



POLICY STATEMENT

Iodine Deficiency, Pollutant Chemicals, and the Thyroid: New Information on an Old Problem

COUNCIL ON ENVIRONMENTAL HEALTH

KEY WORDS

lactation, goiter, perchlorate, iodine, iodide, thiocyanate, water pollution, nitrate, supplements

ABBREVIATIONS

AAP—American Academy of Pediatrics
EPA—Environmental Protection Agency
FDA—Food and Drug Administration
NIS—sodium iodide symporter
TSH—thyroid-stimulating hormone

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abstract

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Many women of reproductive age in the United States are marginally iodine deficient, perhaps because the salt in processed foods is not iodized. Iodine deficiency, per se, can interfere with normal brain development in their offspring; in addition, it increases vulnerability to the effects of certain environmental pollutants, such as nitrate, thiocyanate, and perchlorate. Although pregnant and lactating women should take a supplement containing adequate iodide, only about 15% do so. Such supplements, however, may not contain enough iodide and may not be labeled accurately. The American Thyroid Association recommends that pregnant and lactating women take a supplement with adequate iodide. The American Academy of Pediatrics recommends that pregnant and lactating women also avoid exposure to excess nitrate, which would usually occur from contaminated well water, and thiocyanate, which is in cigarette smoke. Perchlorate is currently a candidate for regulation as a water pollutant. The Environmental Protection Agency should proceed with appropriate regulation, and the Food and Drug Administration should address the mislabeling of the iodine content of prenatal/lactation supplements. *Pediatrics* 2014;133:1163–1166

ADEQUACY OF IODINE INTAKE IN THE UNITED STATES

Adequate iodine intake, usually as iodide, is necessary to produce thyroid hormone. Adequate thyroid hormone production is critical in pregnant women and neonates because thyroid hormone is required for brain development in children.¹ Severe, untreated hypothyroidism in infancy results in irreversible cretinism, but milder iodine deficiency can also affect cognitive development of the child. The “goiter belt” of endemic iodine deficiency in the United States had largely been eliminated by iodizing table salt in 1924; however, iodine deficiency increased from the 1970s through the 1990s, and approximately one-third of pregnant women in the United States are marginally iodine deficient.^{2,3} Processed foods in the United States are prepared with noniodized salt,⁴ and consumption of these processed foods has increased. Although studies of cognitive development in infants whose mothers were marginally iodine deficient revealed inconsistent results,^{5,6} any morbidity resulting from iodine deficiency can and should be prevented. Although there are a few instances in which governments have required the use of

iodized salt in processed foods,⁷ this option has not been well studied and is not likely to occur in the United States soon. The Salt Institute, the trade group for salt manufacturers, has a goal of universal salt iodization, but it claims that companies are reluctant to switch to iodized salt for fear that taste or other characteristics of the processed food would be altered.

The American Thyroid Association⁸ and the National Academy of Sciences⁹ recommend that lactating women have an intake of 290 μg of iodide per day, which generally requires a supplement with 150 μg of iodide. In the United States, although most pregnant and lactating women take supplements, only 15% to 20% take supplements that contain any iodide.¹⁰ Many prenatal/lactation vitamins do not contain iodide, and those containing iodide are often formulated to have 150 μg or less of potassium iodide, which should yield approximately 120 μg or less of iodide, which is below the recommended amount of 150 μg . In addition, there is wide variability in the measured iodide content of supplements.¹¹

POLLUTANT CHEMICALS AND IODINE DEFICIENCY

Commonly encountered environmental chemicals might augment the effects of iodine deficiency by competing for transport by the sodium-iodide symporter (NIS). The NIS is an integral plasma membrane glycoprotein found in the thyroid gland and the lactating mammary gland, among other tissues.¹² The NIS mediates the active transport of iodide into the thyroid follicular cells, making it available to iodinate dehydroxylated tyrosine for the first step in thyroid hormone synthesis. In the mammary gland, the NIS mediates transport of iodide into milk, making it available

to the infant. Although the NIS has a high affinity for iodide, other anions, such as thiocyanate, nitrate, and perchlorate, can compete with (and be transported as) iodide and thus decrease iodide concentration within the thyroid gland or milk. Although such transport might be expected to lead to increased concentrations of nitrate, thiocyanate, and perchlorate in human milk, only perchlorate exposure and excretion have been found to be significantly higher in breastfed infants under normal circumstances.^{13,14}

