

METHEMOGLOBINEMIA

1. The Disease Definition

Methemoglobinemia is a blood disorder caused when nitrite interacts with the hemoglobin in red blood cells.

A. Clinical Description

Nitrate, a relatively non-toxic substance, occurs naturally as part of the nitrogen cycle. However, bacteria can convert nitrate to nitrite in the environment, in foods, and in the human body. Until infants reach about six months of age, their digestive system secretes lower amounts of gastric acid and the pH level in their digestive system is higher than most adults. Adults with a diminished capability to secrete gastric acid also can experience a rise in pH in their digestive systems. In both situations, bacteria can proliferate, increasing the transformation of nitrate to nitrite. Once in the blood, nitrite oxidizes iron in the hemoglobin of red blood cells to form methemoglobin, which lacks hemoglobin's oxygen-carrying ability. The nitrite can come from nitrate in drinking water or from food, some drugs, or other sources.

Although methemoglobin is continually produced in humans, an enzyme in the human body reduces it to hemoglobin. In most people, the conversion is rapid. Typically, less than 1 percent of the total circulating hemoglobin in a healthy adult is present in the form of methemoglobin. Infants, however, have a low concentration (about 60 percent of the adult concentration) of the reducing enzyme, as do some older individuals with an enzyme deficiency. In these people, methemoglobin is not converted to hemoglobin as readily. When methemoglobin levels are elevated, the condition known as methemoglobinemia, often referred to as "blue baby syndrome," can result. The blood lacks the ability to carry sufficient oxygen to individual body cells.

Infants suffering from methemoglobinemia may seem healthy, but show intermittent signs of blueness around the mouth, hands and feet. They may have episodes of breathing trouble, some diarrhea and vomiting. In some cases, an infant with methemoglobinemia has a peculiar lavender color but shows little distress. Blood samples appear chocolate brown and do not turn pink when exposed to air. When the methemoglobin level is high, infants show a marked lethargy, excessive salivation, and loss of consciousness. Convulsions and death can occur at extreme levels.

B. Sources of Exposure

The Environmental Protection Agency (EPA) has set a public water-supply maximum contaminant level (MCL) of 10 milligrams per liter (mg/L), which is equal to 10 parts per million (ppm) for nitrate-nitrogen. This level provides a margin of safety against a significant risk for human health. EPA believes water containing nitrate-nitrogen at or below this level is acceptable for daily drinking over a lifetime and does not pose a methemoglobinemia health risk for infants or adults.

In Iowa, an unusual source of exposure was discovered in 2003. Approximately 63 guests from a wedding reception came to emergency rooms after consuming a peculiar-tasting punch. Within 15 minutes of ingesting the punch, they experienced headaches, dyspnea, dizziness, and nausea. Thirteen had cyanosis, and nine collapsed. Pulse oximetry remained in the mid 80s despite oxygen therapy. Chocolate-brown colored blood was noted in all of the cyanotic patients. Methemoglobin levels for all patients ranged from 1.0 to 60.2 percent. The mean methemoglobin level of the 20 hospitalized patients (13 children, 9 adults) was 14.4 percent. Thirty-five patients (19 hospitalized, 16 treated and released) were treated with methylene blue. All admitted patients were discharged the next day. All food and water was tested and the sodium nitrite concentration in the punch was 500 to 820 mg/L. An investigation revealed that sodium nitrite was accidentally substituted for citric acid during the processing of the punch mix. Two additional batches of the punch mix were recalled before distribution. A fourth batch was distributed and consumed by 13 people at a baby shower. Eight developed symptoms, but none sought medical attention.

C. Population at Risk

Infants under six months of age are the primary population at risk, although preventive measures are also encouraged for pregnant women, women who are breast feeding, and other high-risk people.

D. Diagnosis, Treatment, and Prognosis

Diagnosis is made based on symptoms and the level of methemoglobin in the blood.

If the condition is identified early and is not life-threatening, a change of drinking water to water with less than 10 milligrams per liter of nitrate-nitrogen is usually the only needed treatment. This will reduce methemoglobin to hemoglobin in two to three days. Severely affected infants may be treated with an intravenously administered solution of methylene blue.

Patients should recover promptly and suffer no lingering effects if the condition is identified and treated promptly.

E. Prevention of Exposure

Methemoglobinemia prevention is especially important for infants under six months of age, although preventive measures are also encouraged for pregnant women, women who are breast feeding, and other high-risk people. Water from a source containing nitrate-nitrogen at or below 10 ppm should be used. If the drinking water source contains nitrate-nitrogen above 10 ppm, bottled water should be used. Boiling the water does not reduce nitrate levels. In fact, boiling can concentrate them as some water evaporates as steam.

2. Reporting Criteria

A. Disease Reporting

Methemoglobinemia is reportable whenever there is a blood analysis showing greater than 5 percent of total hemoglobin is methemoglobin.

Methemoglobinemia cases must be reported within a week to the Iowa Department of Public Health Division of Environmental Health by the physician or health practitioner attending any person having a reportable disease and by laboratories performing tests identifying reportable diseases. Reporting can be through the Iowa Disease Surveillance System (IDSS), phone, fax, or mail. The preferred reporting method is through IDSS. To report via fax or mail, please use the Methemoglobinemia Case Report Form available in the Epi Manual and online at

<https://wiki.idph.iowa.gov/Portals/3/userfiles/12/Methemoglobinemia Case Report Form.pdf>

How to report to the Division of Environmental Health (Non IDSS Users)	
Phone (Mon-Fri 8 am-4:30 pm):	800-972-2026
Fax:	515-281-4529
Address:	Iowa Department of Public Health Division of Environmental Health Lucas State Office Building 321 E. 12th Street Des Moines, Iowa 50319-0075
24-hour Disease Reporting Hotline:	800-362-2736

B. References

Methemoglobinemia – Medscape

<https://emedicine.medscape.com/article/204178-overview>