Feeling Blue: 10 Fast Facts About Methemoglobinemia

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1. What is methemoglobinemia?

A condition where hemoglobin's iron is oxidized from ferrous (Fe^{2+}) to ferric (Fe^{3+}), producing methemoglobin that cannot bind oxygen. As a result, oxygen delivery to tissues decreases even though arterial oxygen tension (PaO_2) remains normal. This leads to functional anemia and tissue hypoxia.

2. Normal baseline levels are low.

Methemoglobin normally accounts for <2% of total hemoglobin. NADH- and NADPH-dependent reductase systems maintain this balance by reducing ferric iron back to ferrous iron.

3. Causes: inherited and acquired.

Inherited causes include cytochrome b5 reductase deficiency and hemoglobin M variants.

Acquired cases are far more common, often triggered by oxidizing drugs such as **dapsone**, benzocaine, **lidocaine**, nitrates, nitrites, and aniline dyes.

4. Methemoglobinemia look-alikes.

Cyanosis and hypoxia with a low SpO_2 can also occur in sulfhemoglobinemia, severe hypoxemia, or carbon monoxide poisoning.

Clinical signs include refractory cyanosis.

Your suspicion should increase with known cases of:

- Persistent cyanosis despite high-flow oxygen therapy.
- Blood appears chocolate-brown and does not turn red when exposed to air.

- Symptoms vary with concentration: 10–20% causes headache and fatigue, 30–40% confusion and dyspnea, and >50% can lead to arrhythmias, seizures, and death.

6. Pulse oximetry and ABG can mislead (the 'saturation gap').

In methemoglobinemia, SpO_2 readings plateau around 85% regardless of true oxygenation, while PaO_2 remains normal or elevated on ABG. This is known as the saturation gap. It should raise suspicion for dyshemoglobinemia.

7. Severity depends on methemoglobin level and patient reserve.

Healthy individuals may tolerate levels up to 15–20%, but patients with anemia, cardiovascular disease, or pulmonary disease may deteriorate even at lower levels. Levels >40% are considered life-threatening, requiring immediate antidotal therapy.

8. Methylene blue is first-line therapy.

Indicated for symptomatic patients or levels >30%. Initial dose: **1–2 mg/kg IV over 5 minutes**. Clinical improvement occurs within minutes. If symptoms persist or methemoglobin remains >30% after one hour, a **second dose of 1 mg/kg** may be given. Maximum total dose: 7 mg/kg to avoid paradoxical oxidation.

9. Contraindications and alternatives.

Methylene blue requires NADPH, so it may be ineffective in G6PD-deficient patients. Contraindicated in pregnancy and with SSRI use due to serotonin syndrome risk.

Alternative therapies include high-dose **Vitamin C (ascorbic acid) 1.5–3 g IV every 6 hours** and exchange transfusion in refractory or severe cases.

10. Rebound methemoglobinemia can occur.

Rebound often results from ongoing oxidant exposure or short methylene blue duration. Recheck levels 1–2 hours after treatment and again at 6 hours. Continuous monitoring for recurrent cyanosis and hypoxia is essential in high-risk patients.

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