Chapter 33

Nitrates and Nitrites in Water

Nitrogen, an essential nutrient, is absorbed and incorporated by plants from nitrate or ammonium in soil. The use of nitrogen fertilizer for improved crop yields has generally increased in the United States and globally since the 1950s, peaking in the United States around 1990.[1] Nitrate contamination of water supplies is a potential environmental consequence of modern agricultural activity and increasing urbanization. Nitrate concentrations in shallow groundwater and some surface waters have increased as a result of use of nitrogen fertilizers, intensive livestock operations that produce large amounts of animal waste, substandard private septic systems, and municipal wastewater treatment discharges.[2] A recent US Geological Survey National Water Quality Assessment Program report documents elevated nitrate concentrations in 4 of 33 major aquifers sampled in rural and urban areas.[3] Poorly constructed shallow wells in rural areas are at greatest risk of nitrate contamination. In general, nitrite is not as prevalent in water supplies as nitrate, because nitrite is rapidly converted to nitrate, depending on aerobic and bacterial conditions.[4]

High nitrate concentrations in water can potentially have adverse effects on ecology and public health. Nitrate and other nutrients have been linked to blue-green algal blooms, which can produce toxic bacteria that can negatively affect wildlife and humans.[5,6] Methemoglobinemia in infants may result from ingestion of water contaminated with nitrate.[7] Two cases of methemoglobinemia, also known as "blue baby syndrome," were reported in 2000 by the Wisconsin Department of Health in infants fed formula reconstituted with water from private wells with nitrate-nitrogen (NO_3-N) concentrations of 22.9 and 27.4 mg/L.[8] There is great interindividual variability in risk of methemoglobinemia related to nitrate contamination of drinking water. In adults, genetic reductase deficiencies are potential risk factors. Infants younger than 6 months are at high risk, and those younger than 1 month are at highest risk. It has been suggested that coincident gastrointestinal tract infection may be a significant contribution to risk. Gastrointestinal tract infection, diarrhea, and/or vomiting can lead to methemoglobinemia in infants without exposure to high nitrate concentrations from drinking water or foods.[9]

NITRATE IN US WATER SUPPLIES

The trend for US water supplies has been a general increase in nitrate concentrations.[10] The US Environmental Protection Agency (EPA) drinking water standard (maximum contaminant level [MCL]) for public water supplies is 10 mg/L (10 parts per million [ppm]) for NO_3-N and 1 mg/L (1 part per million) for nitrite.[11] These maximum contaminant levels were set in response to concerns regarding methemoglobinemia in infants. EPA drinking water standards, however, do not apply to private wells, nor are these wells subject to federal regulations of the Navajo Nation (which has its own EPA). Wells are minimally regulated by states. Well owners are usually responsible for their own wells. Approximately 15% to 20% of US households obtain their water from private wells.

It was estimated that approximately 1.5 million people, including 22 500 infants, or 1.2% of those served by private wells, and 3 million people, including 43 500 infants, or 2.4% of those served by public community wells, were exposed to drinking water nitrate concentrations above the maximum contaminant level.[12] The 1994 Midwest Well Water Survey collected water samples from 5500 domestic wells located in 9 states. Of those samples, 13.4% exceeded the nitrate maximum contaminant level, with Kansas (24.6%) and Iowa (20.6%) having the highest proportion of samples with nitrate maximum contaminant level greater than 10 parts per million.[13] Proximity to heavy agricultural activity may exacerbate the situation. A North Carolina study (1998) sampled 1600 wells in 15 counties where intensive livestock facilities were located. Of the wells tested, 10.2% had nitrate greater than 10 parts per million.[14] Nitrates in well water are interpreted as an indication of surface contamination and, thus, are often markers of other contamination, typically of agricultural origin, including fecal coliform bacteria, pesticides, and other land applications.

