

Primary Prevention of Pregnancy Complications

Negative pregnancy outcomes such as spina bifida, preterm delivery and low infant birth weight are tremendously costly to society, in both monetary and human terms. Since 1981, when Laurence et al¹ published their landmark study showing prevention of neural tube defects (NTDs) with folic acid supplementation, both biochemical enzyme defects and nutritional deficiencies have been increasingly studied in their relationship to NTDs. This research has yielded overwhelming evidence that consumption of adequate folate prevents NTDs.

These findings resulted in the 1992 US Public Health Service recommendation that all women capable of becoming pregnant should consume 400 mcg of folic acid daily, in order to reduce their risk of a neural-tube-defect-affected pregnancy.² However, it is becoming clear that for some women (and presumably men), dietary sources of folate are inadequate to achieve this level. Even the proposed fortification of cereal-grain products with folic acid is unlikely to adequately increase folate consumption,³ and those with genetic defects may require even higher folate intake.

At the same time that these researchers were pursuing the folate-NTD association, others were discovering non-pregnancy related folate connections. Elevated plasma homocysteine levels have been identified as an independent risk factor for cardiovascular disease, and folic acid (as well as betaine and vitamins B12 and B6) has been found to reduce hyperhomocysteinemia. This has led researchers to re-examine neural tube defects in terms of homocysteine metabolism; elevated homocysteine levels and certain genetic defects in folate-activating enzymes have been correlated with an increased risk of NTDs.

It is now beginning to appear that negative pregnancy outcomes other than NTDs may also be related to folate-homocysteine metabolism. In this issue of *Alternative Medicine Review*, Miller and Kelly⁴ provide a thorough review of the connections between nutrients related to homocysteine metabolism and negative pregnancy outcomes, including not only neural tube defects, but also spontaneous abortion, placental abruption, pre-term delivery, and low infant birth weight. Supplementation with the appropriate nutritional cofactors offers for the first time the possibility of primary prevention of NTDs and other negative pregnancy outcomes.

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1. Laurence KM, James N, Miller MH, et al. Double-blind randomized controlled trial of folate treatment before conception to prevent recurrence of neural-tube defects. *Br Med J* 1981;282:1509-1511.

2. 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. *Morb Mortal Wkly Rep* 1992;41:1-7.

3. Oakley GP, Erickson JD, Adams MJ. Urgent need to increase folic acid consumption. *JAMA* 1995;274:1717-1718.

4. Miller AL, Kelly GS. Methionine and Homocysteine Metabolism and the Nutritional Prevention of Certain Birth Defects and Complications of Pregnancy. *Alt Med Rev* 1996;1(4):220-235.