IRON DEFICIENCY ANEMIA/ANEMIA OF CHRONIC DISEASE

ANEMIA
Definition

- Decrease in the number of circulating red blood cells
- Most common hematologic disorder by far

ANEMIA
Causes - Decreased Production

- Cytoplasmic production of protein
  - Usually normocytic (MCV 80-100 fl) or microcytic (MCV < 80 fl)
- Nuclear division/maturation
  - Usually macrocytic (MCV > 100 fl)

ANEMIA
Causes - Cytoplasmic Protein Production

- Decreased hemoglobin synthesis
  - Disorders of globin synthesis
  - Disorders of heme synthesis
- Heme synthesis
  - Decreased Iron
  - Iron not in utilizable form
  - Decreased heme synthesis

ANEMIA
Causes

- Blood loss
- Decreased production of red blood cells (Marrow failure)
- Increased destruction of red blood cells
  - Hemolysis
- Distinguished by reticulocyte count
  - Decreased in states of decreased production
  - Increased in destruction of red blood cells

IRON DEFICIENCY ANEMIA
Prevalence

<table>
<thead>
<tr>
<th>Country</th>
<th>Men (%)</th>
<th>Women (%)</th>
<th>Pregnant Women (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. India</td>
<td>6</td>
<td>35</td>
<td>56</td>
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<tr>
<td>N. India</td>
<td>64</td>
<td>80</td>
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<td>Latin America</td>
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<td>Israel</td>
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<td>Poland</td>
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<td>Sweden</td>
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<td>USA</td>
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<td>13</td>
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</tr>
</tbody>
</table>
Iron Deficiency Anemia/Anemia of Chronic Disease

IRON

- Functions as electron transporter; vital for life
- Must be in ferrous (Fe+2) state for activity
- In anaerobic conditions, easy to maintain ferrous state
- Iron readily donates electrons to oxygen, → superoxide radicals, H₂O₂, OH• radicals
- Ferric (Fe+3) ions cannot transport electrons or O₂
- Organisms able to limit exposure to iron had major survival advantage

IRON

Body Compartments - 75 kg man

<table>
<thead>
<tr>
<th>Stores</th>
<th>Tissue 170 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1000 mg</td>
<td></td>
</tr>
</tbody>
</table>

| Red Cells | 2400 mg |

Absorption < 1 mg/day
Excretion < 1 mg/day

Causes of Iron Deficiency

- Blood Loss
  - Gastrointestinal Tract
  - Menstrual Blood Loss
  - Urinary Blood Loss (Rare)
  - Blood in Sputum (Rarer)
- Increased Iron Utilization
  - Pregnancy
  - Infancy
  - Adolescence
  - Polycythemia Vera
- Malabsorption
  - Tropical Sprue
  - Gastrectomy
  - Chronic atrophic gastritis
- Dietary inadequacy (almost never sole cause)
- Combinations of above

IRON CYCLE

INTRACELLULAR IRON TRANSPORT

DAILY IRON REQUIREMENTS

Pregnancies

Absorbed Iron
Requirement (mg/day)

Males

Females
Iron Deficiency Anemia/Anemia of Chronic Disease

**Iron Absorption**

- Iron in Diet
- Iron Solubilized
- Iron Uptake
- Iron Absorbed

**GI Absorption of Iron**

**Iron Deficiency Anemia**

- Stainable Iron, Bone Marrow Aspirate
- Serum Ferritin - Low in Iron Deficiency
- Desaturation of transferrin
- Serum Iron drops
- Transferrin (Iron Binding Capacity) Increases
- Blood Smear - Microcytic, Hypochromic; Aniso- & Poikilocytosis
- Anemia

**Ferritin/Transferrin Regulation**

- Iron Regulators of Blood
- Transferrin
- Transferrin Receptor
- Iron Absorbed

**Progression of Findings**

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Iron Deficiency Anemia/Anemia of Chronic Disease

IRON STORES
Iron Deficiency Anemia

Stores 0 mg

Tissue 170 mg

Absorption 2-10 mg/day
Excretion Dependent on Cause

Red Cells 1500 mg

IRON DEFICIENCY
Symptoms
- Fatigue - Sometimes out of proportion to anemia
- Atrophic glossitis
- Pica
- Koilonychia (Nail spooning)
- Esophageal Web

IRON REPLACEMENT THERAPY
Response
- Usually oral; usually 300-900 mg/day
- Requires acid environment for absorption
- Poorly absorbed

IRON THERAPY
Response
- Initial response takes 7-14 days
- Modest reticulocytosis (7-10%)
- Correction of anemia requires 2-3 months
- 6 months of therapy beyond correction of anemia needed to replete stores, assuming no further loss of blood/iron
- Parenteral iron possible, but problematic

IRON CAUSES OF IRRITATION
- Blood Loss
  - Gastrointestinal Tract
  - Menstrual Blood Loss
  - Urinary Blood Loss (Rare)
  - Blood in Sputum (Rarer)
- Increased Iron Utilization
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ANEMIA OF CHRONIC DISEASE

Findings
- Mild, non-progressive anemia (Hgb c. 10, Hct c. 30%)
- Other counts normal
- Normochromic/normocytic (30% hypochromic/microcytic)
- Mild aniso- & poikilocytosis
- Somewhat shortened RBC survival
- Normal reticulocyte count (Inappropriately low for degree of anemia)
- Normal bilirubin
- EPO levels increased but blunted for degree of anemia

ANEMIA OF CHRONIC DISEASE

Causes
- Thyroid disease
- Collagen Vascular Disease
  - Rheumatoid Arthritis
  - Systemic Lupus Erythematosus
  - Polymyositis
  - Polyarteritis Nodosa
- Inflammatory Bowel Disease
  - Ulcerative Colitis
  - Crohn's Disease
- Malignancy
- Chronic Infectious Diseases
  - Osteomyelitis
  - Tuberculosis
- Familial Mediterranean Fever

IRON STORES
Anemia of Chronic Disease

Stores 2500 mg
Tissue 170 mg
Red Cells 1100 mg

Serum Iron Transferrin Ferritin

Iron Deficiency

ACD
SUMMARY
Iron-Related Anemias

• Most common anemia
• Symptom of pathologic process
• Primary manifestation is hematologic
• Treatment requires:
  - Replacement therapy
  - Correction of underlying cause (if possible)