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Diet and heart health: emerging evidence

The National Service Framework for Coronary Heart Disease (NSF for CHD) sets out clinical targets for both primary and secondary prevention but dietary and lifestyle measures remain a vitally important population-based approach to CHD prevention. Though CHD mortality is falling in the UK, a greater focus on lifestyle measures could help to accelerate this fall and to address ethnic and social class differences in CHD. "Emerging evidence – a multidisciplinary approach" was the theme of the Diet and Heart Health Symposium, held in London in October 2002.

A number of recognised dietary and lifestyle measures which the public can make are highlighted in this report. For example, on page S3 of this report we see a summary of the potential impact of a range of dietary measures on blood lipids and lipoproteins, indicating how small but multiple changes by individuals can result in a useful summation of effects. Soya protein has now been added to this list with the recent approval of a health claim for soya protein and cholesterol reduction in the UK. The approval process for such health claims recently granted in the UK by the approval body, the Joint Health Claims Initiative (JHCI), is highlighted.

The promotion of these measures requires a coordinated multidisciplinary approach, and the evolving field of public health nutrition will be pivotal in improving effectiveness. How best to communicate such messages to the public is far from clear, however.

The symposium was organised by HEART UK (Hyperlipidaemia Education and Research Trust), the new union between the Family Heart Association and the British Hyperlipidaemia Association. The event was funded by an educational grant from Alpro, manufacturers of soya products.

Michele Sadler
Medical Writer

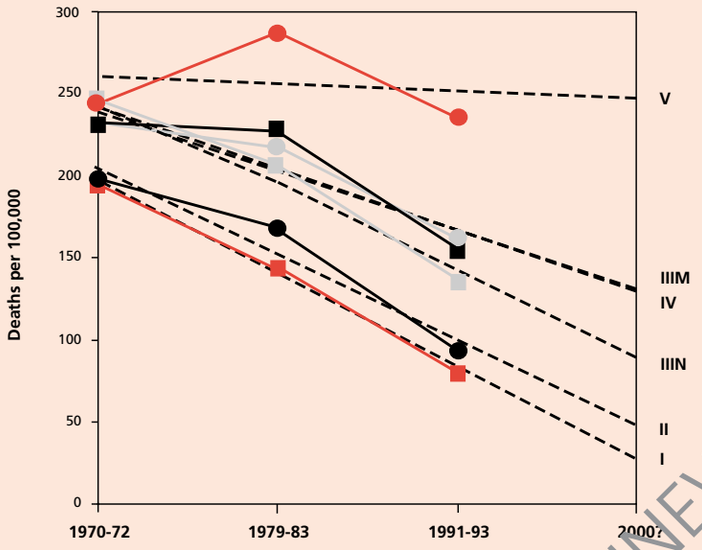
Public health perspective of CHD

The benefit of an integrated and coordinated approach to public health was a key theme of Professor Klim McPherson (Professor of Public Health Epidemiology at the University of Bristol) in his talk "Reduction of risk factors and disease risk".

Across the social classes in the UK there is a consistent trend of increasing CHD mortality from social class I, in which CHD mortality is lower than expected, to social class V, in which it is higher than expected (Department of Health, *Nutritional aspects of cardiovascular disease*, 1994) (figure 1). It is clear that changes in behaviour have contributed to the fall in CHD mortality in social classes I and II, which has fallen at a much faster rate than in social class V. Professor McPherson said that lifestyle changes such as diet and physical activity could, if started at a young age, make CHD essentially avoidable in the under 70s.

