

Letters to the Editor

Re: Exaggerated Claims on Nitrate's Effects on Human Health

Dear Editor:

We read with interest the letters by Dr. Evans and Dr. Gallagher in the September 2010 issue of *CSA News* magazine regarding the statement by Dr. Gallagher and his colleagues in the July 2010 issue (p. 14) that "nitrates are a serious human health concern and have been linked to methemoglobinemia (blue-baby syndrome), various cancers, and birth defects." Dr. Evans indicated his doubt that nitrate qualifies as a serious human health concern and stated "The suggested link to cancer was a scare that was disproved years ago." We disagree, as do consensus reports from experts in public health and cancer. For example, a WHO International Agency for Research on Cancer (IARC) expert working group concluded: "Ingested nitrate or nitrite under conditions that result in endogenous nitrosation is probably carcinogenic to humans" (IARC, 2010; Grosse et al., 2006). Monographs produced by these IARC working groups are used by the USEPA and international agencies in the regulatory review of occupational and environmental chemicals.

Conditions leading to endogenous nitrosation, the formation of N-nitroso compounds (NOC), are common in humans. NOCs are of concern for human health because most are potent carcinogens and teratogens in animals including

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non-human primates. Ingestion of drinking water with nitrate above the regulatory limit results in increased NOC production in humans (Mirvish et al., 1992; Moller et al., 1989; Vermeer et al., 1998). NOC formation can be reduced by concurrent ingestion of antioxidants such as vitamin C, a nutrient found at high levels in certain fruits and vegetables (Mirvish et al., 1998; Vermeer et al., 1999).

Because of endogenous nitrosation, the IARC working group's review gave greater weight to epidemiologic studies that assessed cancer risk in people with high intake of nitrate or nitrite and low vitamin C intake. No increased risk of cancer was found in studies of nitrate in food (vegetables are the primary source). Higher intake of nitrite from foods (cured meats are an important source) was associated with increased risk of stomach and esophageal cancer in

most studies; all studies that evaluated risk among those with high nitrite and low vitamin C intake found the highest risk in this group. Consumption of drinking water with high nitrate levels together with low intake of antioxidants is of most concern; however, few epidemiologic studies assessed risk in this group, and exposure levels in most studies were generally low.

In addition to cancer, Dr. Gallagher and his colleagues mentioned the link between nitrate in drinking water and birth defects. The strongest evidence is for central nervous system defects. In three of four epidemiologic studies, mothers whose drinking-water supplies had higher nitrate concentrations had a greater risk of having a child with a central nervous system birth defect than mothers whose water supplies had low nitrate (Ward et al., 2005). Levels of drinking-water nitrate associated with these birth outcomes were generally below the current maximum contaminant level for public water supplies. We agree with Dr. Evans that there are likely to be beneficial effects of nitrate ingestion, especially for cardiovascular health, but NOC formation from nitrate ingestion is a serious human health concern. To adequately evaluate the human health risks due to consumption of nitrate from drinking-water supplies, we need more studies in populations with high exposures that consider factors affecting endogenous nitrosation.

Finally, while we fully recognize the enormous public health benefits derived from nitrogen inputs to agriculture (e.g., Smil, 2001), we note that the human health concerns of an altered global nitrogen cycle go well beyond drinking-water nitrate (Townsend et al., 2003). Ultimately, the world must strive to maintain the benefits of human-created nitrogen while reducing its unwanted impacts on both human health and the environment.

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References

- Grosse, Y., R. Baan, K. Straif, B. Secretan et al. 2006. Carcinogenicity of nitrate, nitrite, and cyanobacterial peptide toxins. *Lancet Oncol.* 7:628–629.
- IARC. 2010. Monographs on the evaluation of carcinogenic risk to humans. Volume 94: Ingested nitrate and nitrite and cyanobacterial peptide toxins. Available at <http://monographs.iarc.fr> (verified 10 Dec. 2010). International Agency for Research on Cancer, Lyon, France.
- Mirvish, S.S., A.C. Grandjean, H. Moller et al. 1992. N-nitrosoproline excretion by rural Nebraskans drinking water of varied nitrate content. *Cancer Epidemiol. Biomarkers Prev.* 1:455–461.
- Mirvish, S.S., A.C. Grandjean, K.J. Reimers et al. 1998. Effect of ascorbic acid dose taken with a meal on nitrosoproline excretion in subjects ingesting nitrate and proline. *Nutr. Cancer* 31:106–110.
- Moller, H., J. Landt, E. Perderson, P. Jensen, H. Autrup, and O. Jensen. 1989. Endogenous nitrosation in relation to nitrate exposure from drinking water and diet in a Danish rural population. *Cancer Res.* 49:3117–3121.
- Smil, V. 2001. *Enriching the earth: Fritz Haber, Carl Bosch, and the transformation of world food production.* MIT Press, Cambridge, MA.
- Starovoytov, A., R.S. Gallagher, K.L. Jacobsen, J.P. Kaye, and B. Bradley. 2010. Management of small grain residues to retain legume-derived nitrogen in corn cropping systems. *Agron. J.* 102:895–903.
- Townsend, A.R., R.W. Howarth, F.A. Bazzaz, M.S. Booth, C.C. Cleveland, S.K. Collinge et al. 2003. Human health effects of a changing global nitrogen cycle. *Frontiers Ecol. Environ.* 1(5):240–246.
- Vermeer, I.T., E.J. Moonen, J.W. Dallinga, J.C. Kleinjans, and J.M. van Maanen. 1999. Effect of ascorbic acid and green tea on endogenous formation of N-nitrosodimethylamine and N-nitrosopiperidine in humans. *Mutat. Res.* 428:353–361.
- Vermeer, I., D.M. Pachon, J.W. Dallinga, J.C. Kleinjans, and J.M. van Maanen. 1998. Volatile N-nitrosamine formation after intake of nitrate at the ADI level in combination with an amine-rich diet. *Environ. Health Perspect.* 106:459–463.
- Ward, M.H., T.M. de Kok, P. Levallois, J. Brender, G. Gulis, B.T. Nolan, and J. VanDerslice. 2005. Workgroup report: Drinking-water nitrate and health: Recent findings and research needs. *Environ. Health Perspect.* 113:1607–1614.

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