

Getting folic acid nutrition right^{1,2}

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Two articles in this issue of the Journal (1, 2) provide some definitive answers to questions relating to folic acid exposure and folate nutritional status of the US population in the post-fortification era and, by implication, pose other questions. Most convincingly, these reports, which are based largely on National Health and Nutrition Examination Survey (NHANES) data for the 2003–2006 time period, show how the Food and Drug Administration (FDA) models of exposure, which preceded the 1996 mandate that enriched flour be fortified with 140 μg folic acid per 100 g flour to prevent neural tube defect births, got the folic acid dose right. This mandate increased folic acid exposure in women of childbearing age without excessive exposure to those beneficiaries and others in the population. The documentation in these 2 articles of the remarkable predictive value of those models over a decade ago is testimony to the value of prefortification modeling and, at once, a resounding argument for the benefit of such national health and dietary surveys such as NHANES on which the models and their validation is based.

The article by Yang et al (1), from the Division of Birth Defects and Developmental Disabilities of the Centers of Disease Control and Prevention (CDC), focuses on folic acid intake only (the synthetic version of the vitamin folate), which is used in fortification and supplements from enriched cereal grain products, ready-to-eat cereals, and vitamin supplements. Their analysis documents the small exposure (2.7% of the population) beyond the upper level of folic acid intake as suggested by the 1990s Institute of Medicine (IOM) report on Dietary Reference Intakes (DRIs) (3), except in individuals taking dietary supplements with $>400 \mu\text{g}$ folic acid, in which case almost half of adult supplement users were ingesting more than the suggested Tolerable Upper Intake Level (UL). This argues that any putative overexposure in the US population should be attributed to supplement use and not to the FDA's historically successful program of flour fortification to prevent a substantial number of neural tube defect births.

The article by Bailey et al (2), from the National Center of Health Statistics and the Office of Dietary Supplements of the CDC and National Institutes of Health, respectively, presents a more comprehensive analysis of folate and folic acid intake. In this analysis, which included fortified foods beyond ready-to-eat cereals and supplements, the percentage of those aged >50 y who were exposed to folic acid beyond the UL was 5%. This

analysis does not disagree with the conclusions of Yang et al with regard to folic acid supplements and the UL.

These articles, which represent facets of a demonstration of a remarkable policy success story, implicitly raise some additional questions that deserve to be on our national agenda. Some questions relate to the B vitamin DRI report and the standards set therein by the IOM (3). How good is the suggestion that the UL for folate should refer only to folic acid exposure and be based on concern for the folic acid/vitamin B-12 interaction which is somewhat misstated in the Yang et al article as “masking the diagnosis of vitamin B-12 deficiency”? The IOM/DRI report clearly stated that the UL was set to apply “to individuals with B-12 deficiency” in whom “excess supplemental folate intake may precipitate or exacerbate the neurological damage of vitamin B-12 deficiency.” That report was released before several other studies raised questions about the safety of folic acid exposure at high levels, with or without associated vitamin B-12 deficiency (4–6). There is a need for an update and review of this and other upper level recommendations, which were originally meant to be reviewed within a decade. That same report made 3 other recommendations that deserve review. One is that women of childbearing age should be taking 400 μg synthetic folic acid as a supplement. The validity of that target dose at least deserves reconsideration in view of other studies that suggest that benefits might be achieved by half that dose (7). The 400- μg recommendation was really a “convenience” selection from observational studies clustered around that, the dose in most supplements. A second assertion in the report is that the difference between the bioavailability of food folate and synthetic folic acid is sufficiently great so as to institute a formal system of dietary folate equivalents (DFEs) to enshrine this discrepancy for policy purposes. The Bailey et al article, which is forced to use different criteria to judge how well the population meets folate requirements (Estimated Average Requirement) while using another set of criteria to measure exposure beyond the UL, is one argument for reconsidering the practicality of the DFE recommendation. A related error in the DRI report is the designation of human milk

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folate as “natural” folate, and thus inferior in DFEs, although studies support the high efficiency and bioavailability of binding protein bound folate in human milk for the infant gut (8).

Although these 2 excellent articles strengthen our support for the processes and surveys that permit such analyses, we need to seek mechanisms for updating our public health targets in folate nutrition.

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REFERENCES

1. Yang Q, Cogswell ME, Hamner HC, et al. Folic acid source, usual intake, and folate and vitamin B-12 status in US adults, 2003–2006. *Am J Clin Nutr* 2010;91:64–72.
2. Bailey RL, Dodd KW, Gahche JJ, et al. Total folate and folic acid intake from foods and dietary supplements in the United States: 2003–2006. *Am J Clin Nutr* 2010;91:231–7.
3. Food and Nutrition Board. Dietary Reference Intakes for thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin, and choline. Washington, DC: National Academy Press, 1998.
4. Morris MC, Evans DA, Bienias JL, et al. Dietary folate and vitamin B12 intake and cognitive decline among community-dwelling older persons. *Arch Neurol* 2005;62:641–5.
5. Mason JB, Dickstein A, Jacques PF, et al. A temporal association between folic acid fortification and an increase in colorectal cancer rates may be illuminating important biological principles: a hypothesis. *Cancer Epidemiol Biomarkers Prev* 2007;16:1325–9.
6. Morris MS, Jacques PF, Rosenberg IH, Selhub J. Folate and vitamin B-12 status in relation to anemia, macrocytosis and cognitive impairment among older Americans in the age of folic acid fortification. *Am J Clin Nutr* 2007;85:193–200.
7. Daly S, Mill JL, Molloy AM, et al. Minimum effective dose of folic acid for food fortification to prevent neural tube defects. *Lancet* 1997; 350:1666–9.
8. Ek J, Magnus E. Plasma and red cell folate values and folate requirements in formula-fed term infants. *J Pediatr* 1982;100:738–44.