Medical Reference

Corbin Cox

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Methemoglobinemia

2.1 PATHOPHYSIOLOGY

- Oxidant stress converts hemoglobin iron from Fe^{2+} to Fe^{3+}
  - Still binds oxygen, but doesn't release it (shifts binding curve left)
- NADH (glycolosis) pathway detoxifies most methemoglobin (Met-Hgb) during normal situations
- NADPH is upregulated when needed, such as toxin-induced methemoglobinemia

Figure 2.2: Met-Hgb (left), Normal (right)

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2.1.1 Causes

- Conditions
  - Cytochrome b_5 reductase deficiency
  - Hemoglobin M
- Drugs
  - **Dapsone**
  - **Benzocaine** (and other local anesthetics)
  - Nitrite-containing compounds (NTG, nitroprusside, amyl nitrite)
  - Sulfonamides (sulfa antibiotics)
  - Analine dyes
  - Primaquine / chloroquine
  - Many others

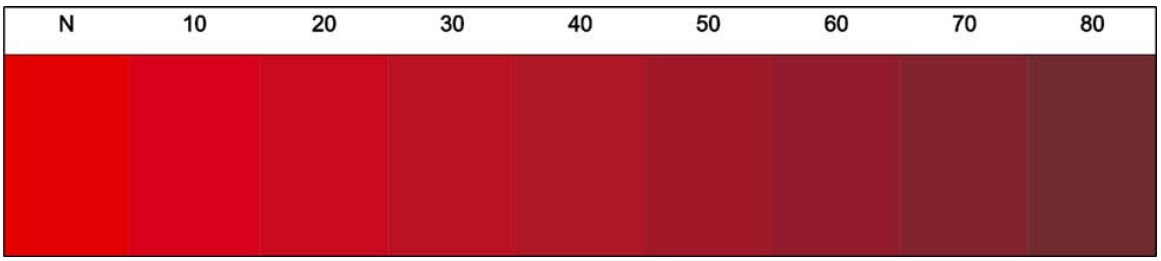
2.2 DIAGNOSIS

- **Be suspicious for methemoglobinemia in cyanotic patients with an SpO2 in the mid-80%'s which is unresponsive to supplemental oxygen, and in patients with chocolate-colored blood**
- Hypoxic cyanosis usually doesn't occur until SpO2 is ≈50%, this is a rare case of cyanosis with "high" SpO2
- **SaO2 - SpO2 >5%** is an indication that something is messing with pulse-ox reading, usually a deviant Hgb like Met-Hgb
  - High Met-Hgb will make SpO2 trend toward ≈ 85%
  - Supplemental O2 will drive up PaO2, and SaO2 on iStat ABGs will increase because it is calculated from PaO2
- Order methemoglobin from lab for confirmation, if symptomatic with high suspicion for methemoglobinemia, can treat empirically

2.3 TREATMENT

- **Treat symptomatic patients or any patient with Met-Hgb >30%**
- Call Toxicology
- Methylene Blue 1-2 mg/kg IV over 5 min
  - Can repeat in 30-60min if needed

Figure 2.3: **Methemoglobin %**



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Place a drop of blood on white paper, allow it to dry, and compare with chart above. Chart Met-Hgb should be within ± 15% of lab value

Table 2.1: Met-Hgb Symptoms

Met-Hgb %	Symptoms
1-3%	Normal
10-20%	Cyanosis
20-30%	Anxiety Headache Dizziness Fatigue
30-50%	Tachypnea Confusion Syncope
50-70%	Szs Coma Metabolic Acidosis
>70%	Death

  - SpO2 may decrease significantly during infusion, caused by interference with pulse-ox, not hypoxia
  - Will discolor body fluids
  - Side effects
    - MAO inhibition $\implies$ serotonin syndrome
    - Methemoglobinemia (doses >7 mg/kg/day)
  - May not be as effective for analine dye overdoses, analine metabolite inhibits entry of methylene blue into RBCs
- Methylene Blue continuous infusion
  - Limited evidence for dosing
    - One case series reported 2 mg/kg over 6hr (0.33 mg/kg/hr, daily dose 8 mg/kg)
    - Some self-reporting from toxicologist starting at 0.1 mg/kg/hr
    - Rates of 0.5-1 mg/kg/hr when used for vasoplegia, so higher doses *may* be safe
    - **Bottom line: Call tox if you have to start continuous methylene blue**
  - Usually not needed, consider if Met-Hgb induced by long-acting agent like dapsone, or if >2 bolus doses needed
- Cimetidine for Dapsone induced Met-Hgb
  - Inhibits CYP450 metabolism of dapsone $\rightarrow$ hydroylamine dapsone, which produces more Met-Hgb than dapsone
- Other Therapies
  - High-Dose Vitamin C (takes a long time to work)
  - Riboflavin (takes a long time to work)
  - Hyperbaric oxygen
  - Red-cell exchange

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