

## Folate Intake Tapers Off; Increased Levels Needed for Veins, Brains

The September issue of the [American Journal of Clinical Nutrition](#) presented numerous study results involving folate, including analysis of existing data on folate levels during the fortification efforts begun in 1998, as well as papers on plasma folate and cognitive performance, and folate intake and endothelial health.

First, researchers from the National Center for Environmental Health at the Centers for Disease Control and Prevention (CDC) joined scientists from the National Center for Health Statistics, National Center for Birth Defects and Developmental Disabilities, FDA and the Office of Dietary Supplements/NIH to determine how population concentrations of serum and red blood cell (RBC) folate and serum vitamin B12 have changed over the past two decades (2007; 85(3):718-27). They reviewed data from the National Health and Nutrition Examination Survey (NHANES, 1988 to 1994), including measurements of blood indicators of folate and B12 in 23,000 subjects from the third of NHANES conducted pre-fortification, as well as like measurements in 8,000 participants from three post-fortification NHANES periods.

They found substantial increases in serum and RBC folate concentrations (by 119 to 161 percent and 44 to 64 percent, respectively) in each age group in the first post-fortification survey period; but, these levels then declined slightly (by 5 to 13 percent and 6 to 9 percent, respectively) in most age groups between the first and third post-fortification survey period. There was no significant change in serum vitamin B12 concentrations. Prevalence estimates of low serum and RBC folate concentrations declined in women of childbearing age from before to after fortification (from 21 to less than 1 percent, and from 38 to 5 percent, respectively), but remained unchanged thereafter. Prevalence estimates of high serum folate concentrations increased in children and older persons from before to after fortification (from 5 to 42 percent and from 7 to 38 percent, respectively), but decreased later after fortification. They concluded there was a significant boost in folate levels immediately following the start of fortification efforts, and a less significant decline in levels longer after fortification began. They noted the decrease is not at the low end of concentrations and, therefore, does not raise concerns about inadequate status.

An accompanying commentary (2007; 85(3):528-30) by folic acid expert Lynn Bailey, Ph.D., health and human nutrition professor at University of Florida and former advisor to numerous government agencies, investigated the possible causes and factors behind the rise and fall of folic acid intake, including concurrent folate supplement use, varying fortification amounts, and reduced consumption of fortified cereal and grain products due to low-carb diet trends. Bailey added there is no way to scientifically compare the 36-percent reduction in neural tube defects (NTDs) charted for the 1995 to 2002 period to current rates, because there is no available post-2002 data, nor is there research showing the effect of the slight decline in folate levels found in the NHANES analysis on the known NTD rates.

The merits of increased folate levels were furthered by a report from a joint trial by researchers from the University of Oxford, England, and University of Oslo, Norway, who investigated plasma folate concentration with cognitive performance, using brain-imaging markers for cerebrovascular disease and brain cell loss. In the study (2007; 85(3):728-34), scientists analyzed data from the population-based Rotterdam Scan Study, including 1,033 non-demented participants aged 60 to 90, who underwent extensive cognitive testing and brain imaging. They used multivariate linear regression to cross-sectionally examine the association between plasma folate concentration and cognitive test performance, and subsequently investigated whether plasma folate was related to the presence of white matter lesions and hippocampal and amygdalar volumes.

Test scores showed improvements in global cognitive function, psychomotor speed and memory function, relative to folate concentration increases; however, there was no association observed between folate status and hippocampal or amygdalar volume. Researchers suggested the performance improvements may be regulated by vascular mechanisms.

Folate's effect on vascular health was highlighted in a meta-analysis of randomized, double blind, placebo-controlled trials in humans (2007; 85(2):610-17). Scientists from Unilever Food and Health Research

Institute, Vlaardingen, Netherlands, looked at the effect of folate on endothelial function—as measured by flow-mediated dilatation (FMD)—using MEDLINE, hand-searched references and interviews with researchers of unpublished trials. Of 163 identified studies, 14 met inclusion criteria and provided data on 732 persons.

In the overall pooled estimate, folic acid improved FMD by 1.08 percentage points over placebo; of the study characteristics, only folic acid dose significantly influenced the outcome. Post hoc analysis seemed to indicate a dose-response effect: the change in FMD was  $-0.07$  percentage points at doses between 400 and 800  $\mu\text{g}/\text{d}$ ; 1.37 percentage points at doses of 5,000  $\mu\text{g}/\text{d}$ ; and 2.04 percentage points at doses of 10,000  $\mu\text{g}/\text{d}$ . They concluded high doses of folic acid improve endothelial function, which could potentially reduce the risk of cardiovascular disease.

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