

Hemoglobin Abnormalities

Arthur Jones, EdD, RRT

<http://rc-edconsultant.com/>

Learning Objective

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

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

Hb Function

- △ 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

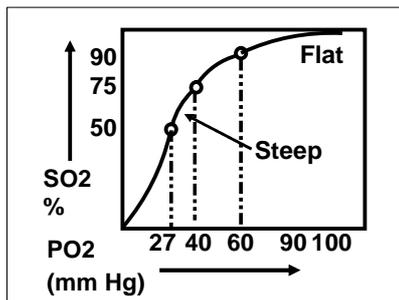
Hb Function

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

FYI - Link to additional information on structure and function of Hb
<http://en.wikipedia.org/wiki/Hemoglobin>

Hb Function

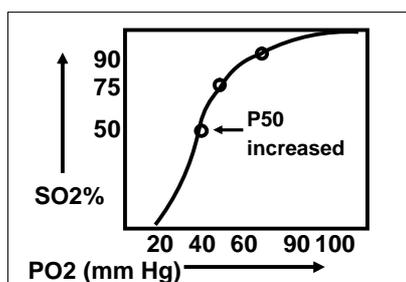
- △ HbO₂ dissociation curve- describes relationship between PO₂ and SO₂

**Hb Function**

- △ 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

Hb Function

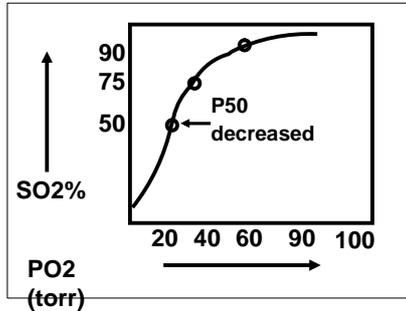
- △ Right shift- lower SO₂ for given PO₂

**Hb Function**

- △ Right shift- lower SO₂ for given PO₂
 - ◆ Hb releases O₂ more readily
 - ◆ increased temperature
 - ◆ increased PCO₂ (Bohr shift)
 - ◆ increased H⁺ (decreased pH)
 - ◆ Hb_{SULF}

Hb Function

△ Left shift- greater SO₂ for given PO₂

**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>

Etiologies

- △ **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**

Etiologies

- △ **secondary polycythemia**
 - ◆ **erythropoietin hypersecretion (tumor)**
 - ◆ **androgenic steroids**
 - ◆ **newborn- fetal asphyxia**

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**

Symptoms

- ▲ Headache
- ▲ Weight loss
- ▲ Weakness, malaise
- ▲ Bruising
- ▲ Bleeding- gums, nose

Symptoms

- ▲ Headache
- ▲ Weight loss
- ▲ Weakness, malaise
- ▲ Bruising
- ▲ Bleeding- gums, nose
- ▲ Itching (pruritus)
- ▲ Joint dysfunctions
- ▲ Gastrointestinal discomfort, constipation

Physical Signs

- ▲ Rubor (redness), esp. facial
- ▲ Hypertension
- ▲ Hepatomegaly
- ▲ Splenomegaly
- ▲ Ecchymoses

Diagnosis

- ▲ History
 - ◆ median age = 60 (primary)
 - ◆ family history of blood disorders
 - ◆ residence at high altitude
 - ◆ medical history
 - ▶ cardiac disease
 - ▶ pulmonary disease

Diagnosis

- ▲ Increased red blood cell mass- essential to confirm erythrocytosis
- ▲ Epo levels- distinguish between types
 - ◆ normal in primary
 - ◆ elevated in secondary
- ▲ Plasma volume- to rule out relative polycythemia

Diagnosis

- ▲ Complete blood count
 - ◆ elevated RBCs, Hb
 - ◆ elevated WBCs (sometimes)
 - ◆ elevated platelets (sometimes)
- ▲ Arterial blood gases- to identify etiology
- ▲ HbCO- to identify etiology

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

Anemia**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

Management

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



Carbon Monoxide Toxicity

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

Manifestations

HbCO Concentration	Signs and Symptoms
0-10%	None
10-20%	Mild headache, angina, dyspnea
20-40%	Severe headache, dyspnea, weakness, cognitive impairment
40-60%	Fainting, tachypnea, tachycardia, convulsion, coma
>60%	Coma, shock, death

Manifestations

- ^ Physical examination
 - ◆ tachypnea, tachycardia
 - ◆ cherry-red coloring
- ^ Diagnosis
 - ◆ HbCO measurement
 - CO-oximetry
 - Pulse CO-oximetry

Masimo Radical 7™

- ^ Hb
- ^ Oxygen content
- ^ HbO₂
- ^ HbCO
- ^ Hb_{MET}



Courtesy of Masimo, Inc.

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

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>

Methemoglobinemia

Methemoglobin

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

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

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

FYI - Link to article on methemoglobinemia
<http://www.emedicine.com/ped/topic1432.htm>

Manifestations

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

Manifestations

- ▲ SpO₂ is unreliable- will display 80-85% with very high Hb_{MET}
- ▲ Diagnosis- CO-oximetry

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

Management

- ▲ O₂ has no beneficial effect
- ▲ Hb_{MET} <30%- no treatment may be needed
- ▲ Hb_{MET} >30%
 - ◆ Methylene blue (IV), unless patient has G6PD deficiency
 - ◆ Ascorbic acid (oral)
 - ◆ n-acetylcysteine (off-label use)

Sulfhemoglobinemia

Sulfhemoglobin

- ▲ 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_{MET}

Manifestations

- ▲ Cyanosis
- ▲ Green-brown blood
- ▲ Otherwise asymptomatic
- ▲ Hb_{SULF} does not carry O₂
- ▲ Hb_{SULF} shifts HbO₂ curve to right, improving tissue O₂ delivery
- ▲ Looks worse than it is

Diagnosis**^ Problems**

- ◆ Hb_{SULF} is not measured by standard CO-oximetry
- ◆ Hb_{SULF} measured as Hb_{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)
<http://www.medscape.com/viewarticle/568376>

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**^ CO poisoning**

- ◆ etiologies- CO inhalation
- ◆ manifestations- depends on Hb_{CO} level
- ◆ diagnosis- Hb_{CO} measurement
- ◆ management- O₂, hyperbaric O₂

Summary & Review**^ Methemoglobinemia**

- ◆ etiologies- nitrites, local anesthetics
- ◆ manifestations- cyanosis
- ◆ diagnosis- Hb_{MET} measurement
- ◆ management- methylene blue

Summary & Review**^ Sulfhemoglobinemia**

- ◆ etiologies- sulfa drugs, constipation, paint
- ◆ manifestations- cyanosis, green blood
- ◆ diagnosis- R/O methemoglobinemia
- ◆ management- none