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The effects of dietary change on serum cholesterol

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Cholesterol is undoubtedly an important cause of coronary heart disease, which adds to the risk associated with other major causes such as smoking and hypertension (Kannel *et al.* 1986). The British are a high-cholesterol population, with more than 40% of middle-aged adults having a serum cholesterol higher than 6·5 mmol/l (Shaper & Pocock, 1985; Tunstall-Pedoe, 1988; Thompson, 1989*a*). If attainable, cholesterol reduction will prevent coronary heart disease. Every 1% reduction in cholesterol reduces coronary events by about 2·5%, so that a 10% reduction in cholesterol will result in a worthwhile 25% coronary prevention (Marmot, 1994). Given these facts the case for lowering cholesterol seems overwhelming.

Recent guidelines for detecting and managing hyperlipidaemia advocate, as a minimum, measurement of cholesterol in those considered at high coronary risk, i.e. those with other risk factors such as hypertension, smoking or diabetes, those with cardiovascular disease, and those with features of familial hyperlipidaemia (International Task Force for Prevention of Coronary Heart Disease, 1992; Betteridge *et al.* 1993). Cholesterol lowering is advocated in these groups. For primary prevention the advice is to lower cholesterol levels which are higher than 6·5 mmol/l, aiming for a target below 5·2 mmol/l. For secondary prevention cholesterol above 5·2 mmol/l is to be lowered below 4·3 mmol/l. Diet change is considered the cornerstone of management, and is expected to be so effective that lipid-lowering drugs will seldom be required; this asks a lot of diet. A reduction in cholesterol from above 6·5 to 5·2 mmol/l requires a cholesterol fall of at least 20%. If diet is not effective the options are to leave the cholesterol high, or to use lipid-lowering drugs. If the diet does not work, neither will the guidelines.

The present review will examine particularly responses to the step-1 diet (American Heart Association, 1984; Table 1), which is the only diet recommended in current guidelines, considering all the published randomized controlled trials of 6 months duration or longer. We discuss briefly more rigorous diets, i.e. the step-2 and -3 diets, which are not recommended in current guidelines and also other dietary measures which may affect serum cholesterol levels.

Table 1. *Diets for reduction of serum cholesterol tested in controlled trials*

Diet . . .	Step 1	Step 2	Step 3
Total fat (% dietary energy)	30	30	<30 and/or
P:S	1·0	1·4	>1·4 and/or
Cholesterol (mg/d)	<300	200	<200
Dietary energy	Reduced to achieve desirable weight for all diets		

P:S, polyunsaturated fatty acids:saturated fatty acids.

Table 2. *Controlled trials of step-1* or equivalent diet to lower cholesterol: individual intervention*

Trial	Setting and subjects	*n*	Men (% total)	Duration (years)	Baseline cholesterol (mmol/l)	Change in cholesterol (%)
UKHDPP	Factories, high risk	1278	100	5–6	6·6	−0·9
WHO Euro†	Factories, high risk	1898	100	4	6·7	−4·0
MRFIT	Employees, high risk	6428	100	6	6·2	−2·0
DART	Hospital, post-MI	982	100	2	6·5	−3·5
Curzio *et al.* (1989)	Hospital, high risk	61	44	0·5	7·1	0·0

MI, myocardial infarction; UKHDPP, United Kingdom Heart Disease Prevention Project (Rose *et al.* 1980, 1983); WHO Euro, World Health Organization European Trial (World Health Organization Collaborative Group, 1982, 1986); MRFIT, Multiple Risk Factor Intervention Trial (Multiple Risk Factor Intervention Trial Research Group, 1982); DART, Diet and Reinfarction Trial (Burr *et al.* 1989).

* For details, see Table 1.

† Excluding results from UK centres.

THE STEP-1 OR GENERAL LIPID-LOWERING DIET

This is the only form of diet advised on current guidelines and entails attaining ideal body weight, reduction of total fat to 30% of dietary energy (from a value of 42% for the population), increase in the polyunsaturated fatty acids (PUFA):saturated fatty acids (SFA; P:S) value to 1·0, and reduction in dietary cholesterol to 300 mg/d (Table 1). Some guidelines claim average cholesterol falls of 20–25% for this diet (International Task Force for Prevention of Coronary Heart Disease, 1992), but this is entirely at odds with the results of long-term controlled trials (Tables 2 and 3).

