Hemoglobin Abnormalities

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This Presentation is Approved for
1 CRCE Credit Hour

Learning Objectives

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

Hemoglobin Structure & Function

Hemoglobin Structure

- Molecule containing four heme groups
- Each heme group contains an iron atom
- One molecule of O_2 binds to each heme group

Hemoglobin Function

- Four molecules O_2 per molecule of Hb = 100% saturation
- Three molecules O_2 per molecule of Hb = 75% saturation

Hemoglobin Function

- One gram of Hb carries 1.34 mL O_2
- At 100% saturation, 15g Hb carries 20.1 mL O_2
- At PaO_2 = 100, 0.3 mL O_2 is carried dissolved in plasma

Hemoglobin Function

- Without Hb, cardiac output must increase to 36 L/min for same O_2 delivery
- Functions in O_2 transport
  - Binds O_2 for transport
  - Transports O_2 to tissues
  - Releases O_2 to tissues

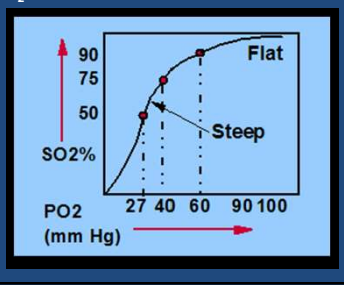
Hemoglobin Function

- Additional functions
  - Buffer
  - CO_2 transport: carries greatest amount of exchanged (excreted) CO_2

FYI see links below for additional information on structure & function of Hb

Hemoglobin Function

- HbO_2 dissociation curve: describes relationship between PO_2 & SO_2

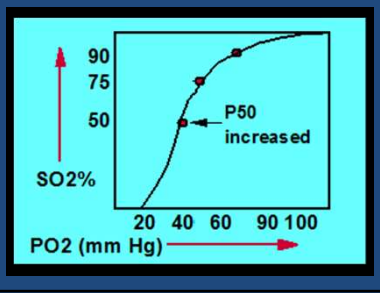


Hemoglobin Function

- HbO_2 dissociation curve: describes relationship between PO_2 & SO_2
  - Upper portion of curve
    - Hb has greater affinity for O_2
    - Facilitates uptake of O_2 in lung
  - Lower portion of curve
    - Hb has lesser affinity for O_2
    - Facilitates release of O_2 to tissues

Hemoglobin Function

- Right shift: lower SO_2 for given PO_2

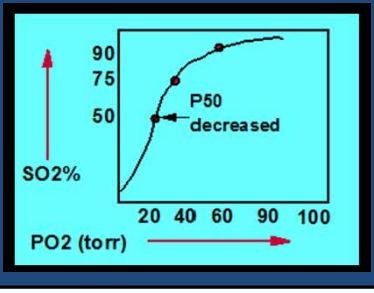


Hemoglobin Function

- Right shift: lower SO_2 for given PO_2
  - Hb releases O_2 more readily
  - Increased temperature
  - Increased PCO_2 (Bohr shift)
  - Increased H+ (decreased pH)
  - Hb_{SULF}

Hemoglobin Function

- Left shift: greater SO_2 for given PO_2



Hemoglobin Function

- Left shift: greater SO_2 for given PO_2
  - Decreased temperature
  - Decreased PCO_2
  - Decreased H+ (increased pH)
  - Fetal Hb
  - Decreased 2,3 diphosoglycerate (DPG): associated with stored blood

Hemoglobin Production

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

Hemoglobin Metabolism

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

Hemoglobin Saturation

- Calculation vs. direct measurement
  - Calculations are based on HbO_2 curve
  - Direct measurement with oximeter or co-oximeter is more accurate
  - Calculated SO_2 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 myeloproliferative disease
  - Origin
    - Inherited mutation
    - Acquired mutation

FYI see links below for article on primary polycythemia

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 see links below for article on secondary polycythemia

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 (pruritis)
- 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 see links below for information on porphyria, vampires, & werewolves

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 times stronger than O_2
  - Binds with myoglobin: myocardial damage
  - Shifts HbO_2 curve to left: interferes with release of O_2 to tissues

Carbon Monoxide

- Effects
  - Binds with Hb 240 times stronger than does O_2
  - Binds with myoglobin: myocardial damage
  - Shifts HbO_2 curve to left: interferes with release of O_2 to tissues
  - 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 Rad 57®

- Hb
- Oxygen content
- HbO_2
- HbCO
- Hb_{MET}

Courtesy of Masimo, Inc.

FYI see links below for information on Masimo

Management

- 100% O_2 decreases HbCO by ½ every 60 minutes
- HbCO > 10%: 100% O_2 until HbCO is less than 5%
- HbCO > 40%: transport for hyperbaric O_2
- Pregnant patients: hyperbaric O_2 for HbCO > 30%

FYI see links below for article on HbCO management

Methemoglobinemia

Methemoglobin

- Hemoglobin that has been oxidized to the ferric state (Fe+++)
- Does not transport O_2 or CO_2

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 see links below for article on methemoglobinemia

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

See links below for case of methemoglobinemia after bronchoscopy

Management

- O_2 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 O_2
- Hb_{SULF} shifts HbO_2 curve to right, improving tissue O_2 delivery
- Looks worse than it is

Manifestations

- 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
  - O_2
  - Methylene blue

FYI see links below for case of sulfhemoglobinemia

Management

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

Summary & Review

- Hemoglobin
  - Structure & 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, erythropoeitin

Summary & Review

- CO poisoning
  - Etiologies: CO inhalation
  - Manifestations: depends on Hb_{CO} level
  - Diagnosis: Hb_{CO} measurement
  - Management: O_2, hyperbaric O_2

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