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NITRATE TOXICITY AND DRINKING WATER STANDARDS – A REVIEW

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Abstract. The current US EPA maximum contaminant level (MCL) for public drinking water supplies and the health advisory level (HAL) for other private water supplies is 10 mg/L, expressed as NO_3-N. Unlike other drinking water standards, the nitrate standard has no safety factor, which typically is about a 10-fold safety factor to account for differences in human susceptibility. Guidance, action, or advisory levels for nitrate in drinking water are lower in several countries, including Germany (4.4 mg/L), South Africa (4.4 mg/L), and Denmark (5.6 mg/L). Clearly health and regulatory officials in other countries believe that the current WHO and USA drinking water standard for nitrate is not adequate to protect their most susceptible population from methemoglobinemia. In addition to acute methemoglobinemia, other potential health effects of nitrate exposure in drinking water include cancer, disruption of thyroid function, birth defects, and developmental disorders in children. Is the current drinking water standard in the US and World Health Organization for nitrate adequate? I think not! Clearly the most susceptible human population (infants under four months of age with existing diarrhea conditions) is not adequately protected from methemoglobinemia. In addition, recent studies suggest other possible linkages between nitrate in drinking water and adverse health consequences for adults. Particularly troublesome is the finding of a positive association between nitrate in drinking water (at levels below the USA drinking water standard) and bladder cancer and ovarian cancer in a large cohort of women in Iowa, USA. Given this framework, the regulatory authorities should establish a safety factor of two, which would reduce the current MCL and HAL for nitrate to 5.0 mg/L NO_3-N. This regulatory mandate would encourage a prudent public health strategy of limiting human nitrate exposure.
Key words: nitrate, drinking water, safety factor, methemoglobinemia

Rezumat. Nivelul maxim admis de contaminare a sistemelor publice de aprovizionare cu apă potabilă, stabilit de Agenția de Protecție a Mediului din SUA pentru nitrați, ca şi nivelul maxim recomandat pentru alte sisteme particulare de apă este de 10 mg/l, exprimat în NO_3-N. Spre deosebire de alte standarde pentru apa de băut, în standardul american pentru nitrat nu s-a aplicat un **factor de siguranță** (de regulă, cu valoarea 10) pentru a se lua în considerare diferențele de susceptibilitate existente în populație. Nivelurile maxime acceptate pentru nitrați în apa de băut sunt mai mici în unele țări ca Germania (4,4 mg/l), Africa de Sud (4,4 mg/L) şi Danemarca (5,6 mg/L). Aceasta înseamnă că, în aceste țări, nivelul maxim acceptat în SUA nu este considerat suficient de scăzut pentru a proteja de methemoglobinemie grupele cele mai susceptibile ale populației. Pe lângă methemoglobinemie, ca efect acut, există şi alte patologii asociate expunerii la nitrații din apă, cum sunt cancerul, unele disfuncții tiroidiene, malformații congenitale şi tulburări de dezvoltare la copii. La întrebarea dacă limita admisă în SUA şi recomandată de OMS pentru nitrați în apă, este corespunzătoare, răspunsul este negativ, fiindcă nu asigură o protecție suficientă, astfel încât grupele cele mai susceptibile ale populației (copii sub vârsta de 4 luni, cu factori favorizanți ai diareei) să nu facă methemoglobinemie. În plus, studii recente sugerează existența unor posibile asocieri între nitrații din apă şi o serie de efecte adverse asupra sănătății adulților. Sunt relevante, în acest sens, rezultatele care indică o asociere pozitivă între nitrații din apă (în concentrații sub limita admisă în SUA) şi cancere de vezică şi ovariene, constatată într-un studiu de cohortă efectuat pe femei în statul Iowa, SUA. Având în vedere aceste aspecte, consider că se impune stabilirea unui factor de siguranță în valoare de 2, care ar reduce limita maximă admisă pentru nitrați la 5,0 mg/L NO_3-N. Această decizie de reglementare ar încuraja o strategie prudentă pentru limitarea expunerii populației la nitrați.

Cuvinte cheie: nitrați, apă de băut, factor de siguranță, methemoglobinemie

Health Effects

The current US EPA maximum contaminant level (MCL) for public drinking water supplies and the health advisory level (HAL) for other private water supplies is 10 mg/L, expressed as NO_3-N. These health-based standards and advisory levels are intended to prevent infant methemoglobinemia. Nitrate generally has a low human toxicity, but becomes a hazard when it is reduced to nitrite by bacterial action in the human gastrointestinal tract. Nitrite coverts oxygen-carrying hemoglobin to methemoglobin, which then cannot transfer oxygen. The resulting condition is methemoglobinemia, or the so-called blue baby disorder.

