Anemia Outline

- Background facts about blood
- Anemia: general information
- Anemia: specific types
Anemia Outline

• Background facts about blood
Normal blood cells
Complete Blood Count (CBC)

- RBC
- Hemoglobin
- Hematocrit
Complete Blood Count (CBC)

MCV
- microcytic
- normocytic
- macrocytic

MCHC
- hypochromic
- normochromic
Additional Red Blood Cell Properties

Size variation

anisocytosis

Shape

poikilocytosis
Normal red blood cells
Anemia Outline

- Background facts about blood
- Anemia: general information
An (without) -emia (blood):

a reduction below normal in hemoglobin or red blood cell number.
Symptoms of Anemia

Pale skin, mucous membranes
Jaundice (if hemolytic)
Tachycardia
Breathlessness
Dizziness
Fatigue
Anemia Outline

• Background facts about blood
• Anemia: general information
• Anemia: specific types
Three Ways to Get Anemic

Lose blood

Destroy too much blood
  • Extracorpuscular reasons
  • Intracorpuscular reasons

Make too little blood
  • Too few building blocks
  • Too few erythroblasts
  • Not enough room
Three Ways to Get Anemic

Lose blood
Anemia of Blood Loss

Things you must know

• Cause: traumatic, acute blood loss
• At first, hemoglobin is normal!
• After 2-3 days, see reticulocytes
• Chronic blood loss is different (it causes iron deficiency anemia).
Reticulocytes
Three Ways to Get Anemic

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  • Extracorpuscular reasons
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Hemolytic Anemias

• Intracorpuscular vs. extracorpuscular
• Chronic vs. acute
• Signs of destruction: ↑ bilirubin, ↑ LDH, ↓ haptoglobin
• Signs of production: ↑ reticulocytes, nucleated red cells in blood
Reticulocytes (supravital stain)
Three Ways to Get Anemic

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  • Extracorpuscular reasons
Microangiopathic Hemolytic Anemia

Things You Must Know

• Physical trauma to red cells
• Schistocytes
• Find out why!
Red cells snagged on fibrin strand
Schistocytes
Triangulocyte
Causes of MAHA

- Artificial heart valve
- Malignancy
- Obstetric complications
- Sepsis
- Trauma
Autoimmune Hemolytic Anemia

Things You Must Know

- Warm AIHA
  - IgG
  - Spleen
  - Spherocytes

- Cold AIHA
  - IgM, complement
  - Intravascular hemolysis
  - Agglutination
Warm AIHA
Cold AIHA
Cold AIHA
patient red cells + AHG = agglutination

Direct antiglobulin test (DAT)
Three Ways to Get Anemic

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  • Intracorpuscular reasons
Sickle Cell Anemia

Things You Must Know

• Hemoglobinopathy (qualitative defect in hemoglobin)

• Single amino acid substitution in beta chain of hemoglobin

• Can be heterozygous or homozygous

• Sickle cells are nasty:
  • Fragile (burst easily)
  • Get stuck in vessels
Hemoglobin
Point mutation in β chain gene

→

abnormal β chains
(substitution of valine for glutamate)

→

Hgb S
Nasty!
Aggregates and polymerizes on deoxygenation
Red cell becomes sickle shaped
Sickles clog up vessels...
...plus, they are fragile
Sickle cell anemia
Sickle cell anemia: foot lesion
Note the "sickled" appearance of the RBC's in the vessels and sinusoids.

Sickle cell anemia: spleen
Clinical Findings in Sickle Cell Anemia

- Blacks (8% are heterozygous)
- Severity of disease is variable
- Chronic hemolysis, vaso-occlusive disease, and ↑ infections (autosplenectomy)
- Treatment: prevent triggers, vaccinate, transfuse
Thalassemia

Things You Must Know

- Quantitative defect in hemoglobin
- Can’t make enough α or β chains
- Variable disease severity
- Hypochromic, microcytic anemia with increased RBC and target cells
Hemoglobin chain development

Hgb F = $\alpha_2\gamma_2$

Hgb $A_2 = \alpha_2\delta_2$

Hgb $A = \alpha_2\beta_2$

Hemoglobin chain development
Thalassemia
Thalassemia: Medullary expansion
Hereditary Spherocytosis

Things You Must Know

- Tons of spherocytes
- Spectrin defect
- Splenectomy is curative
Hereditary spherocytosis
Splenomegaly in hereditary spherocytosis
Glucose-6-Phosphate Dehydrogenase Deficiency

Things You Must Know

- $\downarrow \text{G6PD} \rightarrow \uparrow \text{peroxides} \rightarrow \text{cell lysis}$
- Oxidant exposure
- Bite cells (removal of Heinz bodies)
- Self-limiting
Clinical Findings in G6PD Deficiency

- Some patients asymptomatic
- Others have episodic hemolysis
- Triggers: broad beans (favism), drugs (antibiotics, aspirin)
- Spontaneous resolution
Child with G6PD deficiency: jaundiced sclera
Why Do G6PD-Deficient Red Cells Die?

- They can’t reduce nasties
- Nasties attack hemoglobin bonds
- Heme breaks away from globin
- Globin denatures, sticks to red cell membrane ("Heinz body")
- Spleen bites out Heinz bodies
G6PD deficiency: Heinz bodies
G6PD deficiency: bite cells
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Iron-Deficiency Anemia

Things You Must Know

• Most important cause: GI bleeding
• Microcytic, hypochromic anemia
• Must find out why patient is iron deficient!
Iron-deficiency anemia
Atrophic glossitis in iron-deficiency anemia
Koilonychia in iron-deficiency anemia
Causes of Iron Deficiency

- Decreased iron intake
  - bad diet
  - bad absorption

- Increased iron loss
  - GI bleed
  - menses
  - hemorrhage

- Increased iron requirement
  - pregnancy
Anemia of Chronic Disease

Things You Must Know

• Infections, inflammation, malignancy
• Iron metabolism disturbed
• Normochromic, normocytic anemia
• Anemia usually mild
Megaloblastic Anemia

Things You Must Know

• Defective DNA synthesis
• Nuclear/cytoplasmic asynchrony
• $\downarrow$ B$_{12}$/folate
• Macrocytic anemia with oval macrocytes and hypersegmented neutrophils
methyl $\text{FH}_4$

$\text{B}_ {12}$

$\text{FH}_4$

methylene $\text{FH}_4$

$\text{FH}_2$

dUMP

dTMP

DNA

Need $\text{B}_ {12}$ to make DNA!
Megaloblastic Anemia

- retarded DNA synthesis
- unimpaired RNA synthesis

→ BIG \text{	extsc{cells}!}

- immature nucleus
- mature cytoplasm
Megaloblastic anemia
Megaloblastic anemia
Atrophic glossitis in megaloblastic anemia
What else is B₁₂ good for?

- Homocysteine
  - Homocysteine
  - Endothelial damage
    - Atherosclerosis
    - Thrombosis
  - Methionine
    - Methionine
    - Myelin damage
      - Subacute combined degeneration
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Aplastic Anemia

Things You Must Know

- Pancytopenia
- Empty marrow
- Most are idiopathic
Blood smear in aplastic anemia
Empty bone marrow in aplastic anemia
Empty bone marrow in aplastic anemia
Causes of Aplastic Anemia

- Idiopathic
- Drugs
- Viruses
- Pregnancy
- Fanconi anemia
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Bone marrow full of fibrosis