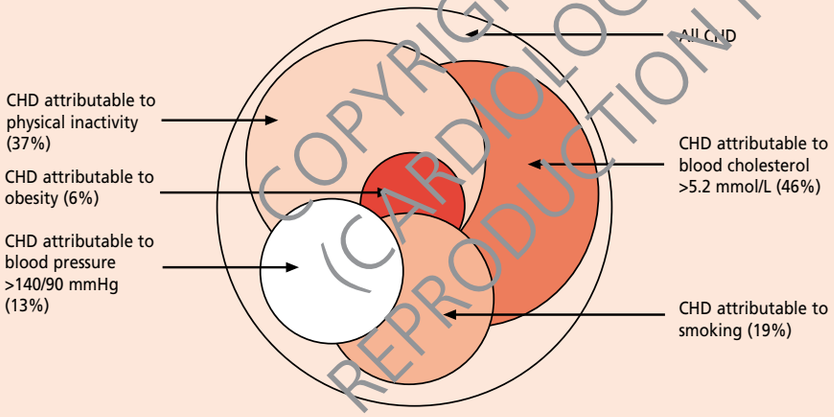
An assessment of the major contributors to preventable coronary heart disease (figure 2) shows that blood cholesterol above 5.2 mmol/L is the largest component of risk, followed by physical inactivity, smoking, high blood pressure and obesity. Professor McPherson has estimated that moderate changes to risk factors (table 1) could reduce CHD cases and deaths in the UK

Figure 1. Standardised (to European population) death rates from coronary heart disease, men aged 20–64, by social class, at three time periods 1970–1993, England and Wales



The dotted lines are extrapolated linear trends. Source: Drever E and Whitehead M. 1997 Health Inequalities: Decennial Supplement. London: The Stationery Office.

Figure 2. Components of preventable coronary heart disease



Source: British Heart Foundation (2000). Coronary Heart Disease Statistics (taken from the above analyses)

From: 'Estimating the Impact of changes in risk factors.' McPherson, Britton & Causer, National Heart Forum, 2002

by 30% by the year 2010. Larger changes might have an even bigger impact: for example the risk of CHD could be reduced by more than 50% in both men and women if the whole population reduced their total blood cholesterol to less than 5 mmol/L. However, achieving such changes is a complicated issue.

Market forces are a major influence on choice, and factors impeding the implementation of effective public health strategies include lack of resources, short-term political expediency, a demand-led healthcare system and vested interests that do not promote health. The importance of focusing on primary prevention is apparent from the Wanless Report (submitted to HM Treasury in April 2002), which predicts that a fully engaged healthcare system embracing modern technology and focused on disease prevention could result in lower NHS spending by the 2020s. Problems within the public health infrastructure highlighted by Professor McPherson include fragmentation, protected clinical leadership, and issues such as the lack of a descriptive noun for public health workers.

Professor McPherson concluded with his own estimate: a really effective CHD healthcare policy could reduce CHD deaths in England and Wales from their current rates of more than 17,000 deaths annually to 3,200 deaths annually in those under 65 years of age; and from 38,000 deaths to 8,340 deaths annually in those aged 65–74 years.

Strategies to reduce cholesterol

In his keynote address "Dietary and lifestyle interventions – do they work?" Dr Andrew Neil (Consultant Physician, Oxford) outlined current clinical guidelines: patients with pre-existing cardiovascular disease, patients with multiple cardiovascular risk factors, and patients with inherited disorders of lipoprotein metabolism warrant treatment with statins. Dietary and other lifestyle measures are an adjunct to all of these, he said.

An overview of six trials of more than two years' duration concluded that an 11% reduction in total cholesterol is associated with a 23% decrease in cardiovascular events (Hooper L. *BMJ* 2001;**322**:757-63). However, evidence shows that the results of cholesterol lowering seen in clinical trials are not reproduced in free-living populations, in which dietary advice is only associated with a 3–5% reduction in total cholesterol. Other strategies are therefore needed to produce a more beneficial cholesterol-lowering effect. These may include functional foods, dietary supplements, and possibly fiscal and legal measures.

