If an exercise training programme, which has the known effects on autonomic balance were added to this spontaneous tendency, it would be easier to accept that physical activity has a beneficial impact on heart rate variability thereby reducing a risk factor.

But if we can accept that physical training could improve autonomic balance, and if a spontaneous trend in this direction is present in coronary patients what happens to myocardial contractility, or more generally the mechanical efficiency of the heart? In other words, improvement of sympatho-vagal interaction due to physical training also plays a counteractive role on ventricular remodelling, and in doing so increases the process of risk reduction after a myocardial infarction? At the moment the question has no clear and definite answer. We probably need larger numbers of patients and a different approach to the analysis of the heart rate variability.

A good suggestion, in our opinion, could be that of our own experience[7] in which to assess heart rate variability as a predictor of myocardial recovery from ischaemia or hypoxia, we used a non-linear dynamic analysis (fractal dimension), which appeared convenient because fractal dimension predicts arrhythmia recurrence in patients treated for life-threatening ventricular arrhythmias. B. CARU*
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References
[6] Malliani A, Pagani M, Lombardi F et al. Cardiovascular disease risk reduction after a myocardial infarction? At the moment the question has no clear and definite answer. We probably need larger numbers of patients and a different approach to the analysis of the heart rate variability.

Vitamin C and coronary vasoreactivity

See page 1676 for the article to which this Editorial refers

Vitamin C, ascorbic acid, has many functions including collagen formation and wound healing, but in this editorial I will focus on its antioxidant properties. Although ascorbate is not lipophilic, it can reduce LDL oxidative susceptibility. Therein lies its potential to attenuate the progression of atherosclerotic plaques and coronary heart disease prevention.

Oxidized LDL is thought to be one of the culprits important in the pathophysiology of atherosclerosis. Studies have generally shown reduced coronary heart disease risk in populations consuming foods high in antioxidant vitamins. However, it is not known whether antioxidant vitamins given as supplements to food will reduce cardiac events or prevent the development of atherosclerosis. The US Nurses Health Study reported 30–40% risk reduction in cardiovascular events in subjects taking the antioxidant vitamin E who were in the highest quintiles[4].

Enstrom et al. in NHAES 1 (National Health and Nutrition Examination survey) reported data from >11 000 US adults[2]. Individuals reporting high intakes of vitamin C exhibited significantly lower risk of death from all causes, particularly from coronary heart disease over a 10-year period. Prospective trials of the antioxidant beta carotene in a 12 year randomized trial in 22 071 male physicians showed neither benefit nor harm in relationship to the incidence of cardiovascular disease or all-cause mortality. In contrast, the Cambridge Heart Antioxidant Study (CHAOS) of patients who had established coronary heart disease, showed a reduction in cardiovascular events but not in all-cause mortality in physicians using vitamin E (400 IU–800 IU per day)[5].

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In this issue, Jeserich and colleagues have shown that vitamin C improves endothelial function of epicardial coronary arteries in patients with hypercholesterolaemia or essential hypertension — assessed by cold pressor testing. They investigated whether the abnormal constriction of epicardial coronary arteries, due to sympathetic stimulation by the cold pressor test in patients with essential hypertension or hypercholesterolaemia could be reversed by the administration of the antioxidant vitamin C. Investigators studied 28 patients with angiographically normal coronary arteries with either hypercholesterolaemia, hypertension or neither. Immersion of the hand and forearm in ice water was used as a stimulus and quantitative angiography was used to determine the diameter of the coronary arteries. Ice water immersion was performed before and after 3 g of vitamin C was given intravenously. Patients were excluded from study if they had unstable angina, myocardial infarction, valvular heart disease, diabetes, were cigarette smokers, had coronary artery spasm or heart failure. All vasodilator drugs were discontinued 24 h before study. Ice water hand and arm immersion was carried out for 90 s.

Results of their investigation are fairly clear-cut and show that vitamin C given intravenously in the doses stated lessens endothelial dysfunction of coronary arteries in hypertensive and hypercholesterolaemic patients when assessed by a stimulus of hand and arm immersion in ice water for 90 s. The clinical relevance of these observations, although suggesting benefit, needs to be elucidated. The dose of vitamin C given seems rather large compared to what the patient might be taking on a daily basis with usual vitamin therapy.

The investigators indicate that the cold pressor testing is more of a physiological test than infusing acetylcholine by the intracoronary route. I suppose that is correct, but I have never thought that immersing a forearm and hand in a bucket of ice water was physiological. Anyone who had done this recognizes immediately that this is a very painful stimulus in most instances and not really comparable to activities of daily living or even exercise testing.

