

## ENDOCRINE HEALTH

## Nitrate May Feed Thyroid Disorders

Thyroid cancer incidence has been rising substantially worldwide since at least the 1970s,<sup>1</sup> but the reasons remain murky. Trend data are scant for two other thyroid diseases, hyperthyroidism and hypothyroidism, but incidence estimates suggest each is at least 5 times more common than thyroid cancer.<sup>2,3</sup> Limited evidence has suggested substances such as polychlorinated biphenyls, polybrominated diphenyl ethers, bisphenol A, and triclosan may be playing a role in these disorders. Nitrate also may belong on that list of suspects, U.S. researchers now report.<sup>4</sup>

The new study is apparently the first to link nitrate ingestion and thyroid cancer. The authors found that the quartile of women who consumed drinking water containing an average concentration of nitrate–nitrogen<sup>5</sup> (NO<sub>3</sub>–N) greater than 2.46 mg/L—about one-fourth the EPA maximum contaminant level of 10 mg/L—were 2.18 times more likely to have thyroid cancer than the bottom quartile, whose water contained less than 0.36 mg/L NO<sub>3</sub>–N. Consuming water containing more than 5 mg/L NO<sub>3</sub>–N for more than five years increased the risk slightly more. The women in the highest quartile of daily nitrate ingestion from food were 2.9 times more likely to have thyroid cancer than the quartile who consumed the least, and were 24% more likely to report having hypothyroidism. Nitrate in food dominated total nitrate intake.

The study was based on records from women who were followed from 1986 to 2004 as part of the larger Iowa Women's Health study. The women were 55–69 years old at recruitment. The researchers had extensive self-reported demographic, behavioral, and medical data, but fewer data on overall diet and none on nitrate levels in individuals. Instead, they had to develop intake estimates based on local public water supply monitoring data and national food nitrate data. The small number of thyroid cancers—40 in the approximately 21,000 women analyzed—also is a limitation, although the findings were statistically significant.<sup>6</sup>

The numerous limitations make Lewis Braverman, a professor of medicine at the Boston University School of Medicine, somewhat

skeptical of the conclusions. “The evidence is fairly soft,” he says. He notes, though, there has been some evidence globally of a nitrate-related association with hypothyroidism, goiter, and other thyroid disorders in subjects such as pregnant women and children exposed to far higher nitrate concentrations than those reported in the present study.<sup>7</sup> Ongoing and planned studies, including one looking at men, may provide additional clues, says Mary Ward, lead author of the current study and a senior investigator at the National Cancer Institute.

Thyroid cancer is estimated to be the seventh leading site of new cancers in U.S. women, according to the American Cancer Society.<sup>8</sup> Incidence is about three times higher in women than in men, similar to the pattern worldwide.<sup>1</sup> Some experts are concluding that increased detection alone is not likely to be responsible for global increases.<sup>9</sup>

Synthetic fertilizer can be an important source of nitrate in water and food.<sup>10</sup> The foods that often have the highest concentrations of nitrate, such as spinach, kale, and beets, often are touted for their nutritional benefits. The women in this study who were hardest hit by thyroid disorders tended to be better educated, physically active nonsmokers—a group Ward says is more likely to eat vegetables.

