Learning Objective
- Explain the etiologies, pathophysiology, manifestations, diagnosis and management of selected hemoglobin abnormalities

Hemoglobin Abnormalities
Arthur Jones, EdD, RRT
http://rc-edconsultant.com/

Hemoglobin Structure and Function

Hb Structure
- Molecule containing four heme groups
- Each heme group contains an iron atom
- One molecule of O2 binds to each heme group

Hb Function
- Four molecules O2 per molecule
  Hb = 100% saturation
- Three molecules O2 per molecule
  Hb = 75% saturation

Hb Function
- One gram Hb carries 1.34 mL O2
- At 100% saturation, 15 g Hb carries 20.1 mL O2
- At PaO2 = 100, 0.3 mL O2 is carried dissolved in plasma
Without Hb, cardiac output must increase to 36 L/min for the same O2 delivery.

Functions in O2 transport
- binds O2 for transport
- transports O2 to tissues
- releases O2 to tissues

Additional functions
- buffer
- CO2 transport - carries greatest amount of exchanged (excreted) CO2

HbO2 dissociation curve - describes relationship between PO2 and SO2

- upper portion of curve
  - Hb has greater affinity for O2
  - facilitates uptake of O2 in lung
- lower portion of curve
  - Hb has lesser affinity for O2
  - facilitates release of O2 to tissues

Right shift - lower SO2 for given PO2

- Hb releases O2 more readily
- increased temperature
- increased PCO2 (Bohr shift)
- increased H+ (decreased pH)
- HbSULF

HbO2 dissociation curve

PO2 (mm Hg) | SO2 %
---|---
27 | 50
40 | 75
60 | 90
90 | 100

P50 increased

PO2 (mm Hg) | SO2 %
---|---
20 | 50
40 | 75
60 | 90
90 | 100

FYI - Link to additional information on structure and function of Hb
http://en.wikipedia.org/wiki/Hemoglobin
Hb Function
- Left shift - greater SO2 for given PO2

- Decreased temperature
- Decreased PCO2
- Decreased H+ (increased pH)
- Fetal Hb
- Decreased 2,3 diphosphoglycerate (DPG) - associated with stored blood

Hb Production
- RBC - production stimulated by erythropoietin
  - Erythropoietin - secreted by kidney
  - Renal disease causes anemia by inhibiting production

Hb Metabolism
- RBC ends life cycle (120D)
- Iron in Hb is recycled
- Iron recycling byproducts
  - Carbon monoxide
  - Bilirubin

Hemoglobin saturation
- Calculation vs. direct measurement
  - Calculations are based on HbO2 curve
  - Direct measurement with oximeter or co-oximeter is more accurate
  - Calculated SO2 does not account for hemoglobinopathies, like:
    - HbCO (carbon monoxide)
    - Methemoglobin
    - Sulfhemoglobin

Hemoglobin Abnormalities
- Polycythemia
- Anemia
- Carboxyhemoglobin
- Methemoglobin
- Sulfhemoglobin
**Polycythemia**

**Definitions**
- Polycythemia: excessive RBCs
  - Primary polycythemia (polycythemia vera): caused by genetic mutation in hematopoietic cells - rare condition
  - Secondary polycythemia: caused by factors extrinsic to RBC precursors
  - Relative polycythemia: decreased plasma volume concentrates RBCs

**Etiologies**
- Primary polycythemia: problem is within bone marrow
  - Classified as a myeloproliferative disease
  - Origin:
    - Inherited mutation
    - Acquired mutation

FYI - Link to article on primary polycythemia
http://www.emedicine.com/ped/topic1848.htm

- Secondary polycythemia: problem is outside of bone marrow
  - Chronic hypoxemia
    - Altitude
    - Cardiac disease
    - Lung disease
    - Chronic hypoventilation
    - Smoking - carbon monoxide
    - Congenital methemoglobinemia
    - Congenital 2,3 DPG deficiency

FYI - Link to article on secondary polycythemia
http://www.emedicine.com/med/topic1863.htm

