Helicobacter pylori infection and coronary heart disease

See page 1257 for the article to which this Editorial refers

The recent discovery that Helicobacter pylori is implicated in the aetiology of gastritis, peptic ulcer disease and gastric cancer illustrates that chronic conditions, considered until now as non-communicable, can have an infectious cause.

The hypothesis that atherosclerosis and its clinical consequences are related to the long-term effects of infectious diseases has existed for decades, but has never been accepted as proof.

More recently, evidence has appeared linking infectious diseases with pathophysiological mechanisms that may influence the atherothrombotic process. There are numerous observations both from epidemiological and from pathobiological research linking viral infections with atherosclerosis and thrombosis, herpes virus and cytomegalovirus are strong potential candidates as aetiological agents, but other infectious agents such as Chlamidia pneumoniae and H. pylori may also be implicated in the multifactorial origin of chronic vascular diseases.

The available information suggests that any relationship between chronic infectious diseases and thrombo-atherosclerosis is likely to be complex.

The epidemiological evidence linking infectious diseases and atherosclerosis is largely based on case-control studies, comparing clinical series of coronary heart disease patients with controls. This approach is vulnerable to severe selection bias. Inconsistencies between studies may be related to differences in defining coronary heart disease and to selection bias of controls, including asymptomatic apparently healthy subjects who nevertheless have already developed advanced atherosclerosis without clinical manifestations.

In this issue McDonagh et al. present results from a population-based study on the association between H. pylori infection and coronary heart disease. Prevalent cases of coronary heart disease are compared with the rest of the population as regards seropositivity to H. pylori.

The authors observe that with the adjustment of age and social class the association between H. pylori seropositivity and coronary heart disease becomes insignificant. From this they conclude that the association between seropositivity to H. pylori and the prevalence of coronary heart disease is likely to be spurious.

This study has the great advantage of being population based and therefore less vulnerable to selection bias. However, the study differs substantially from case-control studies in the definition of coronary heart disease. Prevalent cases are defined as all those with a history of myocardial infarction or angina pectoris according to the Rose questionnaire and/or an abnormal ECG; only a small proportion of all prevalent cases reported a history of myocardial infarction. In contrast, most of the case control studies start off with patients with documented coronary heart disease, either clinically or on angiography. These differences in selection and in definition may influence the final results if the hypothesis linking chronic infections to coronary heart disease also involves the severity and extent of the atherothrombotic process.

In the study by McDonagh et al., the prevalences of angina pectoris and ECG abnormalities were considerably less different between genders than was the difference in self-reported myocardial infarction. This may point to a number of false-positives in the female-prevalent cases; angina pectoris and certain ECG abnormalities are less specific for coronary heart disease in women.
Another striking issue to which the authors refer is the extremely high prevalence of seropositivity to *H. pylori* in the general population of North Glasgow: 65% in men aged 45–54 years, more than 80% in men aged 55–74 years. This small fraction of seronegatives (less than 20%) in the age and sex group most likely to have developed athero-thrombotic disease, limits the possibility of detecting an existing association between *H. pylori* seropositivity and coronary heart disease.

Others have argued whether seropositivity to *H. pylori* is to be interpreted as an indicator of chronic infectious disease and/or as an indicator of childhood poverty.

The increase with age of seropositivity may be a cohort effect although not entirely. However, if we accept that *H. pylori* infection is usually acquired in youth and is a marker of deprivation at that time, it becomes very difficult to separate the effect of childhood deprivation and of socio-economic conditions during adulthood on the risk of developing athero-thrombotic diseases.

Social class, educational level or any other indicator of socio-economic class are strongly related to a large variety of health problems including coronary heart disease, although the association with coronary heart disease was inverse in the 1950s and has changed completely in Northern Europe in the last 40 years. The absence of disease specificity and the time trend suggest that social class is related to health through multiple factors associated with a large variety of living conditions and behavioural factors starting in the prenatal phase and continuing until death.

Adjustment for social class status means adjustment for a battery of factors that are not necessarily independent of the study objective i.e. the association between *H. pylori* seropositivity and the atherothrombotic process.

The observation that the association between *H. pylori* seropositivity and coronary heart disease prevalence is no longer statistically significant after adjustment for social class cannot exclude a possible link between *H. pylori* infection and the atherothrombotic process, through mechanisms that are also related to variables that make up part of the Pandora’s box we label as social class.

This study by McDonagh et al. has certainly contributed to the discussion; what is strongly needed are prospective cohort studies on the issue of chronic infectious diseases and coronary heart disease incidence in specific social class subgroups of the population. The complex entity of social class should be left undisturbed. What should be sought for specifically is the association between pre-existent chronic infection and subsequent incidence of atherothrombotic diseases adjusted only for the major disease-specific coronary risk factors that have been well identified.

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References


