LETTERS TO THE EDITOR

Scope
Heart welcomes letters commenting on papers published in the journal in the previous six months. Topics not related to papers published earlier in the journal may be introduced as a letter: letters reporting original data may be sent for peer review.

Presentation
Letters should be:
- not more than 600 words and six references in length
- typed in double spacing (fax copies and paper copy only)
- signed by all authors. They may contain short tables or a small figure. Please send a copy of your letter on disk. Full instructions to authors appear in the January 1997 issue of Heart (page 89).

Hyperhomocysteinaemia and premature coronary artery disease in the Chinese

Sir,—We were interested by the study by Lolin and colleagues.1 The Chinese patients with premature coronary artery disease had higher concentrations of folate in serum and erythrocytes, and higher serum vitamin B12 than healthy control subjects. There was not a significant difference in prevalence of fasting hyperhomocysteinaemia; however, there was a significantly higher prevalence of hyperhomocysteinaemia following methionine loading in patients versus controls. There was a significant difference in fasting and post-methionine load plasma total homocysteine, and higher serum vitamin B12 with control subjects (P = 0.004 and P = 0.003).

Hyperhomocysteinaemia may emerge due to genetic factors, for instance from deficiency of the enzyme cystathionine β synthase (CBS), which participates in a transsulphuration pathway, or from thrombolytically or mutant enzyme methionin-ethyhydrofotol reductase (MTHFR) which synthesises 5-methyltetrahydrofolate, or from inborn errors of cobalamins transport and metabolism. Lower concentrations of vitamins B12, B6, and B9, cofactor form flavin adenine dinucelotide (FAD), or folate in serum or plasma may also be associated with hyperhomocysteinaemia. Vitamins B12, B6, and B9 are coenzymes for enzymes methionine synthase, CBS, and MTHFR, respectively.5 5-Methyltetrahydrofolate is a methyl donor for methylation of homocysteine into methionine. Deficiency of these vitamins in blood may occur because of dietary or environmental factors.2

Miller and colleagues2 4 have indicated that vitamin B, deficiency in humans or rats may not be associated with fasting hyperhomocysteinaemia. Fasting plasma tHcy concentrations in vitamin B12 deficient rats were not significantly different from those in control rats; however, the folate deficient rats had plasma tHcy concentrations nearly 10-fold higher than control rats (P = 0.001). During methionine loading, vitamin B12 deficient rats exhibited a dramatic elevation of plasma tHcy concentrations which persisted for four hours or longer (P < 0.001). Folate deficient rats did not show any significant increase in plasma tHcy.1 4

My colleagues and I have shown that serum folate and vitamin B12 concentrations had significant influence on fasting plasma tHcy concentrations; however, the influence of vitamin B12 on fasting plasma tHcy was weak, probably due to smoking.2

These findings may indicate that homocysteine response during methionine loading may be different for folate or vitamin B12 deficiency. Folate deficiency may be associated with fasting hyperhomocysteinaemia. Methionine loading test may be used to uncover post-load hyperhomocysteinaemia which may be associated with deficiency of vitamin B12 or homocysteine reductase of CBS.

Therefore, it may be interesting to measure concentrations of vitamin B12 in plasma or whole blood to investigate a potential role of vitamin B12 in the development of hyperhomocysteinaemia. Further studies of these patients might be interesting because patients with premature coronary artery disease had higher concentrations of folate in serum and erythrocytes. Measurement of vitamin B12 in serum from patient and control subjects may also add new information in the study.

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Hyperhomocysteinaemia and coronary athero-sclerosis

Sir,—I read with great interest the article on hyperhomocysteinaemia and premature coronary artery disease in Hong Kong Chinese patients.1 As suggested by the title of the accompanying editorial,2 homocysteinaemia has emerged as an independent risk factor for the development of coronary artery disease.

Homocysteine in human plasma arises solely from the breakdown of the essential amino acid methionine, which is present in many dietary sources. Dietary homocysteine is complexed to various thiols, and does not appear under normal circumstances to influence plasma homocysteine.3 The plasma concentration of homocysteine is strictly controlled and kept within a very narrow range in normal subjects, either by its degradation via cystathionine to cysteine and pyruvate, or by remethylation to methionine.4 Although it can be made to rise by ingestion of a very high so-called “loading dose” of methionine in normal subjects on normal diets, such postprandial increases are small, with plasma homocysteine concentrations declining rapidly to the normal range. The study by Lolin and colleagues suggests that in the Hong Kong Chinese patients hyperhomocysteinaemia is associated with genetically inherited abnormalities in enzymes associated with its metabolism.

Thus, while patients with reduced concentrations of cystathionase, homocysteine methyltransferase, methionine synthase, or 5,10-methylenetetrahydrofolate reductase have a widely varying biochemical outcome, they all have in common an elevated plasma homocysteine.5 Patients with these metabolic distort-
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