**Pathophysiology**
- Increased RBC mass
  - Expanded blood volume
  - Increased metabolism
  - Increased blood viscosity
    - Increased myocardial work
    - Increased risk for thrombus formation

FYI - Link to article on secondary polycythemia
http://www.emedicine.com/med/topic1863.htm
<table>
<thead>
<tr>
<th><strong>Symptoms</strong></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>Headache</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Weight loss</td>
</tr>
<tr>
<td>Weakness, malaise</td>
<td>Weakness, malaise</td>
</tr>
<tr>
<td>Bruising</td>
<td>Bruising</td>
</tr>
<tr>
<td>Bleeding- gums, nose</td>
<td>Bleeding- gums, nose</td>
</tr>
<tr>
<td></td>
<td>Itching (pruritus)</td>
</tr>
<tr>
<td></td>
<td>Joint dysfunctions</td>
</tr>
<tr>
<td></td>
<td>Gastrointestinal discomfort, constipation</td>
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</tbody>
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<table>
<thead>
<tr>
<th><strong>Physical Signs</strong></th>
<th><strong>Diagnosis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubor (redness), esp. facial</td>
<td>History</td>
</tr>
<tr>
<td>Hypertension</td>
<td>◆ median age = 60 (primary)</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>◆ family history of blood disorders</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>◆ residence at high altitude</td>
</tr>
<tr>
<td>Ecchymoses</td>
<td>◆ medical history</td>
</tr>
<tr>
<td></td>
<td>◆ cardiac disease</td>
</tr>
<tr>
<td></td>
<td>◆ pulmonary disease</td>
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</tbody>
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<table>
<thead>
<tr>
<th><strong>Diagnosis</strong></th>
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</thead>
<tbody>
<tr>
<td>Increased red blood cell mass- essential to confirm erythrocytosis</td>
<td>Complete blood count</td>
</tr>
<tr>
<td>Epo levels- distinguish between types</td>
<td>◆ elevated RBCs, Hb</td>
</tr>
<tr>
<td>◆ normal in primary</td>
<td>◆ elevated WBCs (sometimes)</td>
</tr>
<tr>
<td>◆ elevated in secondary</td>
<td>◆ elevated platelets (sometimes)</td>
</tr>
<tr>
<td>Plasma volume- to rule out relative polycythemia</td>
<td>◆ Arterial blood gases- to identify etiology</td>
</tr>
<tr>
<td></td>
<td>◆ HbCO- to identify etiology</td>
</tr>
</tbody>
</table>
Complications
- Thrombotic events
  - deep vein thrombosis
  - stroke
  - myocardial infarction
- Heart failure
- Kidney stones
- Hemorrhage

Management
- Primary polycythemia
  - treatment is palliative
  - phlebotomy
    - maintain normal cell mass
    - control blood viscosity
  - chemotherapy to suppress bone marrow production

Management
- Secondary polycythemia
  - phlebotomy
    - maintain normal cell mass
    - control blood viscosity

Management
- Secondary polycythemia
  - treat underlying cause
    - relocate to lower altitude
    - supplemental oxygen
    - smoking cessation
    - BiPAP for hypoventilation
    - surgery for cardiac defects
    - surgery for renal tumors

Definition & causes
- Anemia - deficient RBCs
- Etiologies
  - inadequate production
  - hemolysis - increased destruction
  - chronic blood loss
Types
- Dietary deficiency
  - vitamin B12
  - folic acid
  - iron
- Autoimmune disease
  - autoimmune hemolytic anemia
  - drug-induced immune anemia—drug causes immune reaction to RBCs

Types
- Secondary aplastic anemia—bone marrow depression
  - chemotherapy
  - immunotherapy
  - toxins; e.g., benzene

Types
- Hereditary disease
  - G6PD deficiency—African, Mediterranean
  - Thalassemia—Middle East, Asia
  - Sickle cell—African

Types
- Hereditary disease
  - Porphyria
    - Europeans
    - vampires
    - werewolves