Dr Neil discussed the evidence for health benefits of particular dietary constituents. Thus, 50–100 g oat bran per day is associated with a 2–3% reduction in total cholesterol in free-living subjects (Rispin CM. *JAMA* 1992;**267**:3317-25). It is suggested that garlic may lower blood pressure and lipids but studies have been hampered by poor methodology and use of different garlic preparations. An overview of 25 studies of plant stanol and sterol esters has demonstrated reductions in both total and low-density lipoprotein (LDL)-cholesterol, and indicated that an intake of 2 g/day results in about a 10% reduction in LDL-cholesterol which was additional to the effects of a standard cholesterol-lowering diet. The efficacy of stanol and sterol esters is equivalent, and both work by inhibiting cholesterol absorption. As regards alcohol, up

Table 1. Impact of predicted changes in risk factors on the percentage reduction in cases and deaths in the UK, by 2010

Risk factor	Most likely change	% reduction in CHD
Cholesterol	All < 6.5 mmol/L	10
Physical activity	All light → moderate, all moderate → intense	9
Blood pressure	All < 76 mmHg diastolic	6
Smoking	All smoking > 10 per day → < 10 per day	5
Obesity	6% men, 8% women with BMI > 30	2
Total		30

Table 2. Summary of the potential impact of a range of dietary measures on blood lipids and lipoproteins

Dietary measure	Amount	Impact
Total fat	25%–35% kcal	TC –3% to –5%
Plant sterol spread	20–25 g/day	TC –7% to –10%
Oat bran	50–100 g/day	TC –2% to –3%
Soya protein*	25 g/day	TC –3% to –4%
Garlic supplement		TC –1% to –2%
Oily fish	1 to 2 portions/wk	Little effect at this intake
Fish oil supplements	2–4 g/day (EPA+DHA)	TG up to –30%
Alcohol	2–3 units/day	HDL +15%
Walking	10 miles/week	HDL +20%
Weight loss	10 kg (22 lb)	TC –0.5 mmol/L; TG up to –30%; HDL +20%

Key: TC = total cholesterol; TG = triglycerides; HDL = high-density lipoprotein; EPA = eicosapentaenoic acid; DHA = docosahexaenoic acid.
* This reduction depends on the baseline cholesterol levels and is discussed further in the section on the health benefits of soya.

to six drinks per day are associated with protection against CHD but more than two drinks per day increase the risk of death from other causes, including cancer, cerebrovascular disease and accidents. Table 2 summarises the potential impact of a number of dietary measures on blood lipids and lipoproteins.

Lifestyle changes and dietary measures are recommended not only for their influence on cardiovascular outcomes but for other diseases, too. For example, in one study lifestyle interventions such as weight loss and regular physical activity in 3,234 subjects with impaired glucose tolerance were associated with a lower incidence of type 2 diabetes (Diabetes Prevention Program Research Group. *NEJM* 2002;**346**:393-403).

Dr Neil concluded that while the impact of changes seen in free-living populations may not be significant for individuals, they may well be important for population-based risk reduction. Also, multiple small behavioural changes by individuals can result in a useful summation of effects.

The health benefits of soya

One strategy to reduce blood cholesterol is inclusion of soya protein in the diet. Following recent approval by the UK's Joint Health Claims Initiative (JHCI), a claim that soya protein reduces blood cholesterol can now be communicated to the public via food packs and in promotional material. The JHCI is an impartial organisation that administers the voluntary code of practice agreed between industry, enforcement authorities and consumer bodies. Melanie Ruffell of the JHCI outlined the approval process for health claims. The scientific dossier to support the soya claim was reviewed by the JHCI's expert committee of seven scientists.

The claim states: "The inclusion of at least 25 g soya protein per day, as part of a diet low in saturated fat, can help reduce blood cholesterol levels." There are, however, certain criteria that products must meet before such a claim can be made, such as meeting the requirements for a 'low saturates' nutrient claim and avoiding the implication that more, or less, than 25 g per day is advantageous. Further details about the criteria can be found on the JHCI website www.jhci.co.uk

Professor Tom Sanders of King's College London, and a member of the JHCI expert committee, discussed the body of evidence that supports the soya protein claim in his presentation "Soya, cholesterol and the heart". A meta-analysis of 38 trials examining the effect of soya protein intake on blood lipids (Anderson JW. *NEJM* 1995; **333**:276-82) reported an average reduction in LDL-cholesterol of 12.9% associated with an average intake of 47 g soya protein/day. For a 25 g soya intake daily, the estimated reduction in blood cholesterol would be 0.23 mmol/L.