In a recent study by Kugiyama et al., patients with coronary spastic angina, although the patients are not comparable to the patients studied by Jeserich et al., there are some similarities that warrant comment. These investigators make the point that oxygen free radicals generated in the arterial walls have been shown to cause endothelial vasomotor dysfunction. They infused intracoronary acetylcholine into the left coronary arteries and measured epicardial artery diameters by quantitative coronary angiography before and during combined intracoronary infusion of vitamin C (10 mg. min⁻¹) or saline as a placebo in 32 patients with coronary spastic angina and 34 control subjects.

The results indicated that vitamin C infusion suppressed a constrictor response of the epicardial diameter to acetylcholine in spasm coronary arteries but had no significant effect in the control coronary arteries. The coronary sinus–arterial difference in plasma thio-barbauric acid reactive substances during acetylcholine infusion, an indicator of lipid peroxidation in coronary circulation, was higher in patients with coronary spastic angina than in control subjects, but was suppressed in patients with coronary spastic angina to comparable levels in control subjects by combined infusion of vitamin C. These investigators concluded that vitamin C attenuates vasomotor dysfunction in epicardial coronary arteries in patients with coronary spastic angina and oxygen free radicals may at least in part play a role in the abnormal coronary vasomotor activity and response to acetylcholine in spasm coronary arteries.

The investigators hypothesize that oxygen derived free radicals may cause endothelial dysfunction or inactivate endothelium derived nitric oxide leading to abnormal vasomotor reactivity in spasm coronary arteries in patients with coronary spastic angina. These investigators are the first to show that vitamin C attenuated the constrictor response of the epicardial spasm coronary artery to acetylcholine while it had no effect on the response to acetylcholine control coronary arteries.

I have never advocated the use of vitamin C in patients with proven coronary artery spasm, but based on this observation I may begin to do so. The two studies mentioned above are hypotheses-generating studies. Vitamin C therapy needs to be tested in large populations of patients with coronary artery disease.

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References


Smoking and coronary heart disease

See page 1630 for the article to which this Editorial refers

‘Not bad — but could do better’ must be the verdict on the EUROASPIRE survey of recorded smoking status and interventions following cardiovascular events reported in this issue[1]. Pre-event recording of status and interventions following cardiovascular events on the EUROASPIRE survey of recorded smoking status was remarkably good with ‘cardiovascular risk’[4]. The mechanisms through which tobacco smoking mediates these effects remain largely unknown, but are certainly multiple; there is, for example, evidence for effects on both atherosclerotic and thrombotic processes — free radical damage to vascular endothelium, effects on platelet survival and aggregation, and elevation of fibrinogen levels[5–7].

Most importantly, stopping smoking reduces cardiovascular risk. In the 20 year follow-up of the British Doctors Study, the excess cardiovascular risk was halved within 2 or 3 years of stopping smoking and by 10 years had returned to that of a non-smoker[3]. Stopping smoking after a heart attack is particularly important as it substantially reduces risk, halving risk of recurrence and of cardiovascular death within 5 years[8–9].

Advice and help to stop smoking is therefore of paramount importance in those with manifest cardiovascular disease, particularly those who have had a vascular event or revascularization procedure. Surveys consistently show that about 70% of smokers say they want to stop and try many times to do so; but only a minority succeed[10]. Of those who do succeed, most do so ‘on their own’, without professional help or aids. Motivation to stop and confidence in the ability to do so are important predictors of success. Relapse in the first few weeks is a common pattern but the tendency for this reduces over time and the majority of those who achieve sustained abstinence for a year remain long-term ex-smokers.

Much research has shown that brief advice to stop smoking, given in a medical consultation about other matters, enhances the chances of smoking cessation. Systematic review of about 30 randomized trials involving many thousands of smokers shows that such brief advice (compared to no advice) increases sustained cessation by over 50% — an enhancement of 2 or 3% in absolute success rate[11].

But for many smokers, particularly those smoking more than 15–20 cigarettes daily, nicotine addiction is a major factor in persistence of the habit and causing relapse following attempts to stop, because of nicotine withdrawal symptoms — anxiety, restlessness, irritability, craving, and so on. Nicotine replacement therapy — chewing gum, transdermal patches, nasal spray, oral inhalator, oral tablets — aids smoking cessation by providing a temporary source of nicotine. The evidence of efficacy and safety of these products is now substantial: systematic review of about 80 randomized, placebo-controlled trials shows that nicotine replacement therapy doubles sustained cessation rates and can achieve absolute success rates of about 10% in medical care settings[12].