Description of trials

The United Kingdom Heart Disease Prevention Project (UKHDPP; Rose *et al.* 1980, 1983) and World Health Organization (WHO) European trial (World Health Organization Collaborative Group, 1982, 1986) aimed to reduce cholesterol concentration, cigarette smoking, body weight and blood pressure, and increase exercise. Men were randomized according to the factory where they worked to intervention or control

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Table 3. *Controlled trials of step-1* or equivalent diet to lower cholesterol: population intervention*

Trial	Setting and subjects	*n*	Men (% total)	Duration (years)	Baseline cholesterol (mmol/l)	Change in cholesterol (%)
	Population intervention					
North Karelia†	Population	2535	49	10	7·1	−2·0
Stanford‡	Population: Cohort	490	47	5·5	5·5	−0·6
	Cross-section	–	–	5·5	5·4	−1·7
	Combined individual plus population intervention					
UKHDPP	Factories, all subjects	5373	100	5–6	5·6	+1·0
WHO Euro§	Factories, all subjects	824	100	4	5·6	−2·1
Gothenburg‖	Male population	1473	100	10	6·5	−0·2
OXCHECK¶	Population	2136	45	1	6·0	−2·3
Family Heart Study**	Population	3436	59	1	5·5	−1·8

UKHDPP, United Kingdom Heart Disease Prevention Project (Rose *et al.* 1980, 1983); WHO Euro, World Health Organization European Trial (World Health Organization Collaborative Group, 1982, 1986).

* For details, see Table 1.

† Puska *et al.* (1979, 1983).

‡ Farquar *et al.* (1990).

§ Excluding results from UK centres.

‖ Wilhelmsen *et al.* (1986).

¶ Imperial Cancer Research Fund OXCHECK Study Group (1994).

** Family Heart Study Group (1994).

groups. The Multiple Risk Factor Intervention Trial (MRFIT) randomly allocated high-risk men to intensive intervention to reduce smoking, blood pressure and serum cholesterol, or to ordinary care (Multiple Risk Factor Intervention Trial Research Group, 1982). The Diet and Reinfarction Trial (DART) included a random controlled trial of dietary cholesterol reduction in men who had survived a myocardial infarction (Burr *et al.* 1989). Curzio *et al.* (1989) randomized hypertensive subjects with serum cholesterol >6·5 mmol/l to diet or control groups.

Serum cholesterol responses

Net falls in serum cholesterol in these trials ranged from 0 to 4·0% over 6 months–6 years, with the average fall being about 2% (Table 2). The reduction in the MRFIT (2·0%) was statistically significant, but changes in the other trials were not. Suggested explanations for these poor responses to the diet have included inadequate statistical power, patient selection, changes in control groups and sub-optimal intervention methods. These are considered further.

Statistical power and patient selection

In the two smallest studies the 95% confidence intervals for changes in cholesterol concentration were +3·0–−3·0% (Curzio *et al.* 1989) and −1·4–−5·6% (Burr *et al.*

1989), and the larger studies evidently had sufficient power to exclude type 2 error as an explanation for the small responses. Selection of subjects is unlikely to have influenced the outcome in the UKHDPP, the WHO European trial, or in MRFIT. In DART, patients who intended to follow an intervention diet were excluded, and there may be some bias against intervention. In the trial of Curzio *et al.* (1989) failure of 12% of patients to complete the study may have biased the outcome in favour of diet.

Changes in control groups

In MRFIT, study end-points changed in the control group, and it was suggested that trial procedures may have influenced control subjects, or that population habits may have changed coincidentally. The authors of DART (Burr *et al.* 1989) and Curzio *et al.* (1989) also advanced changes in control groups to explain, in part, the disappointing outcome. In absolute terms, serum cholesterol concentration increased over 5–6 years in the UKHDPP intervention subjects, and fell by 5·0% in MRFIT, 2·8% in DART and 4·2% in the study of Curzio *et al.* (1989). Reductions in serum cholesterol, therefore, were modest, averaging about 3%, even when examined in this way.

