



Jean Mayer
United States Department of Agriculture
Human Nutrition Research Center on Aging
At Tufts University

**Committee on Government Reform
Subcommittee on Human Rights and Wellness
Representative Dan Burton, Chairman**

**September 22, 2004
Rayburn Building, Washington, DC**

Dietary Supplements: Nature's Answer to Cost Effective Preventative Medicine

Testimony by:

**Jeffrey B. Blumberg, PhD, FACN, CNS
Friedman School of Nutrition Science and Policy
Jean Mayer USDA Human Nutrition Research Center on Aging
Tufts University
Boston, MA**

The Role of Folic Acid and Other Dietary Supplements in the Promotion of Health and Prevention of Chronic Disease

I am a Professor of Nutrition at the Friedman School of Nutrition Science and Policy and the Associate Director of the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University. I also serve as a non-paid member of the Scientific Advisory Board of the Dietary Supplement Education Alliance. I have been investigating the role of dietary supplements in the promotion of health and prevention of chronic disease for almost 25 years. It is now indisputable that nutrition is a key component of any disease prevention strategy and optimal intakes of vitamins, minerals and other nutrients are critical to maintaining wellness. Virtually every nutrition-monitoring survey reveals that most Americans fail to achieve these intakes through their usual diets. Fortunately, dietary supplements represent an affordable, effective, and practical tool to help solve this problem and, thus, ultimately reduce healthcare costs. While I will illustrate this principle with the example folic acid, it is important to recognize there is an extensive body of scientific evidence demonstrating the health benefits of other dietary supplements as you are hearing from other experts today.

Folic acid is a B vitamin essential to the activity of more than a dozen enzymes, amino acid metabolism, and DNA formation. Inadequate intake of folic acid has been associated with anemia, some forms of cancer, heart disease, poor pregnancy outcomes

(including preterm delivery, infant low birth weight, fetal growth retardation), and birth defects, most notably, neural tube defects (NTD) leading to spina bifida and anencephaly but also including cleft lip and palate, limb deficiencies, conotruncal defects of the heart, and Down syndrome. The richest dietary sources of folic acid are liver, mushrooms dried beans, green leafy vegetables, and since 1998, enriched grains fortified with this vitamin. The Recommended Dietary Allowance for folic acid is 400 μg daily. Usual intakes of folic acid before fortification were 200 μg but are now estimated to be about 300 μg with much lower intakes in people following low carbohydrate diets and avoiding fortified breads and other cereals. However, it is important to understand that many people have a greater need for folic acid, including pregnant and lactating women, people who consume alcoholic beverages or take certain medications (e.g., aspirin, methotrexate, pyrimethamine, trimethoprim), patients with certain inflammatory conditions of the intestine (e.g., enteritis with malabsorption such as sprue), and the elderly.

For the last five years, Center for Disease Control and Prevention and the Institute of Medicine has recommended that all women capable of becoming pregnant should consume 400 $\mu\text{g}/\text{day}$ of synthetic folic acid from supplements or fortified food in addition to consuming food folate from a variety of dietary sources. The scientific basis of this recommendation included data from population-based studies and randomized clinical trials as well as extensive experimental studies. Folic acid supplements have been proven to be the most effective and reliable method to reduce the probability of NTD. Nonetheless, two-thirds of American women of child-bearing age do not follow this advice and one of every thousand babies in the US is born with an NTD. The Lewin Group analysis calculated that over the next five years \$1.3 billion in health care costs could be saved if these women took a daily supplement containing 400 μg folic acid.

But folic acid supplements are not just for women. The benefits of daily folic acid supplementation extend well beyond reducing the risk of NTD and other birth defects. Observational studies consistently reveal that men and women taking supplements containing folic acid have the lowest blood levels of the amino acid homocysteine. Some evidence suggests that lowering homocysteine levels could reduce the risk of heart disease by 20 percent. Elevated levels of homocysteine are a significant, independent risk factor for atherosclerotic vascular disease in the coronary, cerebral, and peripheral vessels and for arterial and venous thromboembolism. Many studies reveal that elevated homocysteine may enhance the effect of other established vascular risk factors such as hypertension and smoking. Low intakes of folic acid have now been shown to be the primary determinant of mild-to-moderate elevations of homocysteine. Randomized clinical trials investigating the effect of folic acid supplements on risk of heart disease, stroke, and dementia are now being supported with Federal funds.

Folate inadequacy has a pro-carcinogenic effect by interfering with normal DNA synthesis and regulation (via methylation reactions). An increased risk for some forms of cancer has been associated with poor folate status in several epidemiological studies, with the strongest evidence linked to colorectal cancer. However, studies have also suggested that the increased risk of breast cancer associated with regular alcohol consumption may be reduced by an increased intake of folic acid from dietary supplements. Recent

experimental research has shown that low consumption of folic acid impairs the integrity of the genome, particularly tumor suppressor genes, and this effect can be reversed by supplementing the diet with folic acid.

While many different factors contribute to the risk of poor health and chronic disease, we know that diet and the intake of specific nutrients play a key role in the prevention of cancer, diabetes, heart disease, infectious diseases, macular degeneration, osteoporosis, and other conditions. The power of nutrition to promote health is well established. We need now to find ways to encourage Americans to choose healthful dietary patterns and increase their intake of key nutrients with fortified foods and dietary supplements. If we succeed in doing so, both the personal burden of disease carried by Americans and the associated enormous expenditure for their healthcare will be substantially reduced.

Thank you.

Selected References

Neural Tube Birth Defects and Other Pregnancy-related Topics

Centers for Disease Control and Prevention. Neural tube defect surveillance and folic acid intervention – Texas-Mexico border 1993-1998. MMWR Morb Mortal Wkly Rep 2000; 49:1-4.