The most susceptible population to nitrate/nitrite toxicity is infants less than four months of age. Their high sensitivity is due to a combination of factors: higher gastric pH which allows greater bacterial activity in the stomach and subsequent enhanced conversion of ingested nitrate to nitrite, higher proportion of fetal hemoglobin which is more readily oxidized to methemoglobin than adult hemoglobin, and infant NADH - dependent methemoglobin reductase (the enzyme responsible for converting methemoglobin to normal hemoglobin) has about half the activity of the adult enzyme (1).

Several thousand cases of infant methemoglobinemia have been reported in the literature, with an overall case fatality rate of about 5-10 percent. Recent outbreaks have been reported in Central and Eastern Europe, especially in rural areas utilizing private well-water supplies (2,3). The most recent fatal case of methemoglobinemia in the United States occurred in South Dakota in 1986 (4).

The major source of nitrate intake for infants is from drinking water mixed with infant formula. Boiling of drinking water to kill bacteria (a common practice in rural areas) concentrates the nitrate that is present. Feeding practices that include early introduction of certain fruits and vegetables, which contain naturally high nitrate levels (beets, spinach, carrot or apple juice), can also enhance the risk of infant methemoglobinemia (5,6).

There is presently no evidence to support earlier hypotheses that breast-fed infants may develop methemoglobinemia when their mothers consumed nitrate contained in well water. So far, available data from experimental animals and limited human studies indicate that neither nitrate nor nitrite accumulate or concentrate in the mammary gland or milk (7).

Methemoglobinemia is a syndrome of elevated methemoglobin level, high blood nitrite, and frequently is associated with acute diarrhea. A newly proposed hypothesis being advanced by the Center for Global Food Issues is that nitrates in water or food are not the cause of infant methemoglobinemia, but rather the infant's own body is the primary culprit as it responds to pathogens or an indigestible protein (8). In brief, this theory suggests that when an infant has acute diarrhea or other severe gastrointestinal disturbance, either from a bacterial infection in the gut or a protein intolerance (perhaps from cow's milk supplemental feedings) (9), the entire metabolism of the infant is altered in such a way as to cause methemoglobin formation, irrespective of the infant's nitrate intake from food or water. The proposed mechanism of methemoglobinemia in this case is the release of nitric oxide from the white blood cells responding to the inflammation in the gastrointestinal system. The nitric oxide is converted by the body into nitrate, then to nitrite, and finally to ammonia, which is cleared by the kidneys. This process is known as endogenous nitrate production, and has been described recently in the literature for about 45 infants studied in Israel (10). During such episodes of severe gastrointestinal disturbances, the nitric oxide is overproduced, resulting in an accumulation of nitrite in the body. The outcome has been called endogenous methemoglobinemia.

In addition to acute methemoglobinemia, other health effects including cancer (11,12), disruption of thyroid function (13), birth defects (14), developmental disorders in animals (15) and developmental disorders in children (16) are under current study with respect to their relationship to nitrate exposures in drinking water. Although the recent National Research Council report concluded that the current drinking water standards for nitrate were adequate to protect human health in the United States, this conclusion was hedged somewhat by this same subcommittee's recommendation that limiting infant exposure to nitrate would be a sensible public-health measure (17).

Basis for Drinking Water Standard

The current nitrate standard established in 1987 is based on a literature review of 278 cases of methemoglobinemia reported in the United States between 1945 and 1950. The study reported that none of these cases occurred when nitrate concentrations in drinking water were below 10 mg/L (18). Unlike other drinking water standards, the nitrate standard has **no safety factor**, which typically is about a 10-fold safety factor to account for differences in human susceptibility.

Other studies and case reports in the literature strongly suggest that a safety factor is needed. Studies conducted in Germany in 1964 indicated that about 4% of the 249 cases of methemoglobinemia occurred in infants consuming water containing less than 11 mg/L. of nitrate (19). Other case reports in the literature indicated that infants with severe diarrhea are also susceptible to methemoglobinemia following ingestion of drinking water containing less than 10 mg/L. of nitrate-N (20). A recent report of methemoglobinemia in Wisconsin involved an infant consuming formula mixed with private well water containing 9.9 mg/L of nitrate-N and up to 7.8 mg/L of copper (21). Guidance, action, or advisory levels for nitrate in drinking water are lower in several countries, including Germany (4.4 mg/L), South Africa (4.4 mg/L), and Denmark (5.6 mg/L). Clearly health and regulatory officials in other countries believe that the current drinking water standard for nitrate is not adequate to protect their most susceptible population from methemoglobinemia.

Extent of Nitrate Contamination

Another important issue related to nitrate toxicity and drinking water resources is the current extent of groundwater and surface water contamination in the United States. A national drinking water survey conducted by the US EPA indicated about 1.2% of community-water wells and about 2.4% of rural domestic wells have nitrate levels that exceed the health advisory level. It is estimated that about 1.5 million people, including about 22,500 infants, are served by rural domestic wells and that another 3 million people, including about 43,500 infants, are served by community water wells that exceed health advisory levels for nitrate (22).