Intervention methods

In the UKHDPP and WHO European trial, subjects were given personalized dietary advice based on diary records. The cholesterol response varied with the intensity of intervention. The 4·0% cholesterol reduction at 4 years in the WHO European trial probably reflects maximum effort, whereas the 0·9% reduction at 5–6 years in the UKHDPP typifies responses at other times during the trial. In MRFIT, dietary advice started with weekly small-group sessions, followed by individual counselling by behavioural scientists and nutritionists. In DART, advice was given by hospital dietitians who visited and telephoned regularly to reinforce their instructions. In the trial of Curzio *et al.* (1989) individualized dietary advice was provided by hospital dietitians. Subjects in these trials evidently had the benefit of individual instruction at least equal to that currently available in ordinary practice.

In MRFIT, the diet conformed to step 1 initially, but was intensified later to a P:S of 1·25 and cholesterol intake of 250 mg/d. The 2% reduction in cholesterol at 6 years, therefore, was achieved by a diet more intensive than the step-1 diet. In DART, no mention was made of dietary cholesterol reduction, but this does not influence the response (Edington *et al.* 1987). The diet employed by Curzio *et al.* (1989) was equivalent to step 1 for most patients, but more rigorous in some (J. Curzio, personal communication). The diets employed, therefore, were more intensive than step 1 in two trials, and broadly equivalent to step 1 in the others. Dietary adherence was assessed only in DART and was incomplete.

Summary

These trials encompass different clinical settings, including primary prevention in high-risk men or hypertensive patients, and secondary prevention after myocardial infarction. Despite this, changes in serum cholesterol differed little with a mean fall of about 2 (range 0–4)%. The small reductions in cholesterol cannot be attributed to lack of

statistical power, changes in control groups, or subject selection. The precise contribution of inadequate intervention effort, non-adherence and an insufficiently rigorous diet is uncertain, but diets at least equivalent to step 1 clearly have a meagre effect on cholesterol given the resources available and adherence anticipated in ordinary practice.

Population intervention with step-1 diet

In the controlled but not random North Karelia trial (Puska *et al.* 1979, 1983), population education produced net reductions in serum cholesterol of 2–3% at 5–10 years. Reductions in men (3–4%) were significant but those in women (1%) were not. In the Stanford five-city project, population intervention attained non-significant mean cholesterol reductions of 0·6% by cohort sampling and 1·7% by cross-sectional sampling after 5 years (Farquar *et al.* 1990).

Combined individual and population intervention

Five studies examined population education combined with individual advice to high-risk subjects. In the UKHDPP, serum cholesterol concentration increased by 1·0% at 5–6 years, and in the WHO European trial there was a reduction of 2·1% at 4 years. In the Gothenburg trial the net fall in serum cholesterol concentration at 10 years was 0·2% (Wilhelmsen *et al.* 1986). This small response was attributed to a fall in cholesterol concentration in control subjects. However, intervention reduced cholesterol concentration at 4 years by 1·2% from control values, and 0·6% from baseline values. Changes in control subjects clearly could not explain the small response at 4 years.

More recently the OXCHECK study (Imperial Cancer Research Fund OXCHECK Study Group, 1994) and Family Heart Study (Family Heart Study Group, 1994) employed the same outcome measures as the UKHDPP and WHO European trial, namely changes in cholesterol concentration, cigarette smoking, body weight, blood pressure and exercise. In the former, individuals from five general practices in Bedfordshire were sent a questionnaire from which patients were randomized by household to be offered a health check. The control group consisted of patients offered a health check in the subsequent year. In the Family Heart Study, intervention and comparison practices were selected in each of thirteen towns in Britain. Identification of families suitable for recruitment to the study was by household through the male partner. In the OXCHECK study, 80% of subjects responded to the initial questionnaire and 79% of those in the intervention group returned for rechecks after 12 months. In the Family Heart Study 73% of households approached responded: at 1 year the re-attendance rate of men and women in the intervention group was 88 and 85% respectively. Potential bias was introduced by the non-returners in the intervention groups as their weight at the start of the study was on average higher than that of those who returned. This was allowed for in the analysis. Intervention methods in the OXCHECK study consisted of advice to patients by nurses about risk factors, including diet. Set protocols for repeat measurement were laid down for hyperlipidaemia, but otherwise follow-up was by mutual agreement between the nurse and patient. Initial health checks lasted about 1 h, and follow-up examinations about 15 min. In the Family Heart Study subjects (men and their partners) were interviewed by trained research nurses and life-style changes were personally negotiated. Health Authority pamphlets

were provided where appropriate. The frequency of follow-up was determined by individual risk factors and by coronary risk score for individual patients (derived from the British Regional Heart Study; Shaper *et al.* 1986): the higher the score, the more frequent the follow-up. Table 3 shows the cholesterol reduction attained in the OXCHECK study was 2·3% and in the Family Heart Study 1·8%, both consistent with previous studies.

