significant difference in the prevalence of the antibodies between the sexes (51/61 (84%) in the men versus 55/63 (87%) in the women respectively; $\chi^2=0.341$) or between the patients with and without left ventricular hypertrophy (defined as a left ventricular mass index >134 g/m² in men and >110 g/m² in women on echocardiography) (65/78 (83%) versus 41/46 (89%) respectively; $\chi^2=0.784$).

This preliminary study suggests a relation between *H pylori* infection and hypertension. We did not, however, find any associations with cardiovascular risk factors (including the presence of left ventricular hypertrophy) except for a weak relation with body mass index. Our findings are consistent with a study from a general practice in Gloucester, which showed a significant relation between *H pylori* infection and hypertension.² Our group has also reported data suggesting an association between the presence of antibodies to *C pneumoniae* and hypertension.³ Thus our study and that of Barnes *et al.*² are at variance with that of Patel and colleagues as there seem to be significant relations between both *H pylori* and *C pneumoniae* infections and hypertension.

We thank Ms Pauline Lowe, Dr J Zarifis, and Dr A Blann for technical help.

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Study confirms previous findings

EDITOR,—P Patel and colleagues' study substantiates our observation of an association between infection with *Helicobacter pylori* and coronary heart disease.¹ The first report from the group² prompted our retrospective serological study among patients presenting to the emergency care unit of our hospital.³ Currently we are recruiting all patients admitted to the coronary unit of our hospital with acute myocardial infarction during the time that one of us (MTLR) is on duty there. Patients recruited from 1 July to 30 September 1995 are analysed here. In addition to being tested for antibodies, all patients were assessed for the presence of *H pylori* infection with the carbon-13 urea breath test, which was performed according to the European standard protocol.⁴ Volunteer blood donors attending the blood bank of our hospital served as controls.

Twenty four (89%) of the 27 patients with myocardial infarction and 291 (47%) of the 619 blood donors were found to be infected with *H pylori*. As only two women had been admitted to the coronary unit (both of whom were positive for *H pylori* infection) we assessed only the male patients and compared them with blood donors of similar age. Table 1 gives the results; the Mantel-Haenszel weighted odds ratio was 4.4 (95% confidence interval 1.2 to 20.6).

The preliminary findings from this population case-control study confirm previous reports of an increased risk of acute myocardial infarction in men infected with *H pylori*. In our final analysis several potentially confounding variables will be taken into account. We believe, however, that a randomised study is needed to determine more

Table 1—Prevalence of *H pylori* infection among men with myocardial infarction and controls aged 40 and over. Figures are numbers (percentages)

Age (years)	Patients with myocardial infarction	Controls
40-49	6/6 (100)	80/142 (56)
50-59	5/7 (71)	85/135 (63)
60-69	8/9 (89)	18/33 (55)
≥70	3/3 (100)	—
≥40	22/25 (88)	183/310 (59)

clearly the effect of eradicating *H pylori* infection in patients at high risk of myocardial infarction.

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Association may not be causal

EDITOR,—P Patel and colleagues report a causal relation between infection with *Helicobacter pylori* and the presence of ischaemic heart disease.¹ We do not believe that this assertion is supported by the evidence.

Firstly, their findings were based on a cross sectional survey, and it is difficult to separate cause and effect from such surveys. This means that a person's status with regard to exposure to these infections at the time that he or she was included in the study may have had little to do with the exposure status at the time that the coronary heart disease process began. Coronary heart disease has a high prevalence in the population and may have its origins early in a person's life. The seroprevalence of antibodies to *H pylori* is also high and may be closely linked to childhood living conditions or adult social class. Unless a temporal relation can be established, the cause of the coronary heart disease remains uncertain.

