Hematology Alterations:
Altered Erythrocyte Function
Macrocytic and Microcytic Anemia

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Anemia

Definition
- ↓ total number of circulating erythrocytes
- ↓ quality or quantity of hemoglobin

Causes (individual or combined)
- Impaired erythrocyte production
- Increased erythrocyte destruction
- Blood loss
# Anemia

## Classification

- **Causes**
- **Changes in morphology**
  - *-cytic – changes in cell size*
  - *-chromic – changes in Hgb content*

### Terminology for Erythrocyte Assessment

<table>
<thead>
<tr>
<th></th>
<th>Erythrocyte Volume</th>
<th>Hgb Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normocytic</td>
<td>Normochromic</td>
</tr>
<tr>
<td>Increased</td>
<td>Macrocytic (↑ MCV)</td>
<td>Hyperchromic (↑ Hgb)</td>
</tr>
<tr>
<td>Decreased</td>
<td>Microcytic (↓ MCV)</td>
<td>Hypochromic (↓ Hgb)</td>
</tr>
</tbody>
</table>

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McCance & Huether, 2014, Table 28-2
Anemia

Classification by Etiology

- Decreased RBC Production
  - Decreased Hg Synthesis
    - Examples: Iron deficiency, Thalassemias
  - Defective DNA Synthesis
    - Examples: Vit B12 deficiency, Folic acid deficiency
  - Decreased # of RBC Precursors
    - Examples: Aplastic anemia, Leukemia

- Blood Loss
  - Acute
    - Examples: Trauma, Blood vessel rupture
  - Chronic
    - Examples: Gastritis, Menstruation, Hemorrhoids

- Increased RBC Destruction (hemolytic anemias)
  - Intrinsic
    - Examples: Sickle cell anemia
  - Extrinsic
    - Examples: Physical trauma (prosthetic heart valve), Antibodies, Infections/toxins
Anemia

- Overall effect
  Reduced $O_2$ carrying capacity of the blood $\rightarrow \rightarrow$ Hypoxia

- Compensatory mechanisms
  - $\uparrow$ preload
  - $\uparrow$ HR
  - $\uparrow$ SV
  - $\downarrow$ afterload

  $\uparrow$ CO

  Maintain adequate tissue oxygenation
Anemia: Progression and Manifestations

Etiologic events
(↓ erythropoiesis)
(blood loss)
(↑ destruction)

↓ Red blood cells, ↓ hemoglobin
(anemic condition)

↓ Oxygen-carrying capacity
(hypoxemia)

Ischemia
Claudication (muscle)
Weakness, ↑ fatigue
Pallor (skin/mucous membrane)

Liver
(fatty changes; fatty changes can also occur in heart and kidney)

Tissue hypoxia

Respiratory
(↑ respiratory rate, depth, “exertional dyspnea”)

Central nervous system
(dizziness, fainting, lethargy)

Compensatory mechanisms

Heart (angina)

↑ Oxygen demands for work of heart

↑ Heart rate

Cardiovascular

Capillary dilation

↑ SV

↑ Renin-aldosterone response
↑ Salt and H₂O retention
↑ Extracellular fluid

↑ Extracellular fluid

Hyperdynamic circulation

Cardiac murmurs

High-output cardiac failure

↑ Release of oxygen from hemoglobin in tissues

↑ BPG in cells

McCance & Huether, 2014, Figure 28-2
# Anemia - Clinical Manifestations

<table>
<thead>
<tr>
<th>Body System</th>
<th>Clinical Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>↑ HR, CHF, Angina, MI</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>↑ RR, orthopnea, dyspnea</td>
</tr>
<tr>
<td>Neurologic</td>
<td>H/A, vertigo, depression, impaired cognition</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Anorexia, hepatomegaly, splenomegaly</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Fatigue, bone pain</td>
</tr>
<tr>
<td>Integumentary</td>
<td>Pallor, pruritis</td>
</tr>
<tr>
<td>General</td>
<td>Lethargy, sensitivity to cold, weight loss</td>
</tr>
</tbody>
</table>
Macrocytic (Megaloblastic) Anemias

