as it may be an independent prognostic predictor of survival, as suggested by the study of Pietilä et al.[1].

Incremental prognostic value of C-reactive protein elevation

The most notable finding in the study of Pietilä et al.[1] was the discrepancy between the lack of correlation between prognosis and estimates of infarct size from peak creatine kinase or creatine kinase MB values and the significant association with peak C-reactive protein values of sudden coronary deaths, of death from cardiac failure and of 6 months mortality. As the authors suggest, their finding may be of practical use because a single C-reactive protein value taken 48 h after the onset of acute myocardial infarction may help to identify patients at high risk and can be easily obtained. However, it remains to be established whether C-reactive protein measurements have an independent incremental prognostic value over and above the data already available on a routine basis. This is not possible on the basis of the data provided in the article. The association between high peak C-reactive protein levels and mortality could be mediated by a greater impairment of left ventricular function due to a greater extent of necrosis or to a previous infarction. Also, the lack of association with new acute myocardial infarction cannot be interpreted because the timing of the event (before or after 6 months) is not specified.

Therefore, the prognostic value of markedly elevated levels of C-reactive protein during the acute phase of myocardial infarction above that of

peak values of creatine kinase or creatine kinase MB represents an interesting, novel finding, and the underlying mechanism of its association with an unfavourable prognosis should be investigated further.

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Different significance of hyperventilation-induced electrocardiographic changes in healthy subjects and patients with coronary artery disease

See page 1432 for the article to which this Editorial refers

It is well known that hyperventilation can alter the repolarization phase of the electrocardiogram. However, whether hyperventilation-induced electrocardiographic changes may be more than just a subject of

curiosity and actually become a useful diagnostic tool in coronary artery disease is far less clear. Besides some basic technical aspects (such as the duration of overbreathing and the degree of hypocapnia achieved), the single most important point is the population to which the test is applied, since its results and their interpretation differ greatly in

presumably healthy subjects, patients with variant or unstable angina and, finally, in those with stable exertional angina[1].

In presumably healthy subjects, prolonged hyperventilation may induce electrocardiographic abnormalities resembling ischaemic changes, and the paper by Alexopoulos *et al.*[2], published in this issue, expands our knowledge of the incidence of T wave inversion and ST-segment depression observed with the test. They observed repolarization abnormalities in 15% of 474 individuals without any apparent heart disease, who underwent a 5 min hyperventilation test at a rate of at least 30 respirations per minute. In various smaller studies, this incidence has ranged from less than 2% to as much as 70%, but the following characteristics (also found by Alexopoulos *et al.*) have invariably been described:

(1) by far the most common observation (13% in Alexopoulos' study) is the appearance of accentuation of non-diagnostic T wave inversion (usually in one lead), whereas ST-segment depression (diffuse and not following a coronary distribution) is rare (2% in Alexopoulos's and other studies);

(2) these electrocardiographic changes invariably occur during the overbreathing phase (80% within the first minute) and subside immediately at the end;

(3) they are almost never accompanied by chest pain (no case in this study).

Rather than by the data presented in Alexopoulos' paper, the validity of performing a routine hyperventilation test in order to identify false-positive exercise test responders, is highly questionable on the basis of Bayesian probability, given the very low pre-test likelihood of coronary artery disease in healthy subjects.

The hyperventilation test has been used in order to provoke coronary vasoconstriction in patients with various forms of angina pectoris. The typical response to prolonged hyperventilation in patients with variant angina is ST-segment elevation (rarely ST-segment depression) accompanied by chest pain, and angiographically demonstrated focal spasm in an epicardial coronary artery[3]. These electrocardiographic changes always appear during the recovery phase of the test and subside spontaneously or after nitroglycerin administration. The sensitivity of the test depends on the spontaneous activity of the disease ranging from almost 100% in patients with one or more anginal attacks per day down to 55% in those with infrequent anginal attacks[4]. Thus, in patients with variant angina, the test is a useful diagnostic tool for demonstrating coronary spasm, and

it has been shown that the ability of calcium antagonists to prevent hyperventilation-induced ischaemia predicts the long-term efficacy of these agents[5].