ROUTE AND SOURCES OF EXPOSURE

Drinking water is the main source of nitrate for infants. In breastfed infants, there is no evidence of increased risk of methemoglobinemia from maternal ingestion of nitrate-contaminated water with NO_3-N concentrations as high as 100 parts per million, because these mothers do not produce milk with high nitrate concentrations.[15] It is uncertain whether transplacental transfer of nitrates occurs. Acquired methemoglobinemia has been linked to a variety of oxidizing agents, including topical benzocaine, silver nitrate burn therapy, laundry inks, and other agents.[16]

CLINICAL EFFECTS

Nitrate is rapidly absorbed from the proximal small intestine, and approximately 70% of ingested nitrate is found in urine within 24 hours. Ordinarily, most ingested nitrate is metabolized and excreted unless conditions favor reduction to nitrite. Although few recent data are available, approximately 2000 cases of acquired methemoglobinemia were reported in North America and Europe between 1945 and 1971.[10]

Although nitrate does not cause methemoglobinemia, it can be converted to nitrite by gut flora. In turn, nitrite converts ferrous iron (Fe^{+2}) in hemoglobin to ferric iron (Fe^{+3}), resulting in methemoglobin, which is incapable of carrying oxygen. Infants younger than 6 months who are fed formula reconstituted with well water containing nitrate are at the greatest risk of methemoglobinemia. The gastric pH of infants is higher than that of older children and adults, with resultant proliferation of lower intestinal bacteria that reduce ingested nitrate to more reactive nitrite.[7] The system responsible for reduction of induced methemoglobin to normal ferrous hemoglobin has only about half the activity in infants as in adults.[17] Infants younger than 6 months are particularly at risk of methemoglobinemia as a result of lesser amounts and activity of methemoglobin reductase, the enzyme that reduces ferric iron in methemoglobin back to ferrous iron, regenerating hemoglobin. Infants begin making adult levels of methemoglobin reductase at around 6 months of age.

Methemoglobinemia generally presents with few clinical signs other than cyanosis. Methemoglobin is dark brown and results in obvious cyanosis at concentrations as low as 3%. Symptoms are generally minimal until methemoglobin concentrations exceed 20%. Usually, cyanosis is manifest well before other symptoms appear unless exposure is intense. The mucous membranes of infants with methemoglobinemia-induced cyanosis tend to have a brownish cast. The brown discoloration increases with the concentration of methemoglobin, as do irritability, tachypnea, altered mental status, and complaints of headache in older children. In the absence of respiratory symptoms, history of cardiovascular disease, abnormal pulse, or abnormal oximetry, a diagnosis of methemoglobinemia should be considered in a child who becomes cyanotic and unresponsive to oxygen administration.[18]

TREATMENT OF METHEMOGLOBINEMIA

Health care professionals who suspect that a child has methemoglobinemia should consult with their local poison control center or a toxicologist to help guide management. An asymptomatic child with cyanosis who has a methemoglobin concentration of less than 20% usually requires no treatment other than identifying and eliminating the source of exposure. For methemoglobin concentrations above 30%, methylene blue (dosage 1 mg/kg, intravenously, over a period of several minutes) and 100% oxygen are therapeutic antidotes. Methylene blue acts as an electron carrier for the hexose monophosphate alternate pathway that reduces methemoglobin to hemoglobin. A rapid disappearance of cyanosis in response to methylene blue would be expected within 1 hour but might not occur if the patient has erythrocyte glucose-6-phosphate dehydrogenase (G6PD) or nicotinamide adenine dinucleotide phosphate diaphorase deficiency or if methemoglobinemia is attributable to the ingestion of compounds such as aniline or dapsone. More information on diagnosis and treatment can be found elsewhere.[16,17]

PREVENTION OF METHEMOGLOBINEMIA

Clinical treatment alone for methemoglobinemia is not sufficient. It is critical to identify and eliminate exogenous sources of exposure. Infants with gastrointestinal infection, diarrhea, dehydration, and/or acidosis may be especially susceptible. Assessment of potential nitrate exposure includes asking about family residence, occupation, drinking water, foods ingested, and use of topical medications or folk remedies. Children may be exposed at child care or school or when visiting vacation homes or camps. Prenatal and newborn care for patients with private wells should include a recommendation for testing well water for nitrate contamination.[19] Water with elevated nitrate concentrations should not be ingested by infants younger than 1 year or used to prepare infant formula. Well waters with high nitrate concentrations typically have elevated concentrations of various pesticides and fecal coliform bacteria. Care must be taken when boiling water before mixing formula, because this may concentrate nitrate and other chemical contaminants. Boiling water for 1 minute generally is sufficient to kill microorganisms without overconcentrating nitrate and other chemical contaminants.[20] Effective in-home systems for nitrate removal include ion exchange resins and reverse-osmosis systems, which are available but expensive. Water testing for nitrate, pesticides, and fecal coliforms can be performed by any reference or public health laboratory using EPA-approved laboratory methods.

