results: ↑PT, ↑aPTT, ↓platelets, ↓fibrinogen, ↑D-dimers, schistocytes

Treatment: underlying cause. Transfusion of platelets, clotting factors, or fibrinogen.

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

Schistocytes

Epidemiology: Sporadic. Autoantibody / inhibitor against protease.

Etiology: absense/deficiency of ADAMTS 13 protease that cleaves vWF. UL multimers bind platelets and make platelet plugs in microvasculature.

Clinical Presentation: PENTAD - MAHA, low platelets, fever, neurologic manifestations, renal manifestations

Diagnostic Mechanism: CBC. Peripheral smear. Measure activity levels of ADAMTS-13.

Diagnostic Results: ↓platelets. Schistocytes. ↑LDH and ↑bili.

Treatment: plasma exchange AVOID platelet transfusion.

HEMOLYTIC UREMIC SYNDROME (HUS)

Epidemiology: seen more in pediatrics → better prognosis

Etiology: precipitated by diarrheal illness (E.coli O157:H7 or shiga toxin)

Clinical Presentation: ↓neurological sequelae. ↑renal manifestations. Usually starts w/ bloody diarrhea.
atypical HUS → without diarrheal prodrome. Needs two hits.

Diagnostic Mechanism:

Diagnostic Results:

Treatment: eculizumab and PLEX

HIT Heparin-induced Thrombocytopenia

Epidemiology: 1/3 pts treated with heparin. Older pts and after orthopedic surgeries.

Etiology: caused by antibodies against complex of heparin/PF4.

Clinical Presentation: can lead to thrombosis

Diagnostic Mechanism: CBC

Diagnostic Results: ↓Platelets on heparin.

Treatment: STOP heparin.

ITP Immune/idiopathic thromocytopenia purpura

Epidemiology:

Etiology: provoked by viral illness in children.

Clinical Presentation: isolated thrombocytopenia

Diagnostic Mechanism: No diagnostic test

Diagnostic Results: diagnosis of exclusion.

Treatment: In adults, specific therapy if platelet < 20-30 OR bleeding.
First line = corticosteroids. IVIg if platelet <10K OR bleeding.
Second line = rituximab to kill CD20+ cells. Splenectomy.