Scott JM, Weir DG, Kirke PN. Folate and neural tube defects. In: Bailey LB, ed. Folate in health and disease. New York: Marcel Dekker, 1995;329-60.

Shaw GM, Schaffer D, Velie EM, et al. Periconceptional vitamin use, dietary folate, and the occurrence of neural tube defects. Epidemiology 1995;6:219-26.

Ellison J, Clark P, Walker ID, Greer IA. Effect of supplementation with folic acid throughout pregnancy on plasma homocysteine concentration. Thromb Res 2004;114:25-7.

Megahed MA, Taher IM. Folate and homocysteine levels in pregnancy. Br J Biomed Sci. 2004;61:84-7.

Yang Q, Atkinson M, Erickson JD. Method of weighted proportion of reproductive-aged women taking folic acid supplements to predict a neural tube defect rate decline. Birth Defects Res 2003;67:959067.

Atherosclerotic Vascular Diseases

Boushey CJ, Berford SA, Omenn GS, Motulsky AG. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probably benefits of increasing folic acid intakes. JAMA 1995;274:1049-57,

Brattstrom LE. Vitamins as homocysteine-lowering agents. *J Nutr* 1996;126:1276S-80S.

Kalra DK. Homocysteine and cardiovascular disease. *Curr Atheroscler Rep* 2004;6:101-6.

Kelly JJ, Kohlhagen J. Atherosclerosis and Folic Acid Supplementation Trial: untangling the web of cardiac risk in chronic kidney disease. *Nephrology* 2004;9:112-3.

Moat SJ, Lang D, McDowell IF, Clarke ZL, Madhavan AK, Lewis MJ, Goodfellow J. Folate, homocysteine, endothelial function and cardiovascular disease. *J Nutr Biochem* 2004;15:64-79.

Paradisi G, Cucinelli F, Mele MC, Barini A, Lanzone A, Caruso A. Endothelial function in post-menopausal women: effect of folic acid supplementation. *Hum Reprod* 2004;19:1031-5.

Pena AS, Wiltshire E, Gent R, Hirte C, Couper J. Folic acid improves endothelial function in children and adolescents with type 1 diabetes. *J Pediatr* 2004;144:500-4.

Refsum H, Ueland PM, Nygard O, Vollset. Homocysteine and cardiovascular disease. *Ann Rev Med* 1998;49:31-62.

Splaver A, Lamas GA, Hennekens CH. Homocysteine and cardiovascular disease: biological mechanisms, observational epidemiology, and the need for randomized trials. *Am Heart J* 2004;148:34-40.

Cancer

Basten GP, Hill MH, Duthie SJ, Powers HJ. Effect of folic acid supplementation on the folate status of buccal mucosa and lymphocytes. *Cancer Epidemiol Biomarkers Prev* 2004;13:1244-9.

Choi SW, Mason JB. Folate and carcinogenesis: an integrated scheme. *J Nutr* 2000;130:129-32.

Jacob RA, Greta DM, Taylor PC, et al. Moderate folate depletion increases plasma homocysteine and decreases lymphocyte DNA methylation in postmenopausal women. *J Nutr* 1998;128:1204-12.

Majumdar AP, Kodali U, Jaszewski R. Chemopreventive role of folic acid in colorectal cancer. *Front Biosci* 2004;9:2725-32.

Zhang S, Hunter DJ, Hankinson SE, et al. A prospective study of folate intake and the risk of breast cancer. *JAMA* 1999;281:1632-7.

Diculescu M, Ciocirlan M, Ciocirlan M, Pitigoi D, Becheanu G, Croitoru A, Spanache S. Folic acid and sulfasalazine for colorectal carcinoma chemoprevention in patients with ulcerative colitis: the old and new evidence. *Rom J Gastroenterol* 2003;12:283-6.

Other Health-related Topics

Iskandar BJ, Nelson A, Resnick D, Pate Skene JH, Gao P, Johnson C, Cook TD, Hariharan N. Folic acid supplementation enhances repair of the adult central nervous system. *Ann Neurol* 2004;56:221-7.

Lamers Y, Prinz-Langenohl R, Moser R, Pietrzik K. Supplementation with [6S]-5-methyltetrahydrofolate or folic acid equally reduces plasma total homocysteine concentrations in healthy women. *Am J Clin Nutr* 2004;79:473-8.

Millar WJ. Folic acid supplementation. *Health Rpt* 2004;15:49-52.

Morrell MJ. Folic acid and epilepsy. *Epilepsy Curr* 2002;2:31-4.

Schwammenthal Y, Tanne D. Homocysteine, B-vitamin supplementation, and stroke prevention: from observational to interventional trials. *Lancet Neurol.* 2004;8:493-5.

Whittle SL, Hughes RA. Folate supplementation and methotrexate treatment in rheumatoid arthritis: a review. *Rheumatology* 2004 Jan 6 [Epub ahead of print]

Woitalla D, Kuhn W, Muller T. MTHFR C677T polymorphism, folic acid and hyperhomocysteinemia in levodopa treated patients with Parkinson's disease. *J Neural Transm Suppl* 2004;68:15-20.

McLean RR, Jacques PF, Selhub J, Tucker KL, Samelson EJ, Broe KE, Hannan MT, Cupples LA, Kiel DP. Homocysteine as a predictive factor for hip fracture in older persons. *N Engl J Med* 2004;350:2042-9.

Submitted by:

Jeffrey Blumberg, PhD, FACN, CNS
Associate Director and Professor

Friedman School of Nutrition Science and Policy
Jean Mayer USDA Human Nutrition Research Center on Aging
Tufts University
711 Washington Street
Boston, MA 02111

tel: 617-556-3334
Fax: 617-556-3295
EM: jeffrey.blumberg@tufts.edu