

Folic Acid Supplementation During Pregnancy May Reduce Risk of Down's Syndrome

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It is well-established that folic acid supplementation during pregnancy is associated with a significantly lower risk of having a child with a neural-tube defect (NTD; e.g., spina bifida, anencephaly). However, a recent study in *The Lancet* (2003; 361[9366]:1331-5) provides evidence that folic acid supplementation also is associated with reduced risk of Down's syndrome. Researchers compared medical data from approximately 490 families at high risk for NTD with data from 516 families at high risk for Down's syndrome, and discovered that Down's syndrome was much more prevalent in pregnancies involving families at high risk for NTD. The evidence suggests that mothers of children with Down's syndrome experience an abnormal metabolism of folate and methyl, as well as mutations in their folate gene. These traits are also seen in infants affected by NTD.

Folate (folic acid, a B vitamin) is unique in that it contains a methyl group (CH₃), which it donates to homocysteine to permit its enzymatic conversion to methionine. Once formed within the cells of the body, methionine (a methyl-containing amino acid) extracts the adenosine ring from adenosine triphosphate (ATP) and becomes S-adenosyl methionine (S-AdoMet). S-AdoMet is then able to donate its methyl group (originally derived from folate) to many biochemical reactions, including the synthesis of DNA bases. Consequently, DNA synthesis requires a constant, adequate supply of folate on a daily basis.

During pregnancy, the rapid rate of fetal cell division demands an even greater supply of folic acid; if the demand is not met, DNA defects occur, which most often manifest as neural-tube defects. Evidence from the *Lancet* study suggests the same may be true for Down's syndrome. To complicate matters, some individuals have an inborn error of folate or methyl metabolism, in that they show a defect in the enzyme that converts homocysteine to methionine, and thus produce insufficient amounts of S-AdoMet. However, studies show that these individuals can improve the conversion of homocysteine to methionine significantly if they are provided with higher supplementation levels of folic acid (which is the coenzyme for this reaction) in many cases. Therefore, mothers identified as high-risk for NTD usually express this type of folate or methyl defect and are prescribed higher supplemental levels of folic acid. *The Lancet* study provides evidence that these women are also at higher risk for delivering a child with Down's syndrome, indicating that higher folic-acid supplementation may be of great importance in reducing the risk of NTD and Down's syndrome.

The researchers conclude that because of the links in the development of the two complications, folate supplementation before conception has the potential to reduce NTD and Down's syndrome during pregnancy. Most women would benefit from 400 mcg of folic acid prior to conception (most multiple vitamins contain this amount) and 800 mcg during pregnancy (the amount contained in prenatal vitamins). Women with folate or methyl metabolism problems require additional amounts of supplemental folic acid, which should be prescribed by their attending physicians or specialists, who can best monitor the appropriate biomarkers.

Reference

NNFA Supplement (April 28, 2003).

Vitamin D Supplementation Improves Outcomes in Prostate Cancer Patients

Prostate cancer cells are known to maintain expression of their cell membrane vitamin D receptors. Evidence suggests that vitamin D (1,25 dihydroxy-cholecalciferol, or calcitriol) slows the replication rate of various prostate cancer cell lines under experimental conditions, and enhances cellular differentiation (making these cells appear and behave less malignant and more like normal prostate cancer cells from which they were born). As such, researchers have suspected that vitamin D may be of value as complementary treatment in prostate cancer management. This suspicion was confirmed this year in a study reported in the *Journal of Clinical Oncology* (2003;21[1]:123-8). In this study, calcitriol was administered to men with androgen-independent prostate cancer, in conjunction with the chemotherapy agent, docetaxel. The combination of calcitriol and docetaxel was twice as effective compared to the docetaxel alone. Of the 37 patients in the study, 81 percent (31) who were treated with the calcitriol/docetaxel combination reduced their prostate-specific antigen levels by more than 50 percent. This is an important finding, because androgen-independent prostate cancer is the most stubborn form of this disease; it is inherently resistant to hormone ablation treatment and has few other treatment options.

Reference

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