# ANEMIAS

## MICROCYTIC
MCV < 80 fL

### Hemoglobin Defects

**Defective Heme Synthesis**

STRIKING RBC VARIATION
**IRON DEFICIENCY (late)**
Dx: ↓iron, ↑TIBC, ↓ferritin
Sx: glossitis, cheilosis, Plummer-Vinson (anemia, dysphagia, esophageal webs)

**LEAD POISONING** (some iron defs)
lead → ferrochelatase, ALA D
→ ↓ Heme, ↑ RBC protoporphyrin
Tx Dimercaprol, EDTA, succimer
* Basophilic stipling

**SIDEROBLASTIC ANEMIA**
↑iron, +/- TIBC, ↑ferritin
* Prussian Blue mitochondria
Tx: Pyridoxine (B6)

**ANEMIA of CHRONIC DISEASE**
Tx: underlying cause, blood transfusions, EPO

**Defective Globin Chain**

**α-THALASSEMIA** AFR
αα dd – minima (del α-globin)
αd – – minor
α – – – HbH → β4
– – – – Barts (death)

**β-THALASSEMIA** MED
mut → ↓β-globin
anisopoikilocytosis, "crew-cut" skull X-ray, "chipmunk" facies

* low reticulocytes

## NORMOCYTIC
MCV 80-100 fL

### Non-Hemolytic
reticulocytes ≤ 2%

**IRON DEFICIENCY (EARLY)**
Dx: ↓iron, ↑TIBC, ↓ferritin
Bone Marrow: no blue (Prussian) iron granules
Cells: hypochromic, target
Sx: pallor, pica, koilonychia (spoon nails)
Tx: ferrous sulfate + vit C

**ANEMIA OF CHRONIC DISEASE**
Labs: ↓iron, ↓TIBC, ↑ferritin
inflammation → ↑hepcidin
Associations: RA, SLE, neoplasm, CKD

**APLASTIC ANEMIA**
[pancytopenia + low blasts / hypocellular bone marrow / fat in bone marrow]
Sx: bleed/bruising, fatigue, infections
Tx IV Ab w/ culture if neutropenic fever
Tx immunosupp, alloSCT if <40

**CHRONIC KIDNEY DISEASE**
see Anemia of Chronic Disease shown above
LOW EPO → LOW RBCs

* cancers can also metastasize to bone marrow
* infections, e.g. fungal can directly invade bone marrow

### Hemolytic
reticulocytes > 2%

#### Intrinsic

**Membrane Defects**

**HEREDITARY SPHEROCYTOSIS** AUT DOM
gallstones!
small round RBCs, jaundice, ↑osmotic fragility, ↑spleen
no central pallor (↑MCHC)
Tx: splenectomy
Dx: microspherocytes

**PAROXYSMAL NOCTURNAL HEMOGLOBINURIA** RARE post-viral in kids
C3d + intravascular RBC lysis
Associations: untreated syphilis, acute leukemia, aplastic anemia
Dx: hemoglobinuria post-cold Donath-Landsteiner Test

**Enzyme Deficiencies**

**G6PD DEFICIENCY** AFR X-linked, Rec
→ ↓glutathione → ↓NADPH
→ RBCs prone to oxidative stress
sulfa drugs, fava, antimalarials, infection, etc
Back pain, hemoglobinuria, Heinz bodies, Bite cells

**PYRUVATE KINASE DEFICIENCY** AUT Rec
→ ↓ATP → Rigid RBCs
→ extravascular hemolysis
→ ↑2,3-BPG → ↓$O_2$ affinity
* hemolytic anemia in newborn

**Hemoglobinopathies**

**SICKLE CELL ANEMIA** AUT Rec
HbS point mut GLU → VAL in β chain → hemolysis (both) deox HbS polymerizes → sickle cells
"crew cut" skull xray
Dx hemoglobin electrophoresis
Tx hydroxyurea, hydration

**HbC DISEASE**
point mut GLU → LYS in β chain → extravascular hemolysis
Lab: hemoglobin crystals, target cells

Risks:
- autosplenectomy
- splenic sequestration → encapsulated infections
- vaso-occlusive crisis → priapism, dactylitis, acute chest syndrome, avascular necrosis, stroke

* HbSC (one of each mut) = milder than HbSS

• = micro spherocytes (many) as primary abnormality

#### Extrinsic

**AUTOIMMUNE** • AIHA
Warm (IgG+) - chronic
← drugs e.g. methyldopa, SLE, CLL, Rh
Cold (IgM, C3d+) - acute
← mycoplasma pneumonia, mono, CLL
coombs ⊕ cold agglutinins
Tx: Folate, glucocorticoids, splenectomy, rituximab
PCH: C3d+ DL+

**MICROANGIOPATHIC**
RBCs damaged when passing through obstructed/narrow vessel lumens → schistocytes ("helmet cells")
← e.g. DIC, TTP/HUS, SLE, HELLP, ↑↑BP↑!

**MACROANGIOPATHIC**
mechanical destruction of RBCs due to aortic stenosis or mechanical heart valves
schistocytes on peripheral blood smear

**INFECTIONS**
↑oxidative stress
↑destruction of RBCs (e.g. malaria, Babesia)

## MACROCYTIC
MCV > 100 fL

### Megaloblastic

**Defective DNA Synthesis**

**FOLATE DEFICIENCY**
↑homocysteine only
NO neurologic Sx
Causes: malnutrition / alcoholism, pregnancy, hemolytic anemia, drugs (methotrexate, trimethoprim, phenytoin)

**VITAMIN $B_{12}$ DEFICIENCY**
↑homocysteine, ↑MMA
← veganism, tapeworm, gastrectomy, Crohn's, pernicious anemia
Dx: schilling test
Neuro Sx: dementia, subacute combined degeneration

**OROTIC ACIDURIA** AUT Rec
orotic acid —(UMP synthase, X defect)→ UMP (pyrimidine)
failure to thrive, delayed meg. anemia refractory to folate / B12
NO hyperammonemia
Dx orotic acid in urine
Tx UMP etc bypass bad enzyme

**DEFECTIVE DNA Repair**

**FANCONI ANEMIA** AUT Rec
☆ also depicted as nonhemolytic normocytic as a sub of Aplastic Anemia
← DNA crosslink repair defect
Sx short stature, hypo- & hyperpigment, café-au-lait spots, microcephaly, thumb/radial defects
Labs: pancytopenia
→ ↑incidence of tumors / leukemia
Note: this is NOT Fanconi Syndrome

* sore, smooth tongue, grey hair, pigmentation
* RBC macrocytosis, hypersegmented neutrophils

### Non-Megaloblastic

**DIAMOND-BLACKFAN ANEMIA**
intrinsic defect in erythroid progenitor cells → rapid anemia < 1 yo
↑HbF but ↓total Hb
Sx short stature, abn face, UE abn (e.g. tri-phal thumb)

**LIVER DISEASE**
Sequester RBCs & Platelets → splenomegaly
Liver plays important role in lipid synthesis for cell membranes including RBCs

**ALCOHOLISM**
EtOH causes marrow suppression (mechanism unknown)
Also: → liver disease
→ folate / B12 deficiency

* low reticulocytes
* DNA synthesis NOT impaired
* RBC macrocytosis WITHOUT hypersegmented PMNs



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