Secondly, we found a reverse association from

Fig 1—Relation between prevalence of *H pylori* infection and standardised death rate from ischaemic heart disease in nine countries

that claimed by the authors when we compared the seroprevalence of antibodies to *H pylori* reported by the EUROGAST Study Group² with the age standardised death rate from ischaemic heart disease in nine developed nations.³ Figure 1 shows that deaths from ischaemic heart disease were negatively associated with the seroprevalence of antibodies to *H pylori* ($r=-0.73$, $P<0.05$).

The causation of disease is complex. Patel and colleagues found an association between *H pylori* infection and ischaemic heart disease, but a temporal relation has not been shown and the finding has not been consistent. We remain unconvinced that this association is causal.

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Eradication of the infection on grounds of cardiovascular risk is not supported by current evidence

EDITOR,—P Patel and colleagues report having found an association between *Helicobacter pylori* infection and coronary heart disease in a cross sectional study.¹ As the association based on history alone failed to reach significance when adjusted for other risk factors this finding is based largely on the interpretation of resting electrocardiograms. The authors fail to provide data on the predictive value of left bundle branch block, T wave inversion, and ST depression in a similar population or to explore the sensitivity of their result to these values.

Furthermore, insufficient detail of the logistic regression is given for readers to determine which groups were contrasted and how the group with both *H pylori* and *Chlamydia pneumoniae* infections was treated in the analysis. If the latter group was included in the groups with a single infection the results could be misleading and adjustment for the other infection by an additive covariate may be inadequate. Also, generalised linear interactive modelling is known to give inaccurate results for logistic regression when there are few results in a particular group. There were only 11 patients in the group with electrocardiographic abnormalities but no *H pylori* infection and at least 14 covariates to be adjusted for simultaneously.

We have evaluated a near patient test for *H pylori* infection (Helico G test) in six general practices in Birmingham.² A total of 311 patients were tested, having been recruited from patients aged over 50 who were attending the practices; their medical histories were recorded and validated against their general practice records. The prevalence of angina or myocardial infarction was 13% (41/311). Twenty six (63%) of the 41 patients with a history of ischaemic heart disease were positive for *H pylori*, compared with 198 (73%) of the 270 without a history of the disease. Our results, based on history alone, therefore do not support the findings of Patel and colleagues.

Patel and colleagues have attempted to provide evidence of a causal link. When two common conditions that have known confounding variables³

(such as age and social class) are found to be associated, even after adjustment, it seems sensible to treat such associations with caution until evidence of causality can be obtained—in this case from a prospective randomised controlled trial of the eradication of *H pylori* infection. We therefore believe that eradication of *H pylori* infection on the grounds of the risk of cardiovascular disease alone, like that of gastric cancer alone,⁴ is not supported by the current evidence.

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Authors' reply

EDITOR,—Brendan C Delaney and colleagues point out that the association between seropositivity for antibodies to *Helicobacter pylori* and coronary heart disease (based on history alone) in our study failed to reach significance. It is more important, however, to look at the odds ratio and confidence interval. We suggest that an odds ratio of 1.87 (95% confidence interval 0.87 to 4.02) is important in a common disease like coronary heart disease.

The reason for Delaney and colleagues' failure to find an association between *H pylori* infection and a history of ischaemic heart disease (as ascertained from general practice records) is unclear, but selection bias may have been a problem as the subjects were all attending their general practice. In any event, the confidence interval for the odds ratio that they observed (0.63 (0.32 to 1.26)) overlaps ours. An association of a similar magnitude to that observed in our study has been reported recently in a large population based study of 2000 subjects aged 25-65 that used the Rose angina questionnaire to define coronary heart disease. The odds ratio for *H pylori* infection in patients with coronary heart disease as defined by the questionnaire was 1.68 (0.89 to 3.10) in men after adjustment for age, smoking, and social class.¹ Furthermore, the association between *H pylori* infection and coronary heart disease was shown in patients with disease evident on angiography in our original study² and in patients with myocardial infarction in another study.³

With regard to the predictive value of electrocardiographic findings of coronary heart disease, we would refer Delaney and colleagues to the Whitehall study, in which the abnormalities we chose were validated in relation to subsequent death from coronary heart disease.⁴ Most electrocardiographic abnormalities involved Q waves (22 patients had *H pylori* infection out of 26 with Q wave abnormalities). Rates of infection in those with ST depression (5/6), T wave inversion (7/11), and left bundle branch block (2/4) were slightly lower, possibly reflecting the reduced specificity of these abnormalities for coronary heart disease.

