Lack of Association of Increased C-Reactive Protein and Total Plasma Homocysteine

To the Editor:

We read with great interest the article on circulating vitamin B<sub>6</sub> levels and C-reactive protein (CRP) in cardiovascular disease (CVD) by Friso et al<sup>1</sup> showing that low plasma pyridoxal 5′-phosphate (PLP) is associated with higher CRP levels. Total plasma homocysteine (tHcy), a well-known risk factor for CVD,<sup>2</sup> represents a major determinant of plasma PLP levels.<sup>3</sup> The inverse correlation of CRP and PLP seems to be independent of tHcy levels.<sup>1</sup>

We tested this hypothesis in 100 patients (59 men and 41 women with a mean age of 63.7 years; range, 31 to 82 years) with CVD and stable angina pectoris who were referred for coronary angiography. Subjects were divided into 2 groups according to normal or elevated CRP values. Group 1 had a CRP<sub>0</sub>&lt;6 mg/L (n=60); group 2 had a CRP&ge;6 mg/L (n=40). Fasting plasma tHcy levels did not differ substantially between the groups (12.5±4.5 μmol/L versus 12.9±3.9 μmol/L in groups 1 versus 2; P=0.65).

Our data confirm the results from Friso and colleagues,<sup>1</sup> as well as observations from others,<sup>4</sup> of a lack of association between CRP and tHcy levels. Whereas both elevated levels of CRP and tHcy represent independent risk factors for CVD, the relationship between tHcy, inflammation, and atherosclerosis cannot be explained through a link of tHcy with CRP.<sup>5</sup> Other factors, such as vitamin B<sub>6</sub> use in the presence of an underlying inflammatory process, could represent a possible link between inflammation and homocysteine metabolism in CVD.

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Response

We are grateful to Auer and colleagues for their interest in our recent report on the relationship between vitamin B<sub>6</sub> (PLP) and C-reactive protein (CRP).<sup>1</sup> In the population-based Framingham Heart Study cohort, we described an inverse correlation between PLP and CRP levels.

Auer et al observed no difference in plasma homocysteine (tHcy) levels in their sample set of patients who were divided into 2 groups according to normal or elevated CRP levels using parameters analogous to those of our study.<sup>3</sup>

This observation is similar to that in our report. However, we showed a slight, marginally significant difference in tHcy concentrations between groups (P=0.063). This trend was no longer present after adjustment for PLP, whereas the strong association between PLP and CRP remained highly significant even after adjustment for plasma concentrations of tHcy, a well-known risk factor for coronary artery disease (CAD). CRP is also a risk factor for CAD, and perhaps the independent association between PLP and CAD<sup>2</sup> exists through an interaction with levels of CRP. Indeed, PLP may not only be an important risk factor for CAD because of its connection with tHcy metabolism, but also through different mechanisms that are still unclear.

The principal aim of our study was to analyze the interaction between PLP and CRP. PLP was not considered in Auer et al’s study, and their statement that tHcy is a determinant of PLP is inverted.

PLP has been reported to be low in chronic inflammatory diseases.<sup>3</sup> This coenzyme is widely involved in the amino acid metabolic pathways and has an influence on platelet aggregation, as well as on preserving arterial wall integrity. Therefore, as an alternative speculation to emphasize the importance of PLP in CAD, we proposed an involvement of PLP in the inflammation-associated events related to the process of atherogenesis.<sup>4</sup> We think that our report highlights a potential role of PLP in CAD that is apparently more significant than that confined to its well-known influence on plasma tHcy levels.<sup>5</sup>

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Circulation. 2001;104:e164

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