Conclusions for the step-1 diet

The step-1 diet has only a modest and generally non-significant effect on serum cholesterol whether it is employed as individual intervention, population advice, or in a combined individual and population approach. The mean cholesterol response is a 1–2% reduction, and not the 10–25% reduction suggested in many guidelines.

THE STEP-2 DIET

The step-2 diet is not among recommendations in recent guidelines. Like the step-1 diet, it entails attaining ideal body weight and a reduction in total fat to 30% of dietary energy. In addition, there is a further increase in P:S to 1·4 and reduction in dietary cholesterol to 200 mg/d (Table 1). It has been examined in only one short-term controlled trial in 111 highly-selected and highly-motivated free-living subjects with moderate hypercholesterolaemia (Hunninghake *et al.* 1993). The effectiveness of the diet was maximized by means of extensive dietary advice, reinforcement and monitoring. The mean fall in total cholesterol was only 5%. There was a 5% fall in LDL-cholesterol, which is desirable, but also a 5% fall in HDL-cholesterol, which is theoretically harmful. The LDL:HDL value did not alter, and this would predict no change in coronary risk. The cholesterol-lowering drug lovastatin reduced LDL-cholesterol by 27%, and the combination of the step-2 diet and lovastatin resulted in a 32% decrease in LDL-cholesterol. This demonstrates that the effect of the diet was additive to that of lovastatin.

STEP-3 DIETS

Step-3 diets entail reduction in total fat below 30% of dietary energy, or an increase in P:S to >1·4, or diet cholesterol reduction <200 mg/d, or a combination of these (Table 1). The Oslo study (Hjermann, 1980; Hjermann *et al.* 1981; Table 4) is often cited to support the dietary measures recommended in various guidelines. In this random controlled trial, diet reduced serum cholesterol concentration by 13% over 5 years, and in conjunction with a reduction in cigarette smoking reduced myocardial infarction and sudden death by 47%. Several important points are commonly overlooked. Men were recruited by a single letter of invitation, and the 35% who did not respond probably included those least likely to comply. Subjects were then selected according to their dietary habits. Those following a fat-restricted diet already were excluded, but the number excluded was not stated. The men studied had severe elevation of serum cholesterol concentration, between 7·5 and 9·8 mmol/l. Perhaps because of these selection procedures the subjects had a very high intake of dietary fat, averaging 44% of total energy. This is much higher than the average intake in British men (35–37%; Fehily *et al.* 1987; Burr *et al.* 1989) or the US population (35–40%; National Cholesterol

Education Program Expert Panel, 1988). The diet employed reduced total fat intake to 28% of energy and elevated the P:S from 0·39 to 1·01.

The correct conclusion from the Oslo study is that rigorous dietary intervention in male volunteers with very high serum cholesterol concentrations, and very high dietary fat intake, caused a substantial fall in serum cholesterol. Together with some reduction in cigarette smoking this resulted in an important decline in coronary heart disease. However, its results cannot be extrapolated generally, particularly to those with less severe hyperlipidaemia, to those with more typical dietary fat intake, to women, or to the outcome with the step-1 diet. In short, the Oslo study does not support the policies set out in recent guidelines and, conversely, recent guidelines do not recommend the form of intervention put to the test so successfully in the study.

