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 figures. **Please send a copy of your letter on disk.** Full instructions to authors appear in the July 1997 issue of *Heart* (page 97).

Hyperhomocysteinaemia, *Helicobacter pylori*, and coronary heart disease

SIR,—Sung and Sanderson[1] have suggested that the development of hyperhomocysteinaemia in subjects with *Helicobacter pylori* infection (due to malabsorption and consequent B vitamin deficiency[2]) might provide a link between these two possible causes of coronary heart disease.

We have examined this issue within the framework of our earlier prospective case control study of *H pylori* infection, based on a comparison of incident cases of myocardial infarction (fatal and non-fatal) and controls within the British regional heart study.[3] Residual serum samples were available for 110 of 135 cases of myocardial infarction and 118 of 136 controls for measurement of total homocysteine by reverse phase high performance liquid chromatography with fluorescence detection.[4] Within the control group, geometric mean total homocysteine concentrations were very similar in subjects seropositive (n = 63) or seronegative (n = 55) for *H pylori* (11.9 *v* 11.9 μmol/l; p = 0.98).

In an analysis adjusted for age and town, total homocysteine was positively related to risk of myocardial infarction. For each 5 μmol/l increase in total homocysteine, the odds ratio (OR) increased by 1.38 (95% confidence interval (CI) 1.02 to 1.86; p = 0.03). *H pylori* seropositivity was positively but non-significantly related to risk of myocardial infarction (OR = 1.56; 95% CI 0.86 to 2.82; p = 0.14). However, mutual adjustment had little effect on the respective odds ratios: for total homocysteine, adjusted OR = 1.35; 95% CI 1.00 to 1.83; p = 0.04; for *H pylori*, adjusted OR = 1.47; 95% CI 0.81 to 2.68; p = 0.20.

The findings of this study, while consistent with earlier reports of an association between homocysteine and coronary risk,[5] do not provide strong support for the hypothesis that hyperhomocysteinaemia and *H pylori* infection have interrelated effects on coronary risk.

Analyses of total homocysteine were carried out in the department of pharmacology, University of Bergen, Norway (Professors H Refsum and P M Ueland).

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Hyperhomocysteinaemia, *Helicobacter pylori*, and coronary heart disease

SIR,—Hyperhomocysteinaemia and *Helicobacter pylori* infection have recently been implicated in the pathogenesis of coronary heart disease and a possible link between these factors has been suggested in this journal.[1] Our work has shown that chronic infection with *H pylori* confers a twofold risk of coronary heart disease[2] and this association, like hyperhomocysteinaemia, is independent of hypertension, smoking, and hyperlipidaemia. Our studies have shown that fibrinogen concentrations and total leucocyte counts were higher in *H pylori* seropositive patients with cardiovascular disease.[3] We therefore suggested that the mechanism is chronic infection accompanied by persistent inflammation.

It has recently been postulated that chronic gastritis caused by *H pylori* infection may cause clinical or subclinical cobalamin deficiency. This damage to the gastric parietal cell may be initiated by autoimmune cross reactivity between identical lipopolysaccharides on the bacterium and the gastric parietal cell itself.[4] As a result, either through reduced acid output leading to malabsorption of food bound cobalamin or intrinsic factor production, subclinical cobalamin deficiency may develop. As a consequence of reduced cobalamin, hyperhomocysteinaemia develops.[5] Homocysteine is directly toxic to endothelial cells and can inhibit the secretion of nitric oxide from endothelial cells, therefore facilitating platelet aggregation and vasoconstriction.[6] Thus, the possible link between *H pylori* and serum homocysteine levels lent itself to investigation.

We assessed both the *H pylori* status measured by enzyme linked immunosorbent assay (ELISA), and total homocysteine concentrations measured by reverse phase high performance liquid chromatography with precolumn derivatisation and fluorometric detection based on the method of Fiskerstrand *et al*,[7] on serum from a population of 220 individuals (143 men, 77 women; mean (SD) age 66 (9.4), range 35–86). The mean (SD) serum homocysteine concentration was 22.7 (11) nmol/l. As the data were positively skewed, they was log transformed before statistical analysis (unpaired *t* test).

We found no significant difference (p = 0.30) between the homocysteine concentrations in the *H pylori* seropositive (n = 122, mean 21.8 (8.6) nmol/l) and seronegative groups (n = 98, 24.0 (13.4) nmol/l). There was, however, a non-significant trend (p = 0.20) in patients over the age of 50 towards lower homocysteine in the seropositive (21.7 (8.6) nmol/l) compared to the seronegative group (24.3 (13.8) nmol/l).

It has been suggested that serum homocysteine may exhibit a sex difference, with men having higher concentrations. This was not borne out by our data: seronegative women 23.6 (15.2) nmol/l, seropositive women 21.4 (6.8) nmol/l (p = 0.82); seronegative men 24.2 (12.2) nmol/l, seropositive men 21.9 (9.3) nmol/l) (p = 0.26).

Our data, therefore, do not show that *H pylori* seropositivity is associated with hyperhomocysteinaemia; if anything, there was a trend towards lower homocysteine being associated with *H pylori* seropositivity. This may reflect the age of the study population and we may need to focus measurements on an older group in whom gastric atrophy resulting from *H pylori* gastritis is more advanced.

This shows that serum homocysteine levels are not altered by *H pylori* infection, and that if the association of *H pylori* with coronary heart disease is a true one then other mechanisms must be sought. Chronic inflammation remains the leading candidate.

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