Thiocyanate and nitrate are well-known and commonly encountered chemicals. Exposure to thiocyanate comes from cruciferous vegetables and tobacco smoke (including secondhand smoke), and exposure to nitrate comes from drinking water and some leafy and root vegetables. Perchlorate (ClO_4^-) may be less familiar. It is an inorganic anion used industrially as an oxidizer for rocket fuels and propellants and in explosives. It also occurs naturally, usually in arid regions, such as in the southwestern United States. Perchlorate is 10 to 100 times more potent than iodide or the other anions in competing for the NIS. It has become a widespread environmental contaminant. The Environmental Protection Agency (EPA) detected perchlorate in approximately 4% of US public drinking water systems.¹⁵ Perchlorate has also been detected in cow milk as well as in a variety of other foods. In a nationwide survey, the US Food and Drug Administration (FDA) detected perchlorate in at least 1 sample of 74% of foods analyzed.¹⁶ Analysis of samples gathered in the NHANES (2001–2002) revealed widespread human exposure to perchlorate; all 2820 spot urine specimens analyzed contained perchlorate, and the median urine perchlorate concentration in the US population was 3.6 $\mu\text{g}/\text{g}$ of creatinine.¹⁷ Perchlorate

competitively inhibits iodide uptake, and high-dose exposure will decrease thyroid function.^{18,19} There is some evidence that perchlorate interferes with thyroid hormone economy at background exposures in the United States. In the NHANES (2001–2002), female participants 12 years and older with lower iodide status and higher urinary perchlorate had higher serum thyroid-stimulating hormone (TSH) and lower serum thyroxine concentrations.¹⁷ In a smaller study in infants, both boys and girls with lower urinary iodide and higher perchlorate concentrations had higher urinary TSH and, unexpectedly, higher thyroxine concentrations.²⁰ That study also reported increases in TSH concentration associated with thiocyanate and nitrate concentrations in urine of infants.

The EPA, in February 2011, made a regulatory determination for perchlorate in accordance with the Safe Drinking Water Act.²¹ This is the first of several steps in the direction of limiting the amount of perchlorate in drinking water, which should ultimately decrease exposure to mothers and infants. This action initiates a process to develop and establish a National Primary Drinking Water Regulation. Once the National Primary Drinking Water Regulation is finalized, certain public water supplies will be required to take action to comply with the regulation in accordance with the schedule specified in the regulation.

Iodine deficiency is undesirable per se because of its potential harm to the developing nervous system. Iodine deficiency may also make the mother and child more vulnerable to environmental agents that compete with iodine for transport into thyroid tissue. The effective regulation of perchlorate by the EPA should decrease exposure but it will not do so

quickly. With regard to thiocyanate and nitrate, young infants should not be exposed to tobacco smoke or drinking water with excess nitrate; few consume enough cruciferous, leafy, or root vegetables for these sources to be of concern. For breastfeeding mothers, perchlorate exposure may be currently unavoidable, but breastfeeding should not be discouraged because of the presence of perchlorate or other environmental chemicals. Nitrate and thiocyanate in the maternal diet do not appear to increase a breastfed child's exposure. In summary, many US women of reproductive age are marginally iodine deficient. Iodine deficiency per se can interfere with normal brain development in their offspring; in addition, it increases vulnerability to the effects of certain environmental pollutants. Women should take a prenatal/lactation supplement with adequate iodide. Such supplements are not currently labeled accurately, but the FDA is moving to correct this situation.

RECOMMENDATIONS FOR CLINICIANS

Pediatricians should be aware that pregnant women and breastfeeding mothers, and thus their infants, may be iodine deficient. Breastfeeding mothers should take a supplement that includes at least 150 μg of iodide and use iodized table salt (combined iodide intake should be between 290 and 1100 μg of iodide per day). If the mother is vegan or does not consume dairy or fish, testing urine to check for iodine deficiency may be indicated. If an opportunity arises to advise a woman who is pregnant or planning to become pregnant about supplementation, the pediatrician should provide similar guidance.

Breastfeeding mothers should avoid excess nitrate both to avoid potential

interference with iodide transport and to prevent methemoglobinemia in their infants.²² Water is the usual source of excess nitrate. Municipal water supplies are regulated, but nitrate is a common pollutant of private wells. The American Academy of Pediatrics (AAP) recommends that well water be checked annually.²³

Interested pediatricians should contact the AAP Department of Federal Affairs about ways they can support regulation by the FDA and EPA. Both agencies need to recognize the hazard to children posed by the current situation.

Tobacco smoke is a source of thiocyanate exposure. The AAP has a detailed policy about the prevention of tobacco smoke exposure.²⁴ Pregnant women should be advised not to smoke and to avoid all exposures to secondhand tobacco smoke.

RECOMMENDATIONS FOR GOVERNMENT

The current reported state of discordance between the label and the actual content of iodide in supplements is unacceptable. As Leung et al¹¹ stated, "Manufacturers of prenatal multivitamins in the United States should be encouraged to use only potassium iodide, to maintain consistency in labeling, and to ensure that these vitamins contain 150 μg of supplemental daily iodide by including at least 197 μg of potassium iodide per daily dose, as recommended by the American Thyroid Association." The FDA is aware of this situation and was investigating it as of fall 2013. The FDA should attempt to correct this situation and, if voluntary action on the part of the suppliers is insufficient, do what is necessary to allow consumers to identify and use iodide supplements with confidence.

The EPA has begun the regulatory process to establish a national primary drinking water regulation for perchlorate. Because of the potential effect on children, the AAP encourages the EPA to complete the regulatory process in as expeditious a manner as possible.