In five small trials in free-living subjects (Table 4; Research Committee to the Medical Research Council, 1965, 1968; Leren, 1966; Dayton *et al.* 1968; Watts *et al.* 1992) rigorous low-fat diets reduced serum cholesterol concentration substantially by 6·5–15·1%. In three controlled trials in people living in institutions serum cholesterol was reduced by 12·8–15·5% over 1–4·5 years. These rigorous diets lower total cholesterol concentration substantially, by a mean of 13%, although this is still well short of the 20–25% reduction claimed in some guidelines. These diets appear safe, as they are not associated with the increased non-coronary mortality observed with lipid-lowering drugs

Table 4. *Controlled trials of step-3 diets* to lower cholesterol*

Trial	Setting and subjects	*n*	Men (% total)	Duration (years)	Baseline cholesterol (mmol)/l	Change in cholesterol (%)
		Free-living subjects				
Oslo study†	Population, high risk	604	100	5	8·3	−13·0
Leren (1966)	Hospital, post-MI	206	100	5	7·7	−13·9
MRC committee (soya-bean oil)‡	Hospital, post-MI	169	100	2	7·1	−15·1
Research Committee (low-fat diet)§	Hospital, post-MI	81	100	2	6·8	−8·1
Rose *et al.* (1965) (maize oil)	Hospital, IHD	13	–	2	6·8	−6·5
STARS	Hospital, IHD	26	100	3	7·2	−13·0
		Institutionalized subjects				
Minnesota‖	Mental hospitals	4541	48	1	5·4	−13·5
Finnish Mental Hospital Study¶	Mental hospitals	300	100	4·5	7·0	−15·5
Dayton *et al.* (1968)	Veterans' centre	163	100	2	6·1	−12·8

MI, myocardial infarction; IHD, ischaemic heart disease; STARS, St Thomas' Atherosclerosis Regression Study (Watts *et al.* 1992).

* For details, see Table 1.

† Hjermann (1980), Hjermann *et al.* (1981).

‡ Research Committee to the Medical Research Council (1968).

§ Research Committee to the Medical Research Council (1965).

‖ Frantz *et al.* (1989).

¶ Turpeinen *et al.* (1979).

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(Davey Smith *et al.* 1993). Some have suggested that step-3 diets are 'simple' and 'well-tolerated' (Watts *et al.* 1992), but they are in fact exceedingly difficult to implement as they require intensive supervision by dietitians, and even provision of special foodstuffs. They are poorly tolerated and often given up even in the short term (Rivellese *et al.* 1994). The selection of patients for inclusion in the trials may preclude extrapolation to ordinary practice. In the St Thomas' Atherosclerosis Regression study (STARS) trial (Watts *et al.* 1992) for example, we do not know how many patients were excluded because they were unable to follow the trial regimen. Of the patients who completed the STARS trial, 55% were in social classes I and II, a proportion entirely unrepresentative of the general population. The best evidence that step-3 diets are neither feasible nor palatable in ordinary practice is the fact that they are not recommended, or even mentioned, in recent guidelines for managing hyperlipidaemia.

DIFFERENT FORMS OF FAT AND CHOLESTEROL RESPONSE

Different types of fat affect cholesterol concentration in different ways. Fats may be divided into three major classes based on the degree of saturation of the fatty acids. SFA have no double bonds and are solid at room temperature. Monounsaturated fatty acids (MUFA) contain one double bond and PUFA more than one double bond.

Saturated fatty acids

Not all SFA affect the serum cholesterol levels to the same degree. Stearic acid acts like oleic acid which is found in olive oil and reduces LDL-cholesterol (Bonanome & Grundy, 1988). Similarly it has been recognized for some years that short-chain SFA do not raise blood cholesterol (Keys *et al.* 1965). Thus, the PUFA:SFA (P:S) generally used to characterize diets may be inappropriate because of the differing effects of individual SFA and, as discussed later, PUFA. In a study by McMurray *et al.* (1991), native Mexicans who traditionally consume little fat were given a diet high in animal fat. Serum total cholesterol rose, but so did HDL-cholesterol so that HDL-cholesterol:LDL-cholesterol changed minimally. The reverse is often seen among patients who adopt a low-fat diet (Sacks & Willett, 1991). HDL-cholesterol has protective effects against coronary heart disease. In women a high concentration of LDL is not a risk factor whereas a low concentration of HDL is and, therefore, diets that reduce both types of lipoprotein may not benefit women (Crouse, 1989). It cannot be assumed that lowering of HDL-cholesterol levels by a reduction in fat intake is innocuous (Sacks & Willett, 1991).