FYI - Link to porphyria, vampires, werewolves
http://en.wikipedia.org/wiki/Porphyria

Manifestations
- Pale coloring
- Chronic fatigue
- Shortness of breath
- Laboratory
  - Decreased RBCs
  - Decreased Hb

Management
- RCPs—always consider Hb level part of oxygenation status
- Blood replacement
- Erythropoietin (Epogen, Aranesp)—stimulate RBC production
- Manage underlying cause
  - nutrition
  - avoid, remove toxins
Carbon Monoxide Toxicity

Management
- Silver bullet, crucifix, cardiac stake (vampires, werewolves)

Carbon monoxide
- Endogenous- trace
- Byproduct of incomplete combustion
  - colorless
  - odorless
- Physiologic level of HbCO is 0.2%
  - nonsmoker
  - rural dweller
- Greater in smokers, city dwellers

Carbon monoxide
- Most common fatal poison in USA
  - accidental
  - suicidal

Carbon monoxide
- Effects
  - Binds with Hb 240 stronger than does O2
  - Binds with myoglobin- myocardial damage
  - Shifts HbO2 curve to left- interferes with release of O2 to tissues

Carbon monoxide
- Effects
  - Binds with Hb 240 stronger than does O2
  - Binds with myoglobin- myocardial damage
  - Shifts HbO2 curve to left- interferes with release of O2 to tissues
  - Stimulates release of NO, which increases free-radicals
  - Greater affinity for fetal Hb- fetal asphyxia
### Manifestations

<table>
<thead>
<tr>
<th>HbCO Concentration</th>
<th>Signs and Symptoms</th>
</tr>
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<tbody>
<tr>
<td>0-10%</td>
<td>None</td>
</tr>
<tr>
<td>10-20%</td>
<td>Mild headache, angina, dyspnea</td>
</tr>
<tr>
<td>20-40%</td>
<td>Severe headache, dyspnea, weakness, cognitive impairment</td>
</tr>
<tr>
<td>40-60%</td>
<td>Fainting, tachypnea, tachycardia, convulsion, coma</td>
</tr>
<tr>
<td>&gt;60%</td>
<td>Coma, shock, death</td>
</tr>
</tbody>
</table>

#### Physical examination
- tachypnea, tachycardia
- cherry-red coloring

#### Diagnosis
- HbCO measurement
  - CO-oximetry
  - Pulse CO-oximetry

#### Management
- 100% O2 decreases HbCO by 1/2 every 60 minutes
- HbCO >10% - 100% O2 until HbCO is less than 5%
- HbCO >40% - transport for hyperbaric O2
- Pregnant patients - hyperbaric O2 for HbCO >30%

FYI - Link to article on HbCO management
http://www.emedicine.com/EMERG/topic817.htm

### Masimo Radical 7(TM)

- **Hb**
- **Oxygen content**
- **HbO2**
- **HbCO**
- **HbMET**

Courtesy of Masimo, Inc.

FYI - Link to Masimo
http://www.masimo.com/

### Methemoglobinemia

- Hemoglobin that has been oxidized to the ferric state (Fe+++) 
- Does not transport O2 or CO2

FYI - Link to article on HbCO management
http://www.emedicine.com/EMERG/topic817.htm
Etiologies
- Congenital cytochrome b5 reductase deficiency
  - subtypes (4)
  - chronic cyanosis (blue-gray)
  - may be otherwise asymptomatic

Etiologies
- Acquired- exposure to:
  - Nitrites
    - food preservatives
    - street drugs (poppers)
  - Aniline dyes
  - Silver nitrate- topical disinfectant
  - Nitroprusside, nitric, nitrous oxide
  - Antimalarials
  - Inadequately cooked, contaminated vegetables

Etiologies
- Local anesthetics, esp. when applied to mucosa:
  - bronchoscopies
  - intubations
  - throat lozenges

Etiologies
- Susceptible patients
  - congenital reduced methemoglobin reductase
  - elderly, infants