State and local governments should enact clean-air and smoke-free environment ordinances and legislation in their communities and states, particularly for environments in which children learn, live, and play, such as schools, multiunit housing, public parks, child care settings, public beaches, sidewalks, restaurants, and sporting arenas. These environments should be smoke free, even when children are not present.²⁴

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REFERENCES

1. Rose SR, Brown RS, Foley T, et al; American Academy of Pediatrics; Section on Endocrinology and Committee on Genetics, American Thyroid Association; Public Health Committee, Lawson Wilkins Pediatric Endocrine Society. Update of newborn screening and therapy for congenital hypothyroidism. *Pediatrics*. 2006;117(6):2290–2303
2. Perrine CG, Herrick K, Serdula MK, Sullivan KM. Some subgroups of reproductive age women in the United States may be at risk for iodine deficiency. *J Nutr*. 2010;140(8):1489–1494
3. Hollowell JG, Haddow JE. The prevalence of iodine deficiency in women of reproductive age in the United States of America. *Public Health Nutr*. 2007;10(12A):1532–1539; discussion 1540–1541
4. Renner R. Dietary iodine: why are so many mothers not getting enough? *Environ Health Perspect*. 2010;118(10):A438–A442
5. Costeira MJ, Oliveira P, Santos NC, et al. Psychomotor development of children from an iodine-deficient region. *J Pediatr*. 2011;159(3):447–453
6. Craig WY, Allan WC, Kloza EM, et al. Mid-gestational maternal free thyroxine concentration and offspring neurocognitive development at age two years. *J Clin Endocrinol Metab*. 2012;97(1):E22–E28
7. The Salt Institute. Iodized salt. Available at: www.saltinstitute.org/News-events-media/Salt-Sensibility/Iodized-Salt/%28tag%29/iodized%20salt. Accessed September 3, 2013
8. American Thyroid Association. Iodine deficiency. Available at: www.thyroid.org/patients/patient_brochures/iodine_deficiency.html#treatment. Accessed September 3, 2013
9. Institute of Medicine, Committee on the Scientific Evaluation of Dietary Reference Intakes. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: National Academies Press; 2001
10. Gregory CO, Serdula MK, Sullivan KM. Use of supplements with and without iodine in women of childbearing age in the United States. *Thyroid*. 2009;19(9):1019–1020
11. Leung AM, Pearce EN, Braverman LE. Iodine content of prenatal multivitamins in the United States. *N Engl J Med*. 2009;360(9):939–940
12. Dohán O, De la Vieja A, Paroder V, et al. The sodium/iodide symporter (NIS): characterization, regulation, and medical significance. *Endocr Rev*. 2003;24(1):48–77
13. Dorea JG. Maternal thiocyanate and thyroid status during breast-feeding. *J Am Coll Nutr*. 2004;23(2):97–101
14. Valentín-Blasini L, Blount BC, Otero-Santos S, Cao Y, Bernbaum JC, Rogan WJ. Perchlorate exposure and dose estimates in infants. *Environ Sci Technol*. 2011;45(9):4127–4132
15. Environmental Protection Agency. How frequently is perchlorate found in drinking water? Available at: <http://water.epa.gov/drink/contaminants/unregulated/perchlorate.cfm#one>. Accessed September 3, 2013
16. Murray CW, Egan SK, Kim H, Beru N, Bolger PM. US Food and Drug Administration's Total Diet Study: dietary intake of perchlorate and iodine. *J Expo Sci Environ Epidemiol*. 2008;18(6):571–580
17. Blount BC, Pirkle JL, Osterloh JD, Valentín-Blasini L, Caldwell KL. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. *Environ Health Perspect*. 2006;114(12):1865–1871
18. Kirk AB. Environmental perchlorate: why it matters. *Anal Chim Acta*. 2006;567(1):4–12
19. Wolff J. Perchlorate and the thyroid gland. *Pharmacol Rev*. 1998;50(1):89–105
20. Cao Y, Blount BC, Valentín-Blasini L, Bernbaum JC, Phillips TM, Rogan WJ. Goitrogenic anions, thyroid-stimulating hormone, and thyroid hormone in infants. *Environ Health Perspect*. 2010;118(9):1332–1337
21. Environmental Protection Agency. Drinking water: regulatory determination on perchlorate. *Fed Regist*. 2011;76:7762–7767 Available at: <https://federalregister.gov/a/2011-2603>. Accessed September 3, 2013
22. Greer FR, Shannon M; American Academy of Pediatrics Committee on Nutrition; American Academy of Pediatrics Committee on Environmental Health. Infant methemoglobinemia: the role of dietary nitrate in food and water. *Pediatrics*. 2005;116(3):784–786
23. Rogan WJ, Brady MT; Committee on Environmental Health; Committee on Infectious Diseases. Drinking water from private wells and risks to children. *Pediatrics*. 2009;123(6):1599–1605
24. Committee on Environmental Health; Committee on Substance Abuse; Committee on Adolescence; Committee on Native American Child. Policy statement—tobacco use: a pediatric disease. *Pediatrics*. 2009;124(5):1474–1487