detect small treatment effects—that is, a reduction of $<25\%$.

The first study by Danesh et al leaves little doubt that a systemic, low grade inflammatory response is an integral part of the atherosclerotic process. Measuring that inflammatory response using, for example, C reactive protein might improve the ability to predict future coronary heart disease in people with and without a previous history of coronary heart disease. Ridker et al have shown that measuring concentrations of C reactive protein adds to the available information by measuring the standard lipid profile.[10]

If chronic infection does not explain the inflammatory response, what might be responsible? Frankly, we do not know. Cytokines, such as interleukin 6 and tumour necrosis factor α, trigger the production of C reactive protein by the liver, and recent prospective studies show associations between concentrations of these cytokines in plasma and the risk of myocardial infarction and death from coronary heart disease.[11 12] The same associations have been found between coronary heart disease and adhesion molecules, such as intercellular adhesion molecule-1 and E selectin, which bind blood cells to the endothelium and are one of the early steps in atherogenesis.[13 14] Intervening in the inflammatory response or interrupting the tissue damage associated with increased deposition of C reactive protein in the myocardium[15] or in the arterial wall could provide new strategies for preventing or treating heart disease. It might be possible to tailor prescriptions for various compounds, such as lipid lowering drugs, cyclooxygenase inhibitors, or angiotensin converting enzyme inhibitors, based on the presence of circulating markers of inflammation. Any new possibilities for the prevention or treatment of what is still the most frequent cause of death worldwide should be welcomed.

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Can heart failure be diagnosed in primary care?

Brain natriuretic peptide assays may make it easier

Heart failure is an increasingly important problem for primary care physicians in most healthcare systems in developed countries. The condition is almost as common as diabetes mellitus in older adults, occurring in at least 2% of the adult population and rising to 3% in those aged over 75 years.[1 2] Although the incidence of most cardiovascular diseases has declined over the past 20 years, the incidence of heart failure has continued to rise, due in part to the fact that more people are surviving after acute myocardial infarctions and also to the increasing number of elderly people.[3]

Symptomatic heart failure has a major impact on patients and healthcare systems: it has a worse prognosis than breast cancer or prostate cancer and is second only to stroke in terms of healthcare costs.[4] Heart failure costs the United States over $8bn (£5bn) each year, and 5% of all admissions in the United Kingdom involve some degree of heart failure.[5] In addition to high mortality, patients with heart failure also have morbidity from symptoms such as dyspnoea and fatigue.[6]

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Accurate and early diagnosis is important since angiotensin converting enzyme inhibitors improve both morbidity and mortality in all grades of symptomatic heart failure caused by left ventricular systolic dysfunction and can delay or prevent progression to symptomatic heart failure. More recently, research has shown the prognostic benefits of treatment with β blockers in heart failure caused by left ventricular systolic dysfunction. Unfortunately, heart failure is difficult to

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diagnose accurately on clinical grounds. Only 26% of patients with suspected heart failure referred to a rapid access clinic for echocardiography had the diagnosis confirmed after investigation. Clinical diagnosis by hospital physicians is just as poor.[7]

Unfortunately, most patients with suspected heart failure and preserved systolic function cannot be classed as having the elusively categorised diastolic heart failure. In this issue of the *BMJ*, Caruana et al (p 215) report that of 159 patients referred to hospital with suspected heart failure, 109 had preserved ventricular function; on further investigation, however, only seven of these patients did not have an alternative explanation for their symptoms of "heart failure," such as obesity, respiratory disease, or myocardial ischaemia.[8]

To positively establish a diagnosis of heart failure in primary care, most patients must be referred for cardiac imaging. A recent survey of a random sample of primary care physicians across six European countries reported only 5% (Netherlands) to 37% (United Kingdom) of general practitioners had direct access to echocardiography.[9] This poor access is partially due to a lack of trained staff to run clinics and partially to concerns that providing primary care physicians with direct access would result in inappropriate use (although a trial of open access echocardiography found only 12% of referrals to be "inappropriate").[10]

Are there alternatives to echocardiography in primary care? A normal electrocardiogram usually excludes left ventricular dysfunction.[11] However, changes may be subtle and primary care physicians' lack of skill in interpreting electrocardiograms may mean that referral for specialist opinion is still required.

A potential diagnostic aid in primary care is the assessment of patients by measuring plasma concentrations of brain natriuretic peptide. However, data on the validity of brain natriuretic peptide are conflicting. Brain natriuretic peptide testing had a sensitivity of 97%, a specificity of 84%, a positive predictive value of 70%, and a negative predictive value of 98% in 106 patients with symptoms of recent onset who were referred to a rapid access heart failure clinic.[12] Similar predictive performance for the peptide was reported both in patients with confirmed left ventricular systolic dysfunction (the commonest cause of heart failure) in a population of 1653 adults aged between 25 and 75 years who were screened in Glasgow, an area with high rates of cardiovascular disease,[13] and in another paper in the *BMJ* in which 155 patients aged over 75 were screened in primary care.[14] However, these studies were small, and a study of 134 patients who were stable after a myocardial infarction found that brain natriuretic peptide could not predict the presence of mild to moderate left ventricular systolic dysfunction compared with normal function (McClure SJ et al, 20th Congress of the European Society of Cardiology, Vienna, 1998). For 126 patients in general practice who were referred to an echocardiography clinic, in another recent paper in the *BMJ*, there was only a small diagnostic advantage in adding brain natriuretic peptide to standard investigations of electrocardiography and chest radiographs, although 1 in 7 patients was given a false negative diagnosis.[15] However, these latter findings contrast with a negative predictive value of 98% reported in an accompanying paper on brain natriuretic peptide that appeared in the same issue.[14]

So which data are correct? Obviously, more research is needed before brain natriuretic peptide becomes a routine assay. The most likely initial application will be in triaging symptomatic adults for echocardiography on the basis of a positive test; a negative result is likely to exclude a diagnosis of heart failure. The assay's performance characteristics are likely to preclude its use in screening healthy populations because of the lower positive predictive value of the test. A comparatively high prior probability of heart failure in certain groups at risk (those who have had heart attacks or who have hypertension or diabetes) may make selective screening in these populations worthy of further study. It is possible that brain natriuretic peptide could be used to guide treatment analogous to the use of glycated haemoglobin in the follow up of patients with diabetes.[16]

Primary care physicians need structured approaches to diagnosing heart failure; these approaches should involve stratifying patients into risk groups and assessing them with objective tests. In many cases, there is no immediate alternative to echocardiography to confirm the diagnosis and determine the aetiology. However, the brain natriuretic peptide assay holds an exciting potential to determine who should be listed for echocardiography, with the possibility that it can aid in treatment and predicting prognosis.

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