

Folic Acid–Preventable Spina Bifida

A Good Start but Much to Be Done

Godfrey P. Oakley, Jr., MD, MSPM

Nearly 20 years ago, a randomized trial unequivocally showed that folic acid prevents spina bifida and anencephaly.¹ This publication provided the scientific basis that should have led to the rapid, global disappearance of folic acid–preventable spina bifida and anencephaly. Although these preventable birth defects should be as scarce as polio, globally we continue to have about as many cases as there were cases of polio in 1988 when WHO began the polio eradication program. There are now fewer than 1000 cases of polio each year in the world, while there remain more than 200,000 cases of folic acid–preventable spina bifida and anencephaly. This failure of modern-day preventive medicine is primarily the failure to create the political will to eliminate these diseases.² The CDC has been the institution that provided the inspiration and early funding for the global eradication of smallpox and polio, but it has yet to receive funding to mobilize sufficiently the global elimination of spina bifida and anencephaly. The current annual budget of the CDC for polio eradication is about \$200 million, while the budget for global prevention of folic acid–preventable spina bifida is less than \$5 million. In the meantime, tens of thousands of children each year continue to be born with these preventable birth defects that contribute to infant mortality and life-long paralysis and disability.

An essential part of the Polio Eradication Campaign has been to secure accurate data on the number of cases in each country to guide the prevention program. The Campaign also has a surveillance mechanism used to determine when polio is eradicated from a country. As reported in this issue of the *American Journal of Preventive Medicine*, Tinker and colleagues³ analyzed NHANES data to evaluate how well American women of reproductive age are following the Public Health Service recommendation that all such women consume 400 μg of synthetic folic acid daily from fortified foods or vitamin pills. They found worrisome results. Only one in four women is consuming the recommended amounts of folic acid, either through folic acid supplements or ready-to-eat

breakfast cereals to which manufacturers have voluntarily added folic acid. No women are consuming 400 micrograms a day from FDA-mandated folic acid fortification of flour and other enriched grain products. On the positive side, they find that no women consume more than 1000 micrograms of folic acid from mandatory food fortification.

Spina bifida and anencephaly births have decreased since fortification in the U.S. and Canada. The question is how much more prevention is there to be done.^{4,5} There was a large case–control study that did not find a protective effect from multivitamin consumption, which is consistent with there being little if any prevention needed in the U.S.⁶ It is, however, only one such study. The China study found that women who consumed 400 micrograms of folic acid had a spina bifida and anencephaly rate that approached five per 10,000.⁷ The rates in the U.S. are in the six to seven per 10,000 birth range, and in Canada the post-fortification rates in the provinces vary from seven to 12 per 10,000 births.⁵ These variances suggest that there is more prevention that can be done. We know that corn masa flour remains unfortified, putting Mexican-American women at increased risk of having babies with spina bifida and anencephaly.

Our goal should be to prevent all, not to prevent just some, children from acquiring folic acid–preventable spina bifida and anencephaly. We have work to do. First, we must find a way to eliminate folic acid–preventable spina bifida and anencephaly in one country and know that we have done it. So far this has not been accomplished. I would like to see the U.S. to be the first country to do so. We need to find a way to increase folic acid consumption among the 75% of women of reproductive age not achieving the recommended amounts. Increasing the concentration of folic acid should be considered. The FDA should facilitate the rapid approval of a standard of identity for corn masa flour so that Gruma can fortify its products here as it does in other countries.⁸

We need a way to rapidly assess how well prevention is going in a particular country. Unless there is a vast increase in global resources for spina bifida and anencephaly surveillance, which is unlikely, we need to develop a serum folate–based surveillance model to help us determine where more resources are needed for prevention programs, and possibly to serve as the basis for determin-

From the Rollins School of Public Health, Emory University, Atlanta, Georgia

Address correspondence to: Godfrey P. Oakley, Jr., MD, MSPM, School of Public Health, Emory University, 1518 Clifton Road Northeast, Atlanta GA 30329. E-mail: gpoakley@mindspring.com

0749-3797/00/\$17.00

doi: 10.1016/j.amepre.2010.02.002

ing when these preventable birth defects are eliminated; to develop some agreement on which serum-folate methods are acceptable; to build a back-up system for the training and evaluation of working laboratories; and to determine what serum concentration of folate assures that 95% of women of reproductive age will have no risk for folic acid–preventable birth defects. Until the time that formal committees have met, I suggest that we assume that at a serum concentration of less than 25 nmol/L, women are at risk for folic acid–preventable spina bifida. This is a reasonable default cut-point until there are more data or formal committee recommendations.

The prevention of spina bifida and anencephaly has had a recent major setback in New Zealand, where for some unknown reason the prime minister sought to score short-term political points by stopping the mandatory fortification that was to be instituted in September 2009 in New Zealand and Australia. He has thus done a disservice to the families of New Zealand. Fortunately, fortification occurred as planned in Australia, where the first babies conceived after mandatory fortification are about to be born. The New Zealand prime minister has called for voluntary fortification of bread and encouragement for women of reproductive age to consume vitamins. The paper by Tinker and colleagues³ suggests that the prime minister's strategy will fail, as they have shown that only 25% of women consume folic acid–containing supplements after 20 years of public health messages. Supplement programs should play only a complementary role in prevention. The primary way to increase folic acid consumption for women of reproductive age is to require that grain products be fortified with sufficient folic acid.

No baby should develop a birth defect that can be prevented. Given that birth defects are the leading cause of infant mortality in all developed countries and the proportion will increase in developing countries as the infectious disease causes of infant mortality are controlled, our institutions and political bodies should give increased priority to improving infant mortality and child health by

implementing programs known to prevent birth defects, such as those that prevent folic acid–preventable birth defects.²

GPO gave talks on folic acid in Japan, sponsored by Otsuka, November 2008; is the co-inventor on a CDC patent for folic acid in oral contraception; and has consulted to Johnson & Johnson on folic acid and oral contraception.

No other financial disclosures were reported by the author of this paper.

References

1. MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. *Lancet* 1991;338:131–7.
2. Oakley GP Jr, Brent RL. Birth defects prevention: “The fierce urgency of now.” *Birth Defects Res A Clin Mol Teratol* 2008; 82:745–7.
3. Tinker SC, Cogswell ME, Devine O, Berry RJ. Folic acid intake among U.S. women aged 15–44 years, National Health and Nutrition Examination Survey, 2003–2006. *Am J Prev Med* 2010;38(5):534–42.
4. Honein MA, Paulozzi LJ, Mathews TJ, Erickson JD, Wong LY. Impact of folic acid fortification of the US food supply on the occurrence of neural tube defects. *JAMA* 2001;285:2981–6.
5. De Wals P, Tairou F, Van Allen MI, et al. Reduction in neural-tube defects after folic acid fortification in Canada. *N Engl J Med* 2007;357:135–42.
6. Mosley BS, Cleves MA, Siega-Riz AM, et al. Neural tube defects and maternal folate intake among pregnancies conceived after folic acid fortification in the United States. *Am J Epidemiol* 2009;169:9–17.
7. Berry RJ, Li Z, Erickson JD, et al. Prevention of neural-tube defects with folic acid in China. China-U.S. Collaborative Project for Neural Tube Defect Prevention. *N Engl J Med* 1999; 341(20):1485–90. Erratum in: *N Engl J Med* 1999;341(24):1864.
8. 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;116:753–5.