Monounsaturated fatty acids

MUFA lower serum LDL-cholesterol levels without lowering the HDL-cholesterol level (Mensink & Katan, 1989). Ginsberg *et al.* (1990) showed that a MUFA-enriched step-1 diet with 38% of the dietary energy consumed as fat (10% SFA, 18% MUFA and 10% PUFA with 250 mg cholesterol/d) had effects on plasma lipids similar to those of step-1 diet. However, the duration of the study was only 10 weeks. It has been suggested that the effects of MUFA may explain why some Mediterranean communities have low blood cholesterol despite high-fat diets, as their diets are rich in monounsaturated olive oil

(Keys *et al.* 1986). However, caution is needed as the Mediterranean life style differs from others in many respects. As with SFA, MUFA do not all act similarly. A comparison of diets containing 10% dietary energy from oleic acid, *trans*-isomers of oleic acid, or SFA, showed that the *trans*-isomers raised LDL and lowered HDL, whereas SFA raised LDL but did not lower HDL. LDL:HDL was highest on the diet containing *trans*-isomers of oleic acid, and this may predict increased cardiovascular risk (Mensink & Katan, 1990).

Polyunsaturated fatty acids

PUFA also have varying effects on serum cholesterol. Two classes of PUFA have been studied in most detail, *n*-6 fatty acids whose parent member, linoleic acid, is found in vegetable-seed oils and *n*-3 fatty acids, such as α-linoleic acid, which are found in oily fish and fish oils. The incidence of coronary heart disease has declined in the USA and other countries as dairy products in the diet have been replaced increasingly by fats high in linoleic acid. This has led some to conclude that an increased intake of *n*-6 fatty acids may protect against atheroma. However, the association does not necessarily imply causality: diets high in *n*-6 fatty acids depress HDL as well as lowering LDL (Grundy, 1986). Despite the extraordinary diversity of diets in the world, no population consumes quantities of *n*-6 PUFA as high as those in some clinical trials and, therefore, the long-term consequences of these diets are unknown (Ulbricht & Southgate, 1991).

The effects of *n*-3 fatty acids differ from those of *n*-6 fatty acids (Ulbricht & Southgate, 1991). In primary prevention of coronary heart disease, the consumption of one to two fish per week may be of value. In a longitudinal study information on fish consumption was obtained from 852 men in 1960 (Kromhout *et al.* 1985), and during 20 years of follow-up an inverse relationship was observed between fish consumption and death from coronary heart disease. However, there are numerous possible confounding factors in this type of study. In the DART (Burr *et al.* 1989) study of men who had survived myocardial infarction consumption of fatty fish significantly reduced mortality by 29% over 2 years. Serum cholesterol tended to rise when compared with control patients. In a more recent randomized double-blind controlled trial with 350 patients assigned to placebo (olive oil) or 6 g purified fish oil once daily, there was no significant change in total cholesterol after 6 months (Sacks *et al.* 1994). Furthermore, there was no significant difference in HDL-cholesterol, although the HDL_2 subfraction did rise significantly. Whether this confers benefit remains to be ascertained. The risks and benefits of fish oil on coronary mortality need to be studied directly. The possible benefits on coronary heart disease appear to be independent of total cholesterol concentration. If this is the case, knowledge of total cholesterol is not necessary.

Fatty acid configurations

The double-bonds in MUFA and PUFA can exist in two forms: *cis*- and *trans*-configurations. The industrial hardening of fats by hydrogenation converts the naturally-occurring *cis*-MUFA and -PUFA to the *trans*-configuration. There are suggestions that *trans*-fatty acids increase cholesterol levels as do SFA and, also, may increase the risk of coronary heart disease (Sanders, 1994). In one study of dietary questionnaires completed

by 85 095 women foods that were major sources of *trans*-isomers were each significantly associated with a higher risk of coronary heart disease (Willett *et al.* 1993). This area needs further study.

OTHER DIETARY CONSTITUENTS

Attempts to reduce coronary risk have focused largely on the fat content and composition of diets, but some preliminary evidence indicates that other aspects of diet may warrant rigorous investigation.

