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*Pediatrics* 2006;117;1418-1419

DOI: 10.1542/peds.2006-0011

**This information is current as of April 11, 2006**

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

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American Academy of Pediatrics

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## The Folate Debate

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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

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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.

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