

# PEDIATRICS®

## **The Folate Debate**

Robert L. Brent and Godfrey P. Oakley, Jr

*Pediatrics* 2006;117;1418-1419

DOI: 10.1542/peds.2006-0011

**This information is current as of April 4, 2006**

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://www.pediatrics.org/cgi/content/full/117/4/1418>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2006 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



## The Folate Debate

Robert L. Brent, MD, PhD<sup>a</sup>, Godfrey P. Oakley, Jr, MD, MSPM<sup>b</sup>

<sup>a</sup>Department of Pediatrics, Radiology, and Pathology, Thomas Jefferson University, A.I. duPont Hospital for Children, Wilmington, Delaware; <sup>b</sup>Department of Epidemiology, Rollins School of Public Health of Emory University, Atlanta, Georgia

Financial Disclosure: Dr Brent owns no stock in companies that make or distribute folic acid or sell or distribute grains. Some of his research that is supported by the National Institutes of Health has dealt with the use of folic acid to prevent neural tube defects as well as the metabolism of folic acid and methionine. Dr Oakley is a co-inventor of a patent that covers adding folic acid to contraceptive pills (while at the Centers for Disease Control and Prevention, compensation, if any, will be under the regulations of the Centers for Disease Control and Prevention) and has been a consultant to Ortho McNeil on this issue.

**N**O INFANT ANYWHERE in the world should die from anencephaly or be paralyzed by spina bifida because he or she was conceived and developed in a folate-deficient environment.<sup>1,2</sup> The Medical Research Council Vitamin Study Research Group's randomized, controlled trial showed in 1991 that pregnant women who consume enough synthetic folic acid before and during the early weeks of pregnancy do not have infants with folic acid-preventable spina bifida and anencephaly.<sup>3</sup> There has been unconscionable and unnecessary delay in the implementation of the public health and nutrition policies and programs necessary to prevent all of these preventable birth defects.<sup>2,4-8</sup> As a result of these delays, ~3 million children have been unnecessarily paralyzed or have died. It is past the time when all governments should have implemented programs to prevent all folic acid-preventable spina bifida and anencephaly.

A group of scientists, parents, and policy advocates met at the Ottawa, Canada, headquarters of Micronutrient Initiative and produced recommendations for increasing the pace for prevention of folic acid-preventable spina bifida and other folic acid-preventable diseases. They recommended mandatory folic acid flour fortification as the foundation on which to build this birth defects-prevention program, because in many countries the consumption of wheat and/or corn flour provides the opportunity to prevent birth defects by requiring mills to fortify flour with folic acid.<sup>8</sup>

In the United States, consumption of wheat and corn flour with adequate enrichment of folic acid can provide the opportunity for near-total, if not total, prevention of these severe birth defects that are preventable through fortification. The decision of the US Food and Drug Administration (FDA) to require "folic acid-enriched" grain products such as wheat and corn flour provided

the basis for a marked improvement of public health and has provided an example that ~40 countries have emulated.

In their special article in this issue of *Pediatrics*, Rader and Schneeman<sup>9</sup> note the improvement in serum and red cell folates that occurred after fortification, yet they write that "it is not possible to determine if these values are sufficiently high to protect all women at risk." Said another way, we do not have the evidence that would permit us to conclude that the developing embryos of all pregnant women are being protected; therefore, we do not have the evidence to conclude that all folic acid-preventable spina bifida and anencephaly are being prevented.

The current US Public Health Service and the current Institute of Medicine (IOM) recommendations are that all women of reproductive age should consume 400  $\mu\text{g}$  of synthetic folic acid daily to prevent these birth defects.<sup>10,11</sup> There is evidence to suggest that the median folic acid consumption of women of reproductive age may be as much as 200  $\mu\text{g}$  of synthetic folic acid per day postfortification,<sup>12,13</sup> which means that most women are not getting the 400  $\mu\text{g}$  that is recommended. Increasing the concentration of folic acid required in "enriched" grains would increase the proportion of women who would consume the recommended amount of folic acid

**Abbreviations:** FDA, Food and Drug Administration; IOM, Institute of Medicine

Opinions expressed in these commentaries are those of the authors and not necessarily those of the American Academy of Pediatrics or its Committees.

[www.pediatrics.org/cgi/doi/10.1542/peds.2006-0011](http://www.pediatrics.org/cgi/doi/10.1542/peds.2006-0011)

doi:10.1542/peds.2006-0011

Accepted for publication Jan 5, 2006

Address correspondence to Robert L. Brent, MD, PhD, Room 308 R/A, Box 269, A.I. duPont Hospital for Children, Wilmington, DE 19899. E-mail: rbrent@nemours.org  
PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275). Copyright © 2006 by the American Academy of Pediatrics

and increase the prevention of folic acid–preventable neural tube defects. We may not know the exact number of cases of spina bifida and anencephaly that would be prevented by increasing fortification; however, that fact should not stop the FDA from moving quickly to require an increase in the concentration of folic acid.