Manifestations
- Hb_{MET} >10% cyanosis- refractory to increased FIO2
- Hb_{MET} 20-50%
  - anxiety
  - fatigue
  - tachycardia
- Hb_{MET} 50-70%
  - coma
  - death

FYI - Link to article on methemoglobinemia
http://www.emedicine.com/ped/topic1432.htm
### Manifestations
- **SpO2** is unreliable—will display 80-85% with very high Hb\textsubscript{MET}
- Diagnosis—CO-oximetry

### Management
- O2 has no beneficial effect
- Hb\textsubscript{MET} <30%—no treatment may be needed
- Hb\textsubscript{MET} >30%
  - Methylene blue (IV), unless patient has G6PD deficiency
  - Ascorbic acid (oral)
  - n-acetylcysteine (off-label use)

Click to read case of methemoglobinemia after bronchoscopy
http://www.jmedicalcasereports.com/content/2/1/16

### Sulphemoglobinemia
- Incorporation of a sulfur atom into Hb molecule
- Characterized by cyanosis in absence of hypoxemia

### Etiologies
- Chronic constipation may predispose (elderly patients)
- Aniline dyes (paint)
- Medications:
  - sulfonamides (Bactrim)
  - phenazopyridine (Pyridium)
  - phenacetin (APC, Excedrin)
  - dapsone
    - treats leprosy, malaria
    - also causes Hb\textsubscript{MET}

### Manifestations
- Cyanosis
- Green-brown blood
- Otherwise asymptomatic
- Hb\textsubscript{SULF} does not carry O2
- Hb\textsubscript{SULF} shifts HbO2 curve to right, improving tissue O2 delivery
- Looks worse than it is
Diagnosis

Problems

- Hb\textsubscript{SULF} is not measured by standard CO-oximetry
- Hb\textsubscript{SULF} measured as Hb\textsubscript{MET}
- Some CO-oximeters can be software-calibrated for measurement

Diagnosis

- History of ingestion, exposure
- Cyanosis, unresponsive to:
  - O2
  - methylene blue

FYI - Link to case of sulfhemoglobinemia (need to register with Medscape - free)

Management

- No intervention is necessary
- Stop causative medication
- Treat constipation

Summary & Review

Hemoglobin

- structure and functions
- production
- metabolism
- abnormalities

Summary & Review

Polycythemia

- etiologies- primary, vs. secondary
- manifestations
- diagnosis
- complications
- management

Summary & Review

Anemia

- etiologies- blood loss, low production
- manifestations- deficient Hb
- management- blood replacement, erythropoietin

Summary & Review

Anemia

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Summary & Review

Anemia

- etiologies- blood loss, low production
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<tr>
<th>Summary &amp; Review</th>
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<tbody>
<tr>
<td><strong>CO poisoning</strong></td>
</tr>
<tr>
<td>◆ etiologies- CO inhalation</td>
</tr>
<tr>
<td>◆ manifestations- depends on Hb$_{CO}$ level</td>
</tr>
<tr>
<td>◆ diagnosis- Hb$_{CO}$ measurement</td>
</tr>
<tr>
<td>◆ management- O2, hyperbaric O2</td>
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<tbody>
<tr>
<td><strong>Methemoglobinemia</strong></td>
</tr>
<tr>
<td>◆ etiologies- nitrites, local anesthetics</td>
</tr>
<tr>
<td>◆ manifestations- cyanosis</td>
</tr>
<tr>
<td>◆ diagnosis- Hb$_{MET}$ measurement</td>
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<td>◆ management- methylene blue</td>
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<tr>
<td><strong>Sulfhemoglobinemia</strong></td>
</tr>
<tr>
<td>◆ etiologies- sulfa drugs, constipation, paint</td>
</tr>
<tr>
<td>◆ manifestations- cyanosis, green blood</td>
</tr>
<tr>
<td>◆ diagnosis- R/O methemoglobinemia</td>
</tr>
<tr>
<td>◆ management- none</td>
</tr>
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