In a recent review of studies published since 1995, six studies were identified that met the review criteria (which included an intake of 25 g soya protein/day). Five of these studies showed an average cholesterol reduction of 0.22 mmol/L, demonstrating consistency of the evidence. To determine the possible benefit of lower intakes of soya, a trial of at least 200 people would be needed to ensure sufficient power to detect an effect. Average baseline cholesterol levels in this meta-analysis were 5.6 mmol/L and the average reduction in cholesterol levels was 4.6%. In accordance with Anderson 1995 we could expect greater reductions in those with higher cholesterol levels.

Recent studies have also assessed the impact of soya protein with and without the isoflavones removed. (Isoflavones are compounds found naturally in foods, including soya beans, which are also known as plant oestrogens. Isoflavones have a similar chemical structure to human oestrogen but a much lower potency.) These trials generally show greater benefits of intact soya (containing isoflavones) compared to extracted soya (isoflavones removed) (Crouse JR. *Arch Intern Med* 1999;**159**:2070-6; Teixiera SR. *Am J Clin Nutr* 2000;**71**:1077-84). Isoflavones show activity as

partial oestrogen agonists, inhibitors of tyrosine kinase and *in vivo* antioxidants, but as yet the mechanisms of action for lipid lowering by soya are very poorly understood.

Trials show that soya protein lowers cholesterol in adults and children, in those both with and without existing coronary heart disease. Soya protein may have effects on the cardiovascular system that operate independently from their effects on plasma lipids. Possible mechanisms include:

- Inhibition of LDL oxidation
- Influencing the production of atherogenic cytokines; and
- Conserving endothelial function.

Animal data show that isoflavones in intact soya contribute to cholesterol lowering, reduction in atheroma and improvement in vascular reactivity.

Dr Aedin Cassidy, a former lecturer at Surrey University, looked in more detail at the effects of the isoflavone compounds that are present almost exclusively in soya. Extracts of isoflavones are currently being prepared for commercial use, both as dietary supplements and as functional foods. An intake of 25 g soya/day would provide approximately 35–50 mg isoflavones. Newly emerging evidence suggests that if isoflavones are extracted and then replaced, the potency of effects is reduced compared to intact soya.

Omega-3 fatty acids

In a second presentation, "Omega-3s and the heart", Professor Tom Sanders discussed two omega-3 fatty acids that are protective against CHD – eicosapentaenoic acid (EPA, or 20:5n-3), found in fish oil, and docosahexaenoic acid (DHA, or 22:6n-3), found in oily fish and in meat. At intakes in excess of 2–3 g per day, EPA and DHA reduce inflammation, susceptibility to cardiac arrhythmia, blood clotting, blood pressure and plasma triglycerides, and improve endothelial function. However, high doses increase the risk of lipid peroxidation. An intake of 0.7–1.0 g long-chain n-3 fatty acids per day reduces the risk of fatal CHD, probably by decreasing susceptibility to ventricular fibrillation.

Increasing the intake of EPA results in substitution of arachidonic acid (20:4n-6) in the platelet lipids, which reduces the capacity of arachidonic acid to produce thromboxane. Thromboxane stimulates platelet aggregation and vasoconstriction, and aspirin blocks these effects. EPA ingestion is associated with production of inactive thromboxane A3, such that a higher intake of EPA makes the platelets less likely to adhere to the vascular epithelium. DHA is a circular molecule that is found in the heart muscle and in the vascular epithelium. It regulates the ion channels, and may reduce sensitivity to arrhythmias.