We encourage the FDA to implement a process that would provide for an open, fair, and rapid assessment of the available data and consider implementing the recommendations of the IOM for folic acid intake through fortification of enriched cereal grains. The primary question to be addressed should be, what additional contributions to the total prevention of folic acid–preventable spina bifida should the FDA initiate through changes in enrichment regulations? Because the IOM has recommended that all people  $\geq 50$  years consume 2.4  $\mu\text{g}$  of synthetic vitamin B<sub>12</sub> to prevent vitamin B<sub>12</sub> deficiency, the review should also deliberate the issue of vitamin B<sub>12</sub> deficiency and determine what contribution to preventing vitamin B<sub>12</sub> deficiency the FDA can make by requiring the addition of vitamin B<sub>12</sub> in enriched grains.<sup>11</sup> We think that when such a review is completed, the FDA will increase the folic acid concentration in enriched grains and require that vitamin B<sub>12</sub> be added.<sup>14</sup> These actions would improve the health of our nation's children and adults.

## REFERENCES

1. Oakley G Jr. Global prevention of all folic acid-preventable spina bifida and anencephaly by 2010. *Community Genet.* 2002; 5:70–77
2. Brent RL, Oakley GP Jr, Mattison DR. The unnecessary epidemic of folic acid–preventable spina bifida and anencephaly. *Pediatrics.* 2000;106:825–827
3. MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. *Lancet.* 1991;338:131–137
4. Oakley GP Jr. Inertia on folic acid fortification: public health malpractice. *Teratology.* 2002;66:44–54
5. Oakley GP. Delaying folic acid fortification of flour [published correction appears in *BMJ.* 2002;325:259]. *BMJ.* 2002;324: 1348–1349
6. Brent RL, Oakley GP Jr. The Food and Drug Administration must require the addition of more folic acid in “enriched” flour and other grains. *Pediatrics.* 2005;116:753–755
7. Brent RL, Oakley GP Jr. Triumph and/or tragedy: the present Food and Drug Administration program of enriching grains with folic acid. *Pediatrics.* 2006;117:929–931
8. Oakley GP Jr, Bell KN, Weber MB. Recommendations for accelerating global action to prevent folic acid-preventable birth defects and other folate-deficiency diseases: meeting of experts on preventing folic acid-preventable neural tube defects. *Birth Defects Res A Clin Mol Teratol.* 2004;70:835–837
9. Rader JI, Schneeman BO. Prevalence of neural tube defects, folate status, and folate fortification of enriched cereal-grain products in the United States. *Pediatrics.* 2006;117:1394–1399
10. Centers for Disease Control and Prevention. Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. *MMWR Recomm Rep.* 1992; 41(RR-14):1–7
11. Institute of Medicine. *Dietary Reference Intake: Folate, Other B Vitamins and Choline.* Washington, DC: National Academy Press; 1998
12. Choumenkovitch SF, Selhub J, Wilson PW, Rader JI, Rosenberg IH, Jacques PF. Folic acid intake from fortification in United States exceeds predictions. *J Nutr.* 2002;132:2792–2798
13. Quinlivan EP, Gregory JF 3rd. Effect of food fortification on folic acid intake in the United States. *Am J Clin Nutr.* 2003;77: 221–225
14. Oakley GP Jr. Let's increase folic acid fortification and include vitamin B-12. *Am J Clin Nutr.* 1997;65:1889–1890

**The Folate Debate**  
Robert L. Brent and Godfrey P. Oakley, Jr  
*Pediatrics* 2006;117;1418-1419  
DOI: 10.1542/peds.2006-0011

**This information is current as of April 4, 2006**

**Updated Information  
& Services**

including high-resolution figures, can be found at:  
<http://www.pediatrics.org/cgi/content/full/117/4/1418>

**References**

This article cites 12 articles, 7 of which you can access for free at:  
<http://www.pediatrics.org/cgi/content/full/117/4/1418#BIBL>

**Subspecialty Collections**

This article, along with others on similar topics, appears in the following collection(s):  
**Nutrition & Metabolism**  
[http://www.pediatrics.org/cgi/collection/nutrition\\_and\\_metabolism](http://www.pediatrics.org/cgi/collection/nutrition_and_metabolism)

**Permissions & Licensing**

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:  
<http://www.pediatrics.org/misc/Permissions.shtml>

**Reprints**

Information about ordering reprints can be found online:  
<http://www.pediatrics.org/misc/reprints.shtml>

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

