Letter by Spence Regarding Article,
“Differential Effect of B-Vitamin Therapy by Antiplatelet Use on Risk of Recurrent Vascular Events After Stroke”

To the Editor:
It is likely that there was a problem with reverse causality in the article by Arshi et al., which found that B vitamins were harmful among patients taking antiplatelet agents in the Vitamin Intervention in Stroke Prevention Trial (VISP). Antiplatelet therapy was not randomized in VISP, so the decision to prescribe it may have been taken in patients at higher risk. The mirror finding (benefit of vitamin therapy in patients not taking antiplatelet therapy) was reported from the Vitamins to Prevent Stroke (VITATOPS) trial.

The key issues in understanding reduction of stroke by B vitamin therapy to lower total homocysteine are B12, renal failure, cyanocobalamin, and thiocyanate.2 We showed benefit of vitamin therapy among VISP patients after excluding patients in the lowest decile of estimated glomerular filtration rate (<47)3 and harm in patients with diabetic nephropathy, among patients with glomerular filtration rate <50.4, 5

Patients with renal failure given cyanocobalamin have high levels of cyanide and thiocyanate. Hydrogen sulfide, an endothelium-derived relaxing factor analogous to nitric oxide, is consumed in elimination of cyanide from cyanocobalamin as thiocyanate. Thiocyanate also increases oxidation of low-density lipoprotein. Although cyanocobalamin did not lower levels of asymmetrical dimethylarginine (a nitric oxide antagonist) in the Western Norway B Vitamin Intervention Trial, Koyama showed that methylcobalamin lowered both total homocysteine and asymmetrical dimethylarginine in dialysis patients.

B vitamins do reduce the risk of stroke in patients without renal failure; the harm from high-dose cyanocobalamin is likely because of cyanide. We should be using methylcobalamin for stroke prevention. If the data are available, it would be important for Arshi et al.1 to adjust for serum creatinine or estimated glomerular filtration rate in their analyses.

Disclosures
None.

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