Nitrate and Methemoglobinemia

Drinking water with high nitrate can cause a potentially fatal disorder called methemoglobinemia. Methemoglobinemia is a condition in which more than one percent of the hemoglobin in red blood cells take the form of methemoglobin. Hemoglobin carries oxygen in our blood, delivering it from the lungs to the rest of our body. Methemoglobin does not carry oxygen well and, when it replaces hemoglobin, it can cause a gray-blueness of the skin (cyanosis).

We have a lot of information about how excess nitrate in drinking water behaves in our bodies and leads to methemoglobinemia. Nitrate in water is almost completely absorbed into the blood. Our bodies convert a portion of that nitrate into nitrite. Nitrite reacts with blood to create methemoglobin. The more methemoglobin in the blood, the worse that blood is at carrying oxygen where it is needed. Along with these changes in blood chemistry, a person suffering methemoglobinemia may also experience elevated resting heart rate, weakness, nausea, and in severe cases, death.

Methemoglobinemia in Minnesota and Wisconsin

Research and case reports show that nitrate in well water above 10 milligrams per liter (mg/L) can cause methemoglobinemia in infants less than six months old. In 1945 the hypothesis that high levels of nitrate in well water caused methemoglobinemia was published (Comly 1945). Two years later, an infant near the town of Tyler became the first published case in Minnesota (Rosenfield and Hudson 1950). In the following three years, there were 146 cases voluntarily reported in Minnesota, including 14 deaths. In 1979 and 1980 there were two reported cases of methemoglobinemia in Minnesota. In both cases nitrate concentrations in the wells were over 50 mg/L. Once the source of water was changed in the homes, the methemoglobinemia resolved (Convery 2013).

Most Minnesota cases of methemoglobinemia in infants occurred in the southwestern part of the state, but cases have been reported from the southern border to as far north as Becker County. Some infants developed symptoms after fewer than two days, and other infants were fed formula prepared with well water for up to 60 days before symptoms appeared. It is suspected that many milder cases were resolved by changing the source of the infant's water and were never reported (Rosenfield and Huston 1950). There were no methemoglobinemia cases reported in breast fed babies.

The most recognized symptom of methemoglobinemia is a gray-blue color to the lips that eventually spreads to the whole body. In some cases, the bluish color can be so subtle that it goes unnoticed (Rosenfield and Huston 1950). This was the case when parents in Columbia County, WI brought their child in for immunizations in 1998. They noticed that their child had been "crabbier than normal" and had been vomiting after feeding since they moved to a new house served by a private drinking water well. Concerned that this may be a case of methemoglobinemia, a home nurse visited the family and took water samples. The concentration of nitrate in their well water was 22.9 mg/L. The doctor placed the baby on bottled water and the methemoglobinemia resolved (Knobeloch, Salna et al. 2000).

Other Cases of Methemoglobinemia

Nitrate in well water and methemoglobinemia are not unique to the Midwest. It occurs all over the country, as well as around the world. According to the Centers for Disease Control and Prevention, between 1979 and

1996 there were six infant deaths from methemoglobinemia in Texas, South Dakota, Louisiana, Virginia, and Colorado (Knobeloch, Salna et al. 2000). Additionally, it is a common problem in Eastern Europe, where most methemoglobinemia cases are associated with contaminated water (Knobeloch, Salna et al. 2000).

Infants Are Especially Sensitive to Nitrate in Water

While adults can develop methemoglobinemia due to high levels of nitrate in drinking water, public health actions mainly focus on infants less than six months old because they are an especially sensitive population. Infants fed formula prepared with water high in nitrate are the most highly exposed population. They receive the highest dose of nitrate compared to all other age groups based on body weight (U.S. Environmental Protection Agency (EPA) 2011). In addition to their high exposure, infants have different body chemistries than adults. They convert more nitrate to nitrite, which leads to the creation of methemoglobin, and their bodies are less able to convert methemoglobin back into hemoglobin. This causes methemoglobin to build up in the body of an infant faster than it builds up in the body of an adult.

Scientific Support for 10 Milligrams per Liter

The evidence supporting the 10 mg/L US EPA Maximum Contaminant Level (MCL) for nitrate in drinking water and the Minnesota Health Risk Limit (HRL; which is the adopted MCL) is strong. Because exposure to nitrate and resulting illness has been observed in humans rather than just laboratory animals, values derived to protect people do not have to be adjusted to account for differences in animals and humans.

Additionally, the six Minnesota cases of methemoglobinemia in infants described by Rosenfield and Huston (1950) occurred in water with nitrate levels above 10 mg/L. A nationwide survey performed by the American Public Health Association in 1949 showed this was a national trend. The survey collected details of 278 methemoglobinemia cases, of which 214 included information about drinking water sources. All 214 cases were associated with drinking water that had a concentration of nitrate above 10 mg/L (Walton 1951).

Factors That May Reduce Cases of Methemoglobinemia

Much of what is known about the health risks of nitrate is from reports, surveys, and other work done in the mid-1900s. Physicians and scientists quickly concluded that water with nitrate above 10 mg/L is potentially lethal to infants less than six months old. Since that time, there have been several changes that may have reduced the real or perceived number of methemoglobinemia cases in Minnesota.

- The high number of cases of methemoglobinemia in 1947-1949 lead to a familiarity with the illness in infants and how to treat it (switch water sources). There has been a gradual drop off in the number of cases voluntarily reported by physicians following this awareness. Additionally, new mothers are more aware of their water source and may opt to feed their babies formula reconstituted with bottled water.
- The condition may not be easily recognized by health care providers, particularly in mild cases with symptoms like irritability, lethargy, and/or a blue skin color that may fade and return.
- Methemoglobinemia is not a reportable illness in Minnesota and there is no mechanism in place for a provider to report cases to the state health department. This limits our ability to know how many infants are treated for this condition each year. In a recent review of hospital discharge data and emergency department records in Minnesota from 2000-2016, there were 10 cases of

methemoglobinemia in infants greater than one day old and less than one year old. The majority of the case records lacked supporting information needed to definitively rule out nitrate in drinking water as a cause or contributor to the diagnosis.

- The 1974 MDH Well Code set a new standard for construction for all new wells in Minnesota. Requirements on casing materials, distances from contamination sources, and well construction methods all help reduce nitrate and bacteria contamination. For example, Walton (1951) noted that in Iowa, water samples with nitrate concentrations over 10 mg/L occurred in 39.7 percent of dug wells, 21.5 percent of bored wells, and only 4.5 percent of drilled wells.
- Baby formula ingredients have changed since the 1950s. Formulas now contain antioxidants such as Vitamin C that can turn nitrite into nitric oxide, a beneficial molecule, and block the formation of methemoglobinemia. This is also why vegetables, a source of high nitrate in the diet, have not likely resulted in cases of methemoglobinemia. Their high antioxidant content may be playing a role in converting the nitrite from nitrate to nitric oxide, reducing harmful effects of nitrate.

In sum, the evidence remains compelling that high levels of nitrate in well water cause methemoglobinemia. While methemoglobinemia in infants may be less common today, it has not disappeared, and remains an important public health concern.

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