

# Call for endorsement of a petition to the Food and Drug Administration to always add vitamin B-12 to any folate fortification or supplement<sup>1,2</sup>

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Effective January 1, 1998, the Food and Drug Administration (FDA) mandates fortification of grains with folic acid (pteroylglutamic acid, PteGlu) at 140  $\mu\text{g}$  PteGlu/100 g product to protect fertile American women against having  $\approx 2000$  fetuses with neural tube defects (NTDs) annually. This mandate will do more harm than good unless the FDA mandates that all fortification of grains with PteGlu and all supplements containing PteGlu also include vitamin B-12.

To persuade the FDA to adopt cofortification with folate and vitamin B-12 as the law, we filed a petition with the FDA Dockets Management Branch (FDA Docket no. 96P-0349/CP 1, filed September 26, 1996), asking that the FDA also require a minimum of 25  $\mu\text{g}$  crystalline vitamin B-12/100 g product or per folate supplement.

Implementation of this action will not only prevent  $\approx 2000$  fetal NTDs annually, but also prevent nerve damage from folate-masked pernicious anemia in fertile African American women (1-5) who do not have fetuses with folate-preventable NTDs (4, 5), but do have increased risk of early onset of pernicious anemia in the childbearing years (4, 5) and also in the many millions of Americans age  $> 50$  y who get gastric atrophy with or without pernicious anemia (6). Such nerve damage, which slowly becomes irreversible, will be produced by fortification and supplementation solely with folic acid (6).

The minimal daily absorbed requirement of vitamin B-12 to sustain normality is only 0.1  $\mu\text{g}$  (7). In pernicious anemia, with its absence of secretion of gastric intrinsic factor, one loses the physiologic machinery for the absorption of vitamin B-12 from food. However,  $\approx 1\%$  of any oral dose of crystalline vitamin B-12 will continue to be absorbed via nonphysiologic mass action (8, 9).

There are two etiologic mechanisms for gastric atrophy eventuating in pernicious anemia (6). One is gradually progressive total gastric atrophy, which develops in all humans in a genetically programmed way. Most Americans acquire it between the ages of 50 and 90 (6). The other mechanism is acquired gastric atrophy, resulting from gastric insult, such as by iron deficiency or *Helicobacter pylori* (6).

Because an average of 1% of orally fed crystalline vitamin B-12 is absorbed by mass action in the absence of intrinsic factor and only 0.1  $\mu\text{g}$  absorbed vitamin B-12 will sustain normality with respect to vitamin B-12 nutrition, it would appear superficially that the minimal amount of vitamin B-12 to be added to grain or a supplement is 10  $\mu\text{g}$  (to ensure absorption of 0.1  $\mu\text{g}$ ). However, most grains are fortified with

iron and  $> 40\%$  of Americans take a vitamin C supplement daily (10, 11). When 200 mg vitamin C and amounts of iron matching the recommended dietary allowance (13) reach the stomach together with vitamin B-12 and folic acid, they destroy  $\approx 40\%$  of the vitamin B-12 and about one-sixth of the folic acid within 30 min (12). Thus, 25  $\mu\text{g}$  vitamin B-12 taken orally by these people translates into only  $\approx 13$   $\mu\text{g}$  vitamin B-12 surviving to pass into the small bowel to be absorbed. Thus, the minimum safe daily oral dose becomes 25  $\mu\text{g}$  vitamin B-12.

The grain industry has objected to adding adequate vitamin B-12 to bread and cereal, alleging that it will turn the product pink. Following a standard recipe for white bread, we found no difference from the color of bread without vitamin B-12 when we added 25, 100, or 500  $\mu\text{g}$  vitamin B-12/100 g baked bread. With 1000  $\mu\text{g}$  vitamin B-12/100 g bread, the bread was off-white and had only a trace of pink color.

Mandating by the FDA of the above combined PteGlu-vitamin B-12 supplement will prevent all Americans from ever getting vitamin B-12 deficiency, with its enormous annual cost in morbidity, mortality, and billions of health care dollars (6). The combined supplement will also prevent millions of Americans from getting vasculotoxic hyperhomocysteinemia, with its enormous cost in heart attack, stroke, other vasculotoxic morbidity and mortality, and billions more health care dollars (6, 12). We estimate that  $\approx 20\%$  of all heart attacks, 40% of all thrombotic strokes, and 60% of all peripheral venous thromboses will be prevented by FDA implementation of our petition (6).

We strongly urge all American Society for Clinical Nutrition members, particularly those who can cite in their endorsement letters their several hundred seminal published contributions to this subject over the past quarter century, to write letters of endorsement of our petition to the Dockets Management Branch, Food and Drug Administration, Department of Health and Human Services, Room 1-23, 12420 Parklawn Drive, Rockville, MD 20857 (FAX 301-594-3215). Comments will be received through June 1997.

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