Why Should Mild Hyperhomocysteinemia Be Responsible for CAD?

To the Editor:

Since June 1997, we have measured homocysteine (Hcy) in 42 patients with cervical artery dissection (CAD), and so far, the mean Hcy level has been 17.8 ± 9.1 μmol/L. This finding confirms our previous observations demonstrating that mild hyperhomocysteinemia is associated with CAD. This result was confirmed by another group. It is still unknown whether hyperhomocysteinemia, responsible for endothelial damage, can cause secondary dissection. The role of hyperhomocysteinemia in inducing endothelial damage and early atherogenesis has been documented both in vitro and in vivo. On the other hand, Magyar et al reported that Hcy and inflammatory markers have a significant role in early-onset carotid atherosclerosis. Hcy should have another effect in CAD patients. Except for a few elderly CAD patients in whom atherosclerotic lesions are described together with CAD, no atherosclerotic lesions were found in younger CAD patients with mild hyperhomocysteinemia. So, it seems that Hcy produces an intimal tear with a secondary subintimal wide damage. Thus, there could be a synergic effect coupled with a minor trauma, a pre-existing arterial wall defect, or both.

Another question is whether the increase recorded during CAD and stroke is in fact a temporary condition as believed. Since 2001, Hcy has been re-measured after a median follow-up time of 3.5 years (range, 1 to 7 years) in previously studied CAD patients and in additional consecutive CAD patients. In 5 of the original 26 patients studied, remeasurement was not possible (2 patients died, 3 were lost to follow-up). Hcy was measured in another 16 consecutive CAD patients and was re-measured in 11 after 1 year. After follow-up, the mean Hcy value of all CAD patients was 15.1 ± 6.3 μmol/L. Median age was 48.5 years (range, 16 to 69 years). Sixteen patients presented vertebral dissection; 17 presented carotid dissection. Mild hyperhomocysteinemia was still present after the acute event. During follow-up, no other vascular events were seen. The distribution of vascular factors was as follows: 8 (24%) had hypertension, 2 (6%) had diabetes, 6 (18%) had hyperlipidemia, and 1 (3%) had migraine with aura. None of the other factors, such as arterial redundancies, intracranial aneurysms, aortic root dilatation, common carotid artery distensibility increase, and fibromuscular dysplasia because its end points and pathways are identical in all these pathologies.

In conclusion, mild homocysteinemia seems to be responsible for CAD without producing further detectable vessel wall damage. CAD patients are younger than other stroke patients, so the effects of long-term exposure to these mild Hcy levels have not been seen.

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Stroke. 2003;34:e209; originally published online October 16, 2003;
doi: 10.1161/01.STR.0000099068.07405.6A
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/34/11/e209