In patients with unstable angina and angiographically-proven coronary artery disease, the test is positive in 32–50% of cases, a higher frequency being observed in those with a history of angina only at rest[1]. The characteristic response of these patients is ST-segment depression, which may occur either during overbreathing or during the recovery phase, and which is accompanied by angina in 50–60% of cases[6]. ST-segment depression occurring during hyperventilation has been attributed to increased oxygen demand due to the work of overbreathing; it is prevented by propranolol and is diagnostic of poor coronary reserve in patients with multivessel coronary disease. On the other hand, delayed ischaemia observed during the recovery phase of the test is due to a primary reduction in coronary blood flow, which has been attributed to the vasoconstriction of an eccentric stenosis. This latter response has been observed mainly in patients with single-vessel disease and is prevented by pretreatment by a calcium antagonist[6]. Thus, in patients with unstable angina, the hyperventilation test may help in revealing the prevailing pathogenetic mechanism of myocardial ischaemia and in selecting drug therapy.

Finally, hyperventilation-induced ST-segment depression (accompanied by angina in 75% of cases) has been demonstrated in 20% of patients with stable exertional angina and a positive exercise test[7]. In these patients, ST-segment depression occurred during the recovery phase of the test, has been considered suggestive of an enhanced coronary vasomotion and was effectively inhibited by calcium antagonist pre-treatment. Also in this case, the test was useful in selecting medical treatment, since nifedipine or felodipine significantly prolonged exercise tolerance in patients with a positive but not in those with a negative test[7].

To summarize, the clinical usefulness of the prolonged hyperventilation test depends on the population to which the test is applied. In subjects without a clinical history of suspect chest pain, the pre-test probability of coronary disease is very low and the T wave changes observed during overbreathing have no diagnostic value. In this setting, the test is not even suggested in order to rule out false-positive responses to exercise testing. In patients with the various forms of angina pectoris, the ST-segment changes observed during the test are often accompanied by chest pain and may give useful information relating to both the underlying pathophysiology of the disease and the most appropriate pharmacological approach.

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Time to bid farewell to surgical mitral commissurotomy?

The incidence of rheumatic heart disease in the United Kingdom has shown a dramatic decline since the turn of the century. However, the number of immigrants arriving from countries where rheumatic heart disease is prevalent is increasing. Until the early 1980s, the treatment of mitral stenosis was surgical, by either closed or open commissurotomy. In 1984, Inoue *et al.*[1] introduced a non-surgical technique for the treatment of mitral stenosis by using a balloon catheter. Since then, percutaneous transvenous mitral commissurotomy has evolved into an accepted alternative to surgical commissurotomy. Like closed surgical mitral commissurotomy, the mechanism of balloon dilatation of the mitral valve involves splitting and separation of the fused mitral valve commissures by the inflated balloon. Hence, the technique is most suited for pure mitral stenotic valves, which are pliable, mobile, and non-calcified. Earlier reports have confirmed the immediate and long-term efficacy of this procedure, and defined the criteria for patient selection[2].

However, with the continued refinement in technique, greater operator experience, and equipment evolution, the indications for this procedure have expanded to include patients in whom percutaneous transvenous mitral commissurotomy was previously thought to be contraindicated. Currently, a significant proportion of mitral stenotic valves treated with percutaneous transvenous mitral commissurotomy have a morphology that would be considered as less than ideal. Examples included patients with: calcified and/or non-pliable mitral valves; mild mitral regurgitation; aortic regurgitation; multivalvar stenosis; elderly patients; and coexistent coronary artery disease. There are now only two absolute contraindications to percutaneous transvenous mitral commissurotomy, namely significant mitral regurgitation and mobile left atrial thrombus.

One category of patients in whom percutaneous transvenous mitral commissurotomy is particularly suited are those with mitral restenosis following prior surgical commissurotomy. Mitral restenosis following surgical commissurotomy was first reported by Brock in 1952[3], and can develop in 10% to 30% of patients over a period of 10 years. The mechanisms responsible for restenosis include fusion of the leaflets and/or degenerative changes in both the leaflets and the subvalvar apparatus. Although the operative mortality of surgical commissurotomy has progressively decreased owing to improvement in surgical techniques and postoperative care, repeat surgical commissurotomy has been associated with a greater mortality and morbidity than the initial operation. Surgical mitral valve replacement is an alternative treatment but requires an open chest operation with its related morbidity, prolonged recovery time, and life long anticoagulation. Percutaneous transvenous mitral commissurotomy by