CHRONIC EFFECTS

Epidemiologic studies have reported increased risks associated with elevated concentrations of nitrate in drinking water for a variety of noncancer outcomes, including hyperthyroidism[21] and insulin-dependent diabetes.[22] Several studies have found associations between birth defects and high nitrate concentrations in water supplies.[22-25] Anecdotal reports of spontaneous abortions in Indiana

(1991–1993) describe a case study in which 3 women experienced a total of 6 spontaneous abortions; the women resided in proximity to each other and consumed drinking water from private wells containing high concentrations of NO_3-N (19–26 parts per million).[26]

Cancer risk during adulthood from exposure to nitrate in drinking water is another potential public health concern. Ingested nitrate is reduced endogenously to nitrite through bacterial reactions in the saliva, and nitrite can be converted to N-nitroso compounds via reaction with secondary amines (from common dietary sources or pesticides) in the stomach, intestine, and bladder.[27] N-nitroso compounds are known to induce cancer in a variety of organs in more than 40 animal species including higher primates. Epidemiologic studies on nitrate in drinking water and cancer risk have shown mixed results.[28] Some studies have demonstrated elevated risk of cancer of the esophagus, colon, nasopharynx, bladder, and prostate as well as non-Hodgkin lymphoma.[28,29] Ecologic studies of stomach cancer in Slovakia, Spain, and Hungary with historical measurements and exposure levels near or above the maximum contaminant level have found positive correlations with stomach cancer incidence or mortality.[30-32] In the Slovakian study, incidence of non-Hodgkin lymphoma and colon cancer were significantly elevated among men and women exposed to public water supplies with NO_3-N concentrations of 4.5 to 11.3 mg/L. Despite some uncertainty about nitrate contamination of water's contribution to cancer, the International Agency for Research on Cancer (IARC) reviewed the evidence in 2006 and determined that ingested nitrate or nitrite under conditions that result in endogenous nitrosation is probably carcinogenic to humans (Group 2A).[33]

Frequently Asked Questions

Q *Do commercial treatment systems sufficiently protect against nitrate contamination?*

A Water softeners and charcoal filters do not significantly reduce nitrate concentrations. Reverse–osmosis systems and ion exchange resins do remove nitrate but are expensive.

Q *Is low-grade nitrate contamination a risk for cancer?*

A We don't know for sure. Published studies of exposure to nitrate in drinking water and cancer risk are not all in agreement, but the International Agency for Research on Cancer has determined that ingesting nitrate probably increases the risk for cancer.

Q *Are the current maximum contaminant levels sufficiently strict to protect the population?*

A Most of the population is protected from methemoglobinemia or other potential adverse effects of nitrate at current maximum contaminant levels. The EPA's drinking water standards for nitrate (10 parts per million) and nitrite (1 part per million) are designed to protect the health even of people who are considered most susceptible. These standards, however, only apply to public water supplies.

Q Should I have my well water tested? How often?

A Indications for having a well tested would include having a new baby, recent damage to the well, or living in a neighborhood where there is known well water nitrate contamination. Individuals with private wells should have them tested for nitrates and coliform bacteria on a yearly basis. Risk factors for increased nitrate contamination include shallow well depth and regional nitrate contamination. Collect the sample during wet weather (late spring and early summer), when runoff and excess soil moisture carry contaminants into shallow groundwater sources or through defects in your well. Do not test during dry weather or when the ground is frozen.

Q I have a young baby and will be staying in a vacation home for a couple of weeks. I don't know whether the well has been tested. Can I give my baby the well water?

A The well water should be tested before being offered to an infant. If this is not possible, it may be safer and more convenient to use bottled water for the baby and others staying in the vacation home.

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