A recent meta-analysis of randomised controlled trials of dietary and non-dietary supplementation with n-3 fatty acids supports a protective effect of omega-3 fatty acids against fatal myocardial infarction and sudden death (Bucher. *Am J Med* 2002;**112**:298-304). The speed of the effect suggests that the mechanism is via thrombosis or arrhythmia rather than atherosclerosis. Indeed, there may be novel mechanisms that are not yet understood, and the mechanisms operating at lower levels of intake also need to be elucidated.

Recent data from the Seven Countries Study (Verschuren WA. *JAMA* 1995;**274**:131-8) show that those countries with a high intake of fish – Japan, which has a low-fat diet, and Mediterranean Europe, which has a medium-fat diet – have the lowest risk of CHD. Data show that even a small amount of fish offers protection.

Professor Sanders referred to Willett's data from prospective cohort studies (Willett WC. *Proc Soc Exp Biol & Med* 2000;**225**:187-90). These show that replacing saturated with polyunsaturated fatty acids results in a greater decrease in CHD risk than reducing total fat, demonstrating that the type of fat is more important than the total fat intake. Professor Sanders suggested that simplistic messages are unhelpful and that health professionals need to be more specific when offering dietary advice.

Influence of diet on cardiovascular disease

In 1994 the UK Committee on Food Aspects of Nutrition Policy (COMA, which has recently been replaced by SACN, Scientific Advisory Committee on Nutrition) gave advice to eat two portions of fish per week, one of which should be oil-rich fish such as mackerel or herring. Dr Judy Buttriss, Science Director of the British Nutrition Foundation (BNF), commented in her talk "Diet and cardiovascular disease – emerging evidence" that the evidence to support this recommendation is now even stronger. Using data from the National Food Survey, Dr Buttriss said that total fish consumption in Britain has increased since 1974, and that intake of oily fish is also gradually rising. When asked about the recent issue of toxins in oil-rich fish, Dr Buttriss commented that the advice to eat one portion of oil-rich fish per week remains unchanged.

Dr Buttriss outlined a number of other emerging markers of risk, an area in which the BNF is facilitating a taskforce, which is due to report in 2003. Antioxidants are hypothesised to inhibit oxidation of LDL-cholesterol, and thus to protect against atherosclerosis. Most cross-sectional studies have shown the prevalence of CVD to be inversely related: to plasma dietary antioxidants, particularly β-carotene and vitamin E; to a lesser extent to vitamin C; and to dietary intake of flavonoids. However, intervention studies have produced less convincing data.

Diets rich in plant foods have been reported to be beneficial but it is not yet clear which components are responsible. Attention has been focused on their antioxidant properties but the antioxidant nutrients may exert their effects through other mechanisms. More needs to be learned about the functions and mechanisms of action of plant-derived substances and about the impact of age, ill-health and genetic inheritance on their actions.

Plant foods are a key source of folic acid, increasingly recognised as an important nutrient, particularly in relation to its involvement in the metabolism of methionine and homocysteine. Blood folate and homocysteine levels are inversely related. High homocysteine levels are associated with a greater cardiovascular risk, and supplementation with folic acid has been shown to reduce homocysteine levels. The results of a series of randomised, controlled trials to ascertain whether folate or folic acid supplements have the potential to reduce CVD risk are eagerly awaited. Studies are also needed to clarify the role of other B vitamins such as vitamins B6, B12 and B2.

An area of increasing concern is the rising prevalence of obesity in the population, both among adults and children, in relation to CHD risk. Obesity is associated with higher blood pressure, higher blood cholesterol levels and increased risk of type II diabetes, all risk factors for CHD. Adipose tissue is now considered to be a central integrator of metabolic activity rather than an inert storage organ, and this is an area of active research. Adipose tissue is under the influence of insulin and the catecholamines, and is recognised to secrete substances such as cytokines (IL-6 and TNF-α), adiponectin and leptin, which are thought to be associated with heart disease risk.

Dr Buttriss emphasised the need to consider the impact of emerging evidence on dietary

advice. There may be a need to refine dietary messages in line with new data concerning the quality rather than the quantity of fat intakes, and as more data emerge about the importance of the glycaemic index. However, the question of how best to communicate the message remains unresolved.

