NOTES
METHEMOGLOBINEMIA

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osms.it/methemoglobinemia

PATHOLOGY & CAUSES

- ↑ methemoglobin levels in blood > 10%
  - Normal methemoglobin level < 1%
- Methemoglobin
  - *Hemoglobin form:* contains ferric (Fe^{3+}) iron → ↓ oxygen affinity
  - Overwhelming oxidative stress (in red blood cells) → iron oxidation within heme (Fe^{2+} → Fe^{3+}) → hemoglobin converted to methemoglobin
  - Oxygen binding → ↑ affinity in remaining heme sites that may have been in ferrous (Fe^{2+}) state in heme tetramer → left shift in oxygen curve → overall oxygen to tissue release ability ↓ → tissue hypoxia
- Healthy cells
  - Spontaneous methemoglobin conversion rapidly ↓ by protective enzymes
  - Nicotinamide adenine dinucleotide-reduced (NADH) methemoglobin reductase (diaphorase I)
  - Nicotinamide adenine dinucleotide phosphate (NADPH) methemoglobin reductase
  - Ascorbic acid
  - Glutathione enzyme system

TYPES

Acquired methemoglobinemia

- ↑ methemoglobin formation
- Drugs
  - Antibiotics, local anesthetics, antiemetics
- Industrial chemicals
  - Aniline dyes, chlorates, bromates, nitrates

Congenital methemoglobinemia

- Recessive gene → enzyme diaphorase I deficiency → inefficient methemoglobin ↓ → accumulation
- Abnormal hemoglobin variants (HbM/HbH) → hemoglobin not enzymatic-reduction amenable
- Diaphorase I cofactor deficiency
  - Impaired upstream enzymes → insufficient diaphorase I cofactors production → impaired enzymatic reduction
  - Pyruvate kinase deficiency
  - Glucose-6-phosphate dehydrogenase deficiency

SIGNS & SYMPTOMS

- Arterial blood may develop bluish/chocolate-brown tinge
- Healthy individuals
  - Symptoms may only manifest at methemoglobin levels > 15%
  - Cyanosis → dyspnea, mental status change, headache, fatigue, exercise intolerance, dizziness
- Severe methemoglobinemia (> 50%) → seizure, coma, death

DIAGNOSIS

DIAGNOSTIC IMAGING

Co-oximetry

- Analyses blood-spectrum absorption → methemoglobin peak absorbance at 631nm

LAB RESULTS

- Arterial blood gas
  - Clinical cyanosis in normal arterial PO_2 presence
- Enzyme assays
  - Enzyme assays for specific enzymes involved in maintaining hemoglobin in reduced state may be utilized

TREATMENT

MEDICATIONS

- Specific
  - *Methylene blue*: intravenous reducing agent → reduces heme group from methemoglobin → hemoglobin

OTHER INTERVENTIONS

- Supplemental oxygen
- Vitamin C (ascorbic acid) may improve cyanosis in chronic cases