An Environmental Working Group review of nearly 200,000 public water sampling records found that nearly 2-million people - including an estimated 15,000 infants under the age of four months - drank water from 2,016 water systems that were reported to the US EPA for violating the nitrate standard at least once between 1986 and 1995. All of these water systems were termed "significant noncompliers" by the US EPA and 60% were repeat violators. An additional 3.8 million people drink water from private wells that are contaminated above the 10 mg/L nitrate standard. In seven states - California, Pennsylvania, New York, Illinois, Wisconsin, Minnesota, and Iowa - more than 100,000 rural residents are exposed to nitrate above the federal standard via private drinking water (23).

In a statewide survey conducted in Iowa, about 18% of rural domestic wells had nitrate contamination above the 10 mg/L. limit (24). Similarly, an assessment of Safe Drinking Water Act database in Iowa indicates that from 1988 to 1995, the MCL was exceeded in 21% of the samples, and was greater than 5 mg/L in 43% of the samples. Some trends in the data were also noted. The median concentration of nitrate in finished water supplies decreased from 1991 to 1995, which was also represented in a decline in the percentage of samples exceeding the MCL - 21% in 1991 to 4% in 1995 (25). However, in another study of groundwater sources in Iowa, the trend for nitrate contamination is not as clear. Since 1982 multiple samples of untreated groundwater used for Iowa municipal water supplies indicate no significant temporal trends in either the frequency of detection or median nitrate concentrations in these wells (26).

In the rural areas of America, nitrate contamination of drinking water supplies continues to be an important public health issue. In the event that future research proves a relationship between nitrate exposure to infants and subsequent adverse health effects such as cancer or developmental disorders, the population at risk to excess nitrate exposures will indeed be huge.

Naturally occurring groundwater resources without influence from anthropogenic pollution sources such as fertilizer, sewage sludge, and animal manure generally contain nitrate at levels below 3.0 mg/L (27). For example, the natural background concentration of nitrate in Iowa groundwater is typically less than 2.0 mg/L (28).

Sources of Nitrate in Drinking Water

Within the US, each year there are about 8-billion pounds more nitrogen available in farm fields than can be utilized by the crops (29). This excess nitrogen generally moves through the soil into groundwater, or is transported during rainfall events into surface waters. Some natural degradation (denitrification) also occurs. Other sources of nitrate such as sewage treatment plants, private septic systems, animal manure, legume crops, and atmospheric deposition can be important in specific, localized groundwater systems. In Iowa, the Department of Natural Resources estimates that about 55-60% of the nitrate environmental loading is from commercial fertilizer applications. Moreover, these area sources of nitrate contamination appear to be more significant than point sources or poor well construction. For example, in Iowa's statewide rural well water study, single source problems such as locating near or in animal feedlots accounted for only 3% of the total rural wells, and accounted for only about 1% of the wells exceeding the nitrate standard (1).

Policy Issues

In order to protect pristine groundwater resources and to recognize the uncertainty in current human health-based standards for nitrate toxicity, a non-degradation groundwater protection strategy for nitrate should be established for all areas where the existing groundwater quality is better than the current drinking water standard. In other words, industrial, municipal, and agricultural pollution sources should not be allowed to contaminate groundwater resources up to the current 10 mg/L level for nitrates. A regulatory framework that accepts or encourages the so-called license to pollute concept is unwise, particularly if an allowable level of nitrate pollution is based on the flawed assumption that the current drinking water standard for nitrate is adequate to protect human health.

Is the current drinking water standard for nitrate adequate? I think not! Clearly the most susceptible human population (infants under four months of age with existing diarrhea conditions) is not adequately protected from methemoglobinemia. In addition, recent studies suggest other possible linkages between nitrate in drinking water and adverse health consequences for adults. Particularly troublesome is the recent finding of a positive association between nitrate in drinking water (at levels below the drinking water standard) and bladder cancer and ovarian cancer in a large cohort of women in Iowa (12). If further studies confirm strong associations between nitrate in drinking water and cancer, then a revised regulatory safety factor would be applied. However, in the meantime, a safety factor of at least two is needed to adequately protect the vulnerable, helpless infant population. Given this framework, the regulatory authority should implement a maximum contaminant level goal (MCLG) of 3 mg/L of NO_3-N in order to limit infant exposures to nitrate.

By mandating a safety factor of two, which would reduce the current MCL and HAL for nitrate to 5.0 mg/L NO_3-N, and by promulgating a MCLG of 3.0 mg/L of NO_3-N; the United States regulatory approach for nitrate in drinking water would become consistent with other European countries and would encourage the prudent public health strategy of limiting human nitrate exposure.

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