

Hemoglobin Abnormalities

Arthur Jones, EdD, RRT

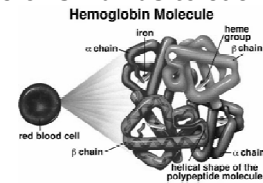
Learning Objectives:

- ^ Describe the functions, production and metabolism of hemoglobin.
- ^ Discuss the etiologies, manifestations, diagnosis, complications and management of the following hemoglobin abnormalities:
 - ◆ polycythemia
 - ◆ anemia
 - ◆ carbon monoxide poisoning
 - ◆ methemoglobinemia
 - ◆ sulfhemoglobinemia
 - ◆ sickle cell disease

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

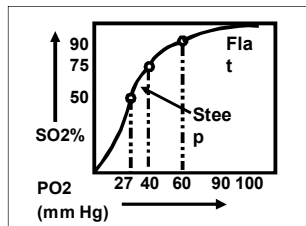
- △ Without Hb, cardiac output must increase to 36 L/min for the same O₂ delivery.
- △ Functions in O₂ transport
 - ◆ binds O₂ for transport
 - ◆ transports O₂ to tissues
 - ◆ releases O₂ to tissues

Hb Function

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

Hb Function

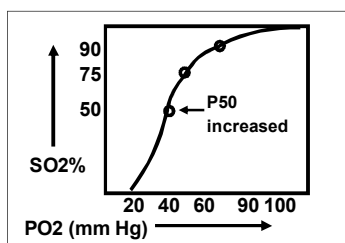
- △ HbO₂ dissociation curve- describes relationship between PO₂ and SO₂

**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

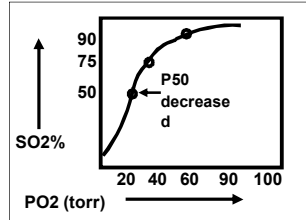
- △ Right shift- lower SO₂ for given PO₂

**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
- ▲ Sickle cell disease

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

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

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

Manifestations

- △ **Pale coloring**
- △ **Chronic fatigue**
- △ **Shortness of breath**
- △ **Laboratory**
 - ◆ Decreased RBCs
 - ◆ Decreased Hb

Management

- △ **RCPs- always consider Hb level as part of oxygenation status**
- △ **Blood replacement**
- △ **Erythropoietin (Epoen, 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
 - ◆ Stimulates release of NO, which increases free-radicals
 - ◆ Greater affinity for fetal Hb- fetal asphyxia

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.

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%

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



Hbmet blood sample

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 FIO_2
- △ $Hb_{MET} 20-50\%$
 - ◆ anxiety
 - ◆ fatigue
 - ◆ tachycardia
- △ $Hb_{MET} 50-70\%$
 - ◆ coma
 - ◆ death

Manifestations

- △ SpO_2 is unreliable- will display 80-85% with very high Hb_{MET}
- △ Diagnosis- CO-oximetry

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)
 - ◆ loperamide (Imodium)- antidiarrheal
 - ◆ 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

**Manifestations**

- △ Patient with green blood



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**

Management

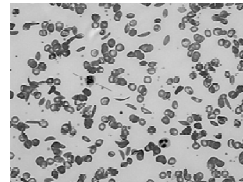
- ▲ **No intervention is necessary**
- ▲ **Stop causative medication**
- ▲ **Treat constipation**

Sickle Cell Disease**Etiology - hereditary**

- ▲ **X-linked recessive gene for HbS**
 - ◆ **primarily among persons of African descent**
 - ◆ **carrier has one HbS gene - sickle cell trait**
 - ◆ **sickle cell disease has two HbS genes**
 - ◆ **those with sickle cell trait are resistant to malaria**

Pathophysiology

- ▲ **HbS does not carry oxygen, causing anemic hypoxia**
- ▲ **HbS accumulates, blocking blood vessels**



Manifestations

- ▲ Chronic hemolytic anemia
- ▲ Recurrent infections
- ▲ Abnormalities of the spleen
- ▲ Avascular necrosis- death of bone tissue
- ▲ Chest pain

Symptoms

- ▲ Pain- may be severe
- ▲ Tiredness
- ▲ Dizziness
- ▲ Dyspnea
- ▲ Pallor
- ▲ Jaundice
- ▲ Growth retardation
- ▲ Delayed puberty

Diagnosis

- ▲ Medical history
- ▲ Physical examination
- ▲ Laboratory testing - visualization of sickle cells
- ▲ Newborn screening - Baby's First Test

Complications

- ▲ Sickle cell crisis - episodes of severe pain
- ▲ Infections
- ▲ Acute chest syndroms
 - ◆ chest pain
 - ◆ cough
 - ◆ dyspnea
 - ◆ fever
- ▲ Splenic sequestration

Complications

- ▲ Leg ulcers
- ▲ Stroke
- ▲ DVT, pulmonary embolism
- ▲ Vision loss - blockage of retinal vessels

Prevention of crises

- ▲ Hydroxyurea - prevents crises
- ▲ L-glutamine - prevents crises
- ▲ Hydration
- ▲ Avoidance of thermal stress
- ▲ Avoidance of hypobaric conditions
- ▲ Avoidance of extreme physical stress

Treatment

- ^ Pain relief- may require opiates
- ^ Oxygen
- ^ Hydroxyurea - prevents crises
- ^ L-glutamine - prevents crises
- ^ Infection prevention
 - ◆ hand washing
 - ◆ antibiotics
 - ◆ vaccines
- ^ Blood transfusions

Treatment

- ^ Medications for DVT, emboli
- ^ Splenectomy for chronic splenic sequestrations
- ^ Bone marrow transplant from matched donor can cure SCD

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

Summary & Review**^ Sickle cell disease (SCD)**

- ◆ etiology - X-linked recessive heredity
- ◆ pathophysiology - anemic hypoxia, clotting
- ◆ manifestations
- ◆ complications
- ◆ treatment