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### REFERENCES AND NOTES

1. Kilfoy BA, et al. *Cancer Causes Control* 20(5):525–531 (2009).
2. Michalek AM, et al. *J Fam Pract* 49(7):638–640 (2000).
3. Emiliano AB, et al. *J Clin Endocrinol Metab* 95(5):2227–2233 (2010).
4. Ward MH, et al. *Epidemiology* 21(3):389–395 (2010).
5. The term “nitrate–nitrogen” (NO<sub>3</sub>–N) refers to the total nitrogen present in the form of the nitrate ion. This differentiates it from nitrite–nitrogen (NO<sub>2</sub>–N) or ammonia–nitrogen (NH<sub>3</sub>–N).
6. The 19-year span of the study and the changing accuracy and diagnostic patterns for thyroid cancer make it difficult to say how this incidence compares with national rates. But for one perspective, the American Cancer Society estimated 17,640 new thyroid cancers were diagnosed in U.S. women aged 75–90 in 2004, the year data collection for this study ended and the approximate age range for the women at that time. According to the U.S. Census Bureau, the U.S. female population for that age range was 9.8 million in 2004. That equates to 0.18% of the larger population of women aged 75–90 having thyroid cancer, compared with 0.20% in the current study.
7. For instance, Gatseva Penka and Argirova [Int J Hyg Environ Health 211(5–6):555–559 (2008)] showed high nitrate levels in drinking water may be a risk factor for thyroid dysfunction in rural Bulgarian children and pregnant women, and Rádiková et al. [Thyroid 18(3):353–362 (2008)] demonstrated possible thyroid effects of nitrates and organochlorines in highly polluted areas of Slovakia.
8. ACS. *Cancer Facts & Figures 2009*. Atlanta, GA: American Cancer Society (2009).
9. For instance, Enewold L, et al. *Cancer Epidemiol Biomarkers Prev* 18:784–791 (2009).
10. European Union Scientific Panel. *ESPA J* 689:1–79 (2008).

## The Beat

by Erin E. Dooley

### EPA Proposes New Coal Ash Rules

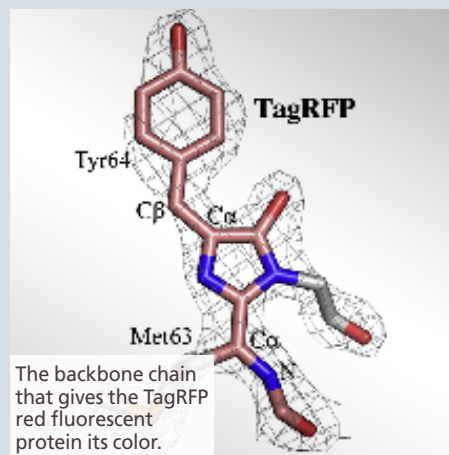
Amid growing concerns about the health impacts of coal ash, the waste produced at coal-fired power plants, the U.S. EPA on 4 May 2010 issued a prepublication version of two options for the management and cleanup of such facilities.<sup>1</sup> The agency is requesting public comments on two approaches to regulation

More stringent regulation as hazardous waste under Subtitle C of the Resource Recovery and Conservation Act (RCRA) would require the development of permit programs, allow for mandatory monitoring and federal enforcement, and more strictly control the use of impoundment liners and groundwater monitoring. Regulation as nonhazardous solid waste under Subtitle D puts more control in the hands of individual states. The EPA also seeks comment on potential refinements to the list of beneficial uses allowed. The proposals will be subject to the EPA's usual 90-day period for public comment upon publication in the *Federal*

*Register*; at press time, the proposals had not yet been published.<sup>2</sup>

### Study Shines Light on the Molecular Structure of Fluorescent Proteins

Researchers have determined the crystal structures of two key fluorescent proteins, one blue and one red, that can be used to highlight molecules in cells being studied.<sup>3</sup> This discovery could allow



scientists to more systematically design novel fluorescent proteins for pinpointing structures and processes in living cells, with more choices of color allowing the simultaneous observation of more individual processes within cells.

### Stream Quality May Predict Human Health

An interdisciplinary study by Nathaniel Hitt and Michael Hendryx looked at the relationship between human cancer mortality in West Virginia and the ecologic integrity of nearby stream ecosystems.<sup>4</sup> They found that people living near the most biologically impoverished streams—as reflected by the numbers and proportions of bottom-dwelling macroinvertebrates living there—had the highest cancer rates, even after adjusting for known risk factors such as smoking, income level, and urbanization. Spatial analyses also revealed more cancers in areas where more coal mining occurred. Their results suggested that proximity to coal surface mines can potentially lead to adverse effects in both aquatic and human communities.