

## THE CLINICAL PICTURE

### RIVA RAIKER, MD

Junior Resident, Department of Internal Medicine, University of Kentucky Medical Center, Lexington, KY

### WILLIAM C. LIPPERT, MD, MPH

Senior Resident, Department of Internal Medicine, University of Kentucky Medical Center, Lexington, KY

### ROMIL CHADHA, MD, MPH, FACP, SFHM

Assistant Professor of Medicine, University of Kentucky Medical Center, Lexington, KY

# Methemoglobinemia in an HIV patient



**Figure 1.** The patient's hands on presentation (top) and after treatment with intravenous methylene blue (bottom).

**A** 45-YEAR-OLD MAN with known human immunodeficiency virus infection presented with a 5-day history of dyspnea. When his dyspnea had become symptomatic, he had restarted his home dapsone prophylaxis, but his dyspnea had progressively worsened, and his urine became dark.

doi:10.3949/ccjm.85a.17004

On presentation to our institution, he was tachycardic, tachypneic, hypoxic, and cyanotic (**Figure 1**). Chest radiography revealed multifocal bilateral airspace opacities. He was started on vancomycin and piperacillin-tazobactam for treatment of presumed pneumonia, and his dapsone was continued for prophylaxis against *Pneumocystis jirovecii* pneumonia.

During the next several hours, his hypoxia worsened, and his peripheral capillary oxygen saturation was 87% despite use of a Venturi mask at a 35% fraction of inspired oxygen. Arterial blood gas testing revealed an elevated partial pressure of oxygen (143 mm Hg) and chocolate-brown colored arterial blood. Due to the low peripheral capillary oxygen saturation, high partial pressure of oxygen, and abnormal color of his blood (**Figure 2**), serum methemoglobin testing was ordered and revealed a concentration of 22.9% (normal value < 1.5%).

Based on these test results, the patient's dapsone was stopped and replaced with atovaquone. Intravenous infusion of methylene blue was started, with subsequent improvement of the hypoxia and cyanosis (**Figure 1**). His urine became green, but it returned to a normal color in a matter of hours. He was ultimately diagnosed with *P jirovecii* pneumonia and completed a course of atovaquone with total resolution of his symptoms.

## ■ THE MECHANISMS BEHIND METHEMOGLOBINEMIA

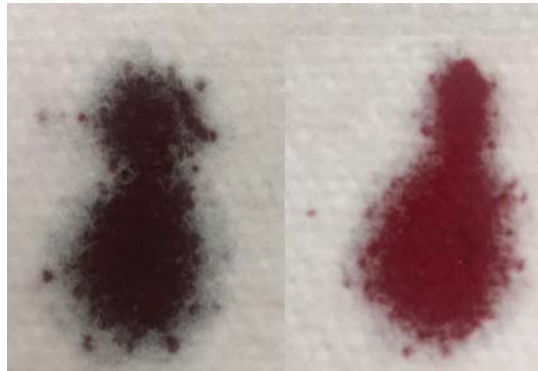
Heme iron is normally in the ferrous state ( $\text{Fe}^{2+}$ ), which allows for hemoglobin to carry oxygen and release it to tissues.<sup>1</sup> Exposure to an oxidative stress can lead to methemoglobinemia from an increase in abnormal hemoglobin that contains iron in a ferric state ( $\text{Fe}^{3+}$ ).<sup>1,2</sup>

Methemoglobin reduces oxygen-carrying capacity in two ways: it is unable to carry oxygen, and its presence shifts the oxygen dissociation curve to the left, causing any remaining normal hemoglobin to be unable to release oxygen to the tissues.<sup>1,2</sup>

Causes of acquired methemoglobinemia include topical anesthetics (eg, benzocaine, lidocaine) and antibiotics (eg, dapsone).<sup>2,3</sup> Signs and symptoms include cyanosis, headache, fatigue, dyspnea, lethargy, respiratory distress, and dark-colored urine.<sup>1,2</sup>

### MANAGEMENT

Treatment consists of intravenous methylene blue, which reduces the hemoglobin from a ferric state to a ferrous state.<sup>1-4</sup> Methylene blue is a water-soluble dye excreted primarily in the urine, and common side effects include dizziness, nausea, and green urine.<sup>5-7</sup> The blue pigments from methylene blue combine with urobilin (a yellow pigment in the urine), producing a green color.<sup>7</sup> This is not pathological



**Figure 2.** The patient's arterial blood on presentation (left) compared with a sample of normal arterial blood (right).

and requires no treatment, as the urine returns to normal color after the body fully excretes the dye.<sup>5-7</sup>

If intravenous methylene blue fails to produce a response, other treatments to consider include hemodialysis, blood transfusion, exchange transfusion, and hyperbaric oxygen therapy.<sup>2</sup>

### REFERENCES

1. Umbreit J. Methemoglobin—it's not just blue: a concise review. *Am J Hematol* 2007; 82:134–144.
2. Ash-Bernal R, Wise R, Wright SM. Acquired methemoglobinemia: a retrospective series of 138 cases at 2 teaching hospitals. *Medicine (Baltimore)* 2004; 83:265–273.
3. Coleman MD, Coleman NA. Drug-induced methaemoglobinemia. *Treatment issues. Drug Saf* 1996; 14:394–405.
4. Sikka P, Bindra VK, Kapoor S, Jain V, Saxena KK. Blue cures blue but be cautious. *J Pharm Bioallied Sci* 2011; 3:543–545.
5. Stratta P, Barbe MC. Images in clinical medicine. Green urine. *N Engl J Med* 2008; 358:e12.
6. Miri-Aliabad G. Green urine secondary to methylene blue. *Indian J Pediatr* 2014; 81:1255–1256.
7. Prakash S, Saini S, Mullick P, Pawar M. Green urine: a cause for concern? *J Anaesthesiol Clin Pharmacol* 2017; 33:128–130.

**ADDRESS:** William C. Lippert, MD, MPH, University of Kentucky Medical Center, Charles T. Wethington Building, Suite 304B, 900 South Limestone Street, Lexington, KY 40536; [william.lippert@uky.edu](mailto:william.lippert@uky.edu)

**Causes of acquired methemoglobinemia include antibiotics and topical anesthetics**