Benefits of physical activity

In the UK seven in 10 men and eight in 10 women do not undertake enough physical activity to benefit health. Physical inactivity is a strong marker for CHD: it is associated with a doubling of risk, and the relationship is strong, inverse and graded (figure 3). At least 20 of 23 major studies published since 1958 provide support for a dose-response relationship between physical activity and CHD risk (Kohl HW. *Med Sci Sports Exerc* 2000;**33**: S472-83). Professor Adrianne Hardman of Loughborough University, in her talk "Exercise and heart health – how much, how often and how hard?" addressed the specifics of these three variables.

The amount of physical activity is assessed from energy expenditure, and this is determined by the intensity, frequency and duration of activity. Data from the Harvard Alumni Study (Sesso *et al*. *Circulation* 2000;**102**:975-80) suggest a possible threshold in men of 2,000 kcal/week. Men expending this level of energy had only 75% the risk of cardiovascular events compared with their peers with lower energy expenditure. In women, data from the Nurses Health Study (Manson JE *et al*. *NEJM* 1999;**341**:650-8) show a graded response across quintiles of activity, with the greatest benefit at an activity level equivalent to 10 hours' leisurely cycling or eight hours' slow swimming per week. More recent data showed that women who walked for four hours per week (approximately 18 miles) had only 58% the cardiovascular risk of women who did no walking (Manson JE *et al*. *NEJM* 2002; **347**:716-25).

Fitness, a measure of the attributes acquired by being active, is also related to cardioprotection. Blair's data (Blair S *et al*. *JAMA* 1989; **262**:2395) show that the greatest fall in risk occurs between the least fit and the next least fit groups (figure 3). These data were highly influential in the American Surgeon-General's advice regarding the benefits of moderate exercise.

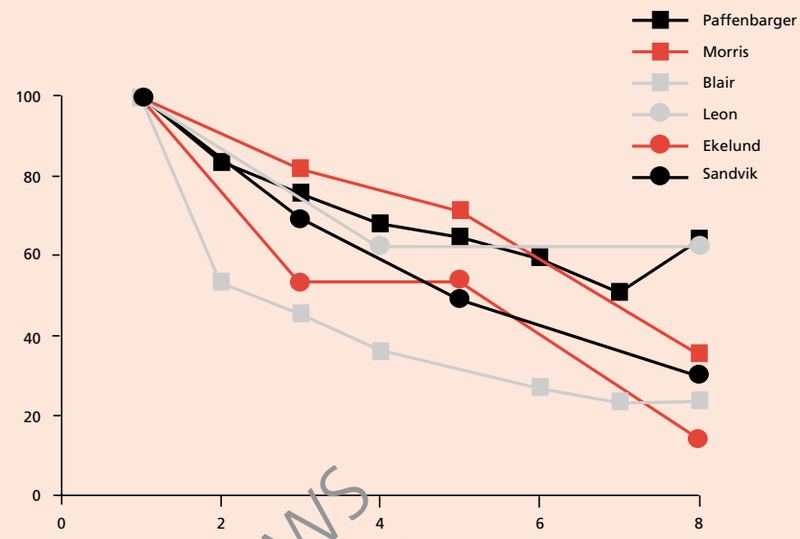
Physical activity influences the metabolic handling of nutrients in a manner likely to decrease cardiovascular risk; studies that have measured the impact of exercise on post-prandial lipaemia can help to assess the 'how often' variable. A study in which subjects underwent a 90-minute brisk walk at 60% capacity the day before a meal (80 g fat load) showed a beneficial effect on serum triglyceride levels for up to six hours post-prandially in both trained and untrained women (Tsetsonis *et al*. *Am J Clin Nutr* 1997;**65**:525). Professor Hardman's data (Hardman AE *et al*. *J Appl Physiol* 1998;**84**: 1895) show that the effects are short-lived but that they are repeated after each session, suggesting that frequency of exercise is important. A single 30-minute walking session or three 10-minute sessions are equally beneficial (Murphy *et al*. *Int J Obesity* 2000). Similar effects have been reported on insulin/glucose dynamics (King *et al*. *J Appl Physiol* 1995;**78**:17-22).

