Anemia

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Terms

- RBC = red blood cells
- Hgb = hemoglobin
- MCV = mean cell volume
- Fe = iron
- SD = standard deviation
- TIBC = total iron binding capacity
- RDW = red cell distribution width
Hemoglobin

• Tetramer of 4 globin chains (proteins)
• Each with a heme group containing iron
• Can be distinguished by electrophoresis
• Chain types
  – Alpha
  – Beta
  – Gamma
  – Delta
  – Zeta and epsilon are embryonic
The Hemoglobin Molecule

Heme group
# Fetal and Neonatal Hemoglobins

<table>
<thead>
<tr>
<th>Hemoglobin type</th>
<th>Designation</th>
<th>Amount %</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Birth</td>
<td>&gt; 1 year</td>
</tr>
<tr>
<td>Fetal</td>
<td>Hgb F</td>
<td>60-85</td>
<td>0-2</td>
</tr>
<tr>
<td></td>
<td>(alpha2 gamma2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult (major)</td>
<td>Hgb A</td>
<td>15-40</td>
<td>96-98</td>
</tr>
<tr>
<td></td>
<td>(alpha2 beta2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult (minor)</td>
<td>Hgb A2</td>
<td>1</td>
<td>1-3</td>
</tr>
<tr>
<td></td>
<td>(alpha2 delta2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
About Hemoglobin

- Hemoglobin binds oxygen and carries it to tissues
- Erythrocytes (red blood cells) consist mainly of hemoglobin
- Function of red blood cell dependent on:
  – Hemoglobin type and content
  – Membrane stability
  – Energy production
Survival and Production of RBC

- Formed in bone marrow
- Life span is 120 days (+/- 20 days)
- Cleared in spleen
- Reticulocytes are newly formed RBC in circulation
- If no new production, Hgb drops 1 gm/week
Definition of Anemia

• Hgb > 2 standard deviations below the mean for age

(see chart)
# Age and Sex Adjusted Hgb and MCV Values

<table>
<thead>
<tr>
<th>Age and Sex</th>
<th>Hgb Mean (-2 SD)</th>
<th>MCV Mean (-2 SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>16.5 (13.5)</td>
<td>108 (98)</td>
</tr>
<tr>
<td>1-3 days</td>
<td>18.5 (14.5)</td>
<td>108 (95)</td>
</tr>
<tr>
<td>2 weeks</td>
<td>16.6 (13.4)</td>
<td>105 (88)</td>
</tr>
<tr>
<td>1 month</td>
<td>13.9 (10.7)</td>
<td>101 (91)</td>
</tr>
<tr>
<td>2 months</td>
<td>11.2 (9.4)</td>
<td>95 (84)</td>
</tr>
<tr>
<td>6 months</td>
<td>12.6 (11.1)</td>
<td>76 (68)</td>
</tr>
<tr>
<td>6-24 months</td>
<td>12.0 (10.5)</td>
<td>78 (70)</td>
</tr>
<tr>
<td>2-6 years</td>
<td>12.5 (11.5)</td>
<td>81 (75)</td>
</tr>
<tr>
<td>6-12 years</td>
<td>13.5 (11.5)</td>
<td>86 (77)</td>
</tr>
<tr>
<td>12-18 year male</td>
<td>14.5 (13)</td>
<td>88 (78)</td>
</tr>
<tr>
<td>12-18 year female</td>
<td>14.0 (12)</td>
<td>90 (78)</td>
</tr>
<tr>
<td>Adult male</td>
<td>15.5 (13.5)</td>
<td>90 (80)</td>
</tr>
<tr>
<td>Adult female</td>
<td>14.0 (12)</td>
<td>90 (80)</td>
</tr>
</tbody>
</table>
Anemia

• Physiologic: hgb below the level needed to deliver adequate oxygen to cells

• Clinical features:

<table>
<thead>
<tr>
<th>Mild</th>
<th>Mild dyspnea on exertion, palpitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>As with MILD ANEMIA, may also have excessive fatigue</td>
</tr>
<tr>
<td>Severe</td>
<td>Dyspnea at rest, tachycardia with pounding pulse, weakness, dizziness, syncope, headache, insomnia</td>
</tr>
</tbody>
</table>
Anemia

• General mechanisms
  – Increased hgb loss (usually bleeding)
  – Decreased hgb production
  – Increased destruction of RBC
Workup for Anemia

• History
  – Diet
  – Blood loss
  – Family history
  – Recent illness or immunization
  – History of anemia and cause
Workup of Anemia

• Physical Examination
  – Evaluate conjunctiva and mucous membranes for paleness
  – Cardiovascular system for murmur
  – Liver
  – Spleen
  – Nodes
  – Look for jaundice or purpura
Workup of Anemia

• Labs
  – Complete blood count with differential and platelets
  – Evaluation of smear with red cell indices
  – Reticulocyte count