The relation between *H pylori* and *Chlamydia pneumoniae* infection and coronary heart disease was assessed by logistic regression models with the outcome variables being, in turn, history of angina or myocardial infarction; electrocardiographic

evidence of ischaemia or infarction; and prevalent coronary heart disease (defined as either a history of the disease or electrocardiographic evidence of it). In the model *H pylori* and *C pneumoniae* infections were individually treated as dichotomous variables (0,1) and no separate term for both infections was included as they correlated with each other weakly (as shown in table I in our paper). Furthermore, there was no evidence of statistical interaction between *H pylori* and *C pneumoniae* infection as suggested by the unadjusted data, nor was there an a priori biological reason to suspect this.

Delaney and colleagues are incorrect in saying that generalised linear interactive modelling gives inaccurate results for logistic regression when there are few results in a particular group. The validity of unconditional estimates of regression variables depends on whether the number of variables fitted approaches the total number of independent observations (study subjects). In our study this ratio was less than 10%.

We appreciate the comment on confounding by age and social class, but residual confounding was unlikely or small because there was little difference in the odds ratio after adjustment. Finally, we agree (as we stated clearly in our paper) that further studies including interventional and prospective trials need to be carried out to address this issue further.

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Increasing prescription of drugs for secondary prevention of myocardial infarction

Authors' recommendations are too restrictive

EDITOR,—Janet Smith and Kevin S Channer state that "there are few published data on the efficacy of multiple combinations for secondary prophylaxis" after acute myocardial infarction.¹ Consequently, they recommended to colleagues the long term use of aspirin and one other drug. We assume that the second drug was most commonly either a β blocker or an angiotensin converting enzyme inhibitor. We believe that this commonly adopted approach is much too restrictive.

The Norwegian timolol trial² and the β blocker heart attack trial of propranolol³ reported a major survival benefit in patients with clinical evidence of heart failure. Indeed, the criteria used to define this subgroup in the β blocker heart attack trial formed the basis of the inclusion criteria in the acute infarction ramipril efficacy study.⁴ Furthermore, in the latter study, as with the other trials of angiotensin converting enzyme inhibitors, at least a quarter of patients selected for treatment were receiving a β blocker at the time of randomisation.⁵ This subgroup also showed a sizeable reduction in all cause mortality as a result of treatment with an

angiotensin converting enzyme inhibitor. Taken with similar findings in the survival and ventricular enlargement trial and thetrandolapril cardiac evaluation study,⁶ these data strongly support the use of both agents in some patients.

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Lipid lowering drugs should be considered too

EDITOR,—Janet Smith and Kevin S Channer describe the lack of translation into clinical practice of evidence from trials of secondary prevention of myocardial infarction.¹ It is notable that lipid lowering interventions were not included in the list of treatments used for secondary prevention. While further definitive evidence of the effect on total mortality of lowering cholesterol concentrations in this context was published recently,² a considerable number of studies—for example, the St Thomas's atherosclerosis regression study³—have shown regression of coronary atherosclerosis, and meta-analysis has shown a reduction in mortality from coronary heart disease.⁴ The problem of objectivity in discussions of drug interventions in cardiovascular disease has been described before.⁵

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Managing cleft lip and palate

EDITOR,—The letters¹ commenting on Tony Markus and Peter Ward Booth's editorial on the management of cleft lip and palate² raise the spectre of two surgical specialties at public loggerheads. Unfortunately, the dispute has had important consequences for those who should be able to