Capability for exercise depends on age, and the question of how hard to exercise can be assessed both in absolute terms and relative to an individual's capacity. Though half of the published studies show that 'vigorous' activity is necessary for cardioprotection, the description of 'vigorous' relates to activities such as cycling at a moderate pace rather than exhausting squash. More gentle exercise will improve fitness in older people, whereas younger people need to undertake more vigorous physical activity to improve their fitness.

Professor Hardman concluded that the aim should be to accumulate at least 30 minutes of moderate-intensity activity on most, preferably all, days of the week. More is probably better. For many benefits to cardiovascular risk, intensity can be traded for duration, provided that total energy expenditure is high. Public health strategies should include encouraging physical activity for personal transportation. Individuals need to decide what they want to achieve from activity, e.g. fitness, cardioprotection or skeletal benefits, and to select activities which fit with other demands on time. Above all, those who have been inactive should start gently and progress gradually.

Is it better to be fat and fit, or thin and unfit? Professor Hardman replied that the lowest risk (of all-cause mortality) has been reported among men who were both fit and lean (Lee *et al*. *Am J Clin Nutr* 1999;**69**:373). However, obese men (defined as BMI >30) who were fit experienced a lower risk than those who were lean but unfit, so it could be argued that physical activity is even more important than avoiding weight gain. But of course, the highest risk was seen among those who were fat as well as unfit.

Figure 3. Physical activity or fitness and CHD mortality



Haskell *MSSE* 1994;**26**:649

Workshop discussions

Two workshops that addressed various practical issues were a useful part of the conference. The general practitioner Dr Jonathan Morrell facilitated "Diet and drugs in the real world – the primary care perspective". He described the challenge faced by GPs and other health professionals in achieving the NSF for CHD Standard 3, namely:

"General practitioners and primary care teams should identify all people with established cardiovascular disease and offer them comprehensive advice and appropriate treatment to reduce their risks." Dr Morrell acknowledged that "the future is multidisciplinary". The workshop demonstrated that lifestyle messages need to be communicated simply to patients, with recommendations that they can both keep to and afford. The parallel workshop run by Ms Jacqui Lynas, the dietitian for HEART UK, focused on "Resources and information for diet and the heart".

Concluding discussion

The Chairman, Dr Tony Leeds of King's College London, asked the speakers to predict likely developments over the next five years. The speakers highlighted the following areas as the most exciting ones to watch:

- Folic acid, homocysteine and CHD risk
- Phytochemicals, particularly in terms of elucidating which constituents are effective and the mechanisms involved
- Accumulating data on the dose response to exercise
- Evidence about the quality versus the quantity of dietary fat, which may influence dietary advice about low-fat, high-carbohydrate diets
- Technological changes that would enable genetic diagnosis to become a reality at an affordable price, the launch of third-generation statins that reduce LDL-cholesterol by 70%, and the development of drugs that reduce LDL-cholesterol by different mechanisms

Further resources

- The HEART UK website: www.familyheart.org
- The Joint Health Claims Initiative website: www.jhci.co.uk
- The British Nutrition Foundation website: www.nutrition.org.uk
- The website put together by Alpro for health professionals: www.soya.co.uk

A second diet and heart health symposium is being planned for Spring 2003. If you would like to be placed on the mailing list for announcements, please email your contact details to hearthealth@alpro.be.

This symposium highlight supplement has been sponsored by Alpro UK. It was written by Dr Michele Sadler, a medical writer (michelejs@aol.com) and independently reviewed by members of the editorial board. The report was edited by supplements editor, Dr Rachel Arthur.

The views expressed in this supplement are not necessarily those of The British Journal of Cardiology or HEART UK.