- Pathophysiology

  Vitamin deficiencies (B₁₂ or Folate)
  \[ \downarrow \]
  Defective erythrocyte precursor
  DNA synthesis
  \[ \downarrow \]
  Unusually large stem cells in bone marrow
  \[ \downarrow \]
  Erythrocyte changes:
  Unusually large size
  No pale center
  Normal Hgb

- Types
  - Pernicious
  - Folate Deficiency
Pernicious Anemia – Vit $\text{B}_{12}$

- Most common megaloblastic anemia
- Deficiency of $\text{B}_{12}$
- Common over age 50

**Pathophysiology**

- Absence of Intrinsic Factor (IF) (gastric parietal cells)
- ↓ IF binding with dietary $\text{B}_{12}$
- ↓ small intestine absorption of $\text{B}_{12}$
- Defective DNA synthesis in erythrocytes
Pernicious Anemia – Vit B$_{12}$

**Causes**
- **Chronic atrophic gastritis (autoimmune) – Type A**
  - Genetic
  - Other endocrine autoimmune disorders

- **Excessive damage to gastric mucosa**
  - Alcohol, caffeine, smoking

- **Gastrectomy (partial/full)**

- **Helicobacter pylori gastritis - Type B**

**Unique Clinical Manifestations**
- **Insidious onset – B$_{12}$ liver storage**
- **Severe at time of diagnosis**
Folate Deficiency Anemia

Pathophysiology

- ↓ RBC production and maturation:
  - Altered DNA synthesis → Megaloblastic cells with clumped nuclear chromatin
  - Apoptosis of erythrocytes during late stage of erythropoiesis
Folate Deficiency Anemia

- Complications of Folate deficiency
  - Pregnancy - Neural tube defects
  - ↑ circulating homocysteine → atherosclerosis
  - Colorectal cancers

- Unique Clinical Manifestations
  - Ulcerations of lips, mouth, buccal mucosa
Microcytic Anemia

Characteristics

- Erythrocytes: Small
- Reduced Hgb

Caused by disorders of:

- Iron metabolism
- Synthesis of hemoglobin components:
  - Heme (porphyrin) - pigment
  - Globin - protein
Iron-deficiency Anemia

- Most common anemia world-wide
- Causes
  - Inadequate dietary intake
    - Infants, small children, adolescents, pregnant women
  - Chronic blood loss
    - GI bleeding
      - Pathologic
      - Medication-induced (ASA, NSAIDS)
    - Menorrhagia
  - Impaired GI absorption
    - Decreased gastric acid production – proton pump inhibitors – Omeprozole
  - Lead Poisoning
Pathophysiology

1. Depletion of iron stores
   - Inadequate iron intake
   - Excessive blood loss
   - Less iron available in bone marrow
   - ↓ Hgb Synthesis

2. Metabolic dysfunction
   - Insufficient iron delivery to bone marrow
   - Impaired iron use by bone marrow
   - ↓ Hgb Synthesis
## Iron-deficiency Anemia

### Pathophysiology:
Iron needs > iron availability

<table>
<thead>
<tr>
<th>Stage</th>
<th>Pathophysiology</th>
<th>Erythropoiesis</th>
</tr>
</thead>
</table>
| Stage 1 | • Depletion of iron stores  
        • Serum ferritin level drops                                                   | • Normal – Hgb normal                                |
| Stage 2 | • Ferritin depletion  
        • ↓ transportation of iron to bone marrow  
        • Serum iron level drops                                                   | • Iron-deficiency erythropoiesis  
        • ↓ Hgb production                                                         |
| Stage 3 | • Iron-deficient RBC in circulation outnumber mature RBC  
        • Iron stores depleted                                                      | • Erythrocytes are hypochromic and microcytic  
        • ↓↓↓ Hgb production  
        • S/S Iron-deficiency anemia                                                 |
Iron-deficiency Anemia

Unique Clinical Manifestations

- **Early**
  - Fatigue, weakness, SOB

- **Progressive**
  - Epithelial tissue changes (nails)
  - Glossitis
  - Dysphagia
    - Hyposalivation
    - Esophageal web development

*McCance & Huether, 2014, Figure 28-4*
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