• Other tests
  – Serum bilirubin, LDH, urinary hemosiderin, hgb electrophoresis, quantitative hgb A2 and F
Reticulocytes
Approach to Anemia

- Smear indices
  - Hypochromic microcytic
  - Normochromic normocytic
  - Macrocytic
Anemias
Hypochromic Microcytic Anemia

• Appearance:
  – Weakly staining, small in size

• Mechanism:
  – Decreased hgb synthesis secondary to decreased heme synthesis

• Causes:
  – Iron deficiency
  – Thalassemia
  – Lead poisoning
Hypochromic, Microcytic Anemia: Iron Deficiency

• Mechanism
  – Decreased hgb synthesis secondary to decreased heme synthesis

• Major differential diagnosis
  – Beta thalassemia minor

• Incidence
  – 3-24% of children age 6-24 months
Iron Deficiency Anemia
Iron Deficiency Anemia: Causes

• Lack of adequate iron at birth
  – Low birth weight
  – Low hgb at birth
• Poor iron intake
• Loss of iron (GI bleeding)
Iron Deficiency Anemia

• Symptoms
  – Irritability
  – Anorexia with poor weight gain
  – Behavioral changes
    *Some of these changes may not be readily reversible with Fe treatment*

• Diagnostic tests
  – Hgb and MCV are decreased
  – Ferritin decreased
  – TIBC increased
Iron Deficiency Anemia: Treatment

Elemental iron 4-6 mg/kg/day

- In a 1-2 year old with a poor diet, therapy may consist of empiric course of oral iron without a full workup
- Reticulocyte count will rise in 4-5 days
- Hgb starts to rise at 1 week
- Once normalized, continue Fe therapy 1-2 months to replace Fe stores in marrow
Iron Deficiency Anemia: Note

- Make sure there is no source of GI bleeding
- Consider malignancy if there is GI bleeding
Lead Poisoning

- Blocks placement of Fe into heme
- May cause neurological damage and anemia
- Usually related to lead-based paints and industrial exposures
- Test for a SERUM LEAD LEVEL
- Treatment – chelation with deferoxamine
Thalassemia

• Genetically determined, often familial defects in the production of Hgb
• Two processes involved
  – Decreased production of Hgb
  – Imbalance of globin chain production
THALASSEMIA

Victims of this hereditary anemia produce very little functional hemoglobin. The cells are also prone to rupture. The result is a severe form of anemia. This disease affects persons from the lands surrounding the Mediterranean Sea.
Thalassemia
Beta-Thalassemia

• Due to deficiency of one or both Beta-globin genes

• Heterozygotes
  – Defect in one chain
  – Mild hypochromic microcytic anemia
  – Normal life expectancy
  – Potential for homozygous children
  – Confirmed by electrophoresis
Beta-Thalassemia

• Homozygotes
  – Beta-Thalassemia major
  – Defect in both beta chains
  – Decreased or no production of Hgb A
  – Hgb F 60-90%

• Clinical
  – Presents with severe anemia at 4-6 months

• Treatment
  – Transfusions
# Differentiating Between Iron Deficiency and Beta-Thalassemia Trait

<table>
<thead>
<tr>
<th>Test/Finding</th>
<th>Beta-Thal trait</th>
<th>Iron Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Fe/ferritin</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
<tr>
<td>TIBC</td>
<td>Normal</td>
<td>Increased</td>
</tr>
<tr>
<td>Fe/TIBC</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
<tr>
<td>Hgb A2</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Hgb F</td>
<td>Increased</td>
<td>Normal</td>
</tr>
<tr>
<td>MCV/RBC</td>
<td>&lt; 13</td>
<td>&gt; 13</td>
</tr>
<tr>
<td>FEP</td>
<td>Normal</td>
<td>Increased</td>
</tr>
<tr>
<td>RDW</td>
<td>Normal (13.4 +/- 1.2)</td>
<td>Higher</td>
</tr>
<tr>
<td>RBC morphology</td>
<td>Abnormal</td>
<td>Slightly abnormal</td>
</tr>
<tr>
<td></td>
<td>Basophilic stippling</td>
<td></td>
</tr>
</tbody>
</table>
Basophilic Stippling
Normochromic, Normocytic Anemia

- Decreased reticulocyte count
  - Hyopproliferative anemia
  - Malignancy

- Increased reticulocyte count
  - Coombs +
    - Intracorpuscular
      - Abnormal hgb
    - Extracorpuscular
      - Membrane defect
      - Enzyme defect
  - Coombs -
    - Antibody mediated

- Acute blood loss
Normochromic, Normocytic Anemia
Macrocytic Anemia

- **Appearance:**
  - Large cells

- **Causes:**
  - Vitamin B12 deficiency
  - Folate deficiency
Macrocytic Anemia