Antioxidants

Free radicals, that is to say atoms or molecules that contain one or more unpaired electrons, are potentially injurious to living organisms, for example by lipid peroxidation to form lipid peroxides. Antioxidants may play a role in protecting against such effects. Two epidemiological studies showed that the use of large doses of vitamin E supplements, an antioxidant vitamin, was associated with a decreased risk of coronary heart disease (Rimm *et al.* 1993; Stampfer *et al.* 1993). However, epidemiological correlations alone, no matter how high the level of statistical significance, cannot establish causal relations, as the authors of these papers recognize (Steinberg, 1993). Whether the relationship is causal remains to be determined and this will require long-term double-blind clinical trials.

Fibre

Cholesterol reduction has been observed in some clinical trials of isolated forms of dietary fibre but the type of fibre seems important. In subjects with mild to moderate hypercholesterolaemia already on step-2 diet a diet high in soluble fibre from barley, dried lentils, peas, beans and oat bran was compared with a diet containing a large amount of insoluble fibre from wheat bran, high-fibre crackers and bread with wheat bran and gluten. The soluble-fibre diet caused a 5% greater reduction in total cholesterol, but HDL-cholesterol was also lowered by 3·5% (Jenkins *et al.* 1993). In healthy subjects, the cholesterol-lowering effect of dietary fibre may be indirect, through replacement of dietary saturated fat and cholesterol (Connor, 1990). Studies using complete foods to raise dietary fibre intake have generally yielded results less convincing than those employing isolated forms of fibre. The amounts of fibre used in studies of fibre isolates have been high (10–30 g/d for guar gum or pectin, and 50–100 g oat bran/d), and may not be acceptable in practical diets (Burr *et al.* 1989). There are no prospective long-term outcome trials of fibre, and one should reserve judgement until they are available.

Garlic

The effect of garlic on plasma cholesterol was examined in a meta-analysis of sixteen randomized controlled trials of at least 4 weeks duration and this purported to show a 12% reduction in total cholesterol with garlic therapy (Silagy & Neil, 1994). However, many of these trials had serious methodological shortcomings and rigorously designed and analysed trials are needed. There are no long-term outcome trials. The longest trial was 12 months and most were only of a few weeks duration.

CONCLUSIONS

The step-1 diet which is advised in current guidelines (International Task Force for Prevention of Coronary Heart Disease, 1992; Betteridge *et al.* 1993) has been shown repeatedly and consistently to have little effect on serum cholesterol concentration in free-living subjects. In trials of individual intervention in high-risk subjects reductions in cholesterol have averaged about 2 (range 0–4)% over 6 months–6 years. These small responses could be due to inadequate intervention effort in some but not all studies, or to incomplete adherence, but above all reflect an insufficiently rigorous diet. Responses were similarly small in trials of population education, and when population education was combined with individual advice for subjects at higher risk, with cholesterol falls averaging about 1%. Changes in control groups do not explain the small responses as cholesterol falls from baseline values averaged only 3%. Health-education measures require the same rigorous evaluation as new treatments (Rose *et al.* 1980) and should be judged by the same yardstick. The true worth of an intervention is measured only by the net difference between intervention and control groups. Subjects treated by diet are sometimes classed as 'responders' or 'non-responders' (Reid *et al.* 1984). When the mean effect of diet is close to zero, as in these trials, 'responders' must be balanced by a similar number who respond adversely. If reductions in cholesterol in individuals are regarded as real, and not simply due to random variation, elevations of cholesterol must also be considered real and potentially harmful. It is wrong to count as successes 'responders' and disregard those whose cholesterol moved in the wrong direction.

The efficacy of the step-1 diet has been questioned surprisingly little, based as it is on epidemiological considerations (Steinberg, 1985) and short-term studies (Lewis, 1980). Ahrens (1979, 1985), one of the few to express reservations about current dietary recommendations, predicted a reduction in serum cholesterol of 6% given the adherence expected in ordinary practice. In the event, this projection has proved over-optimistic. The best estimate of cholesterol reduction is 2%, and even the smallest trials had sufficient power to exclude reductions as large as 6%. These small responses occurred despite deployment of resources at least equal to those currently available in ordinary practice. What benefit might be expected from the reductions of serum cholesterol observed in these trials of step-1 diet? Using as a rule of thumb a 2·5% reduction in coronary events for a 1% fall in total cholesterol (Marmot, 1994), a 2% cholesterol fall may translate to a reduction in coronary events of about 5%.

A more rigorous diet would be required to attain any important reduction in serum cholesterol. The step-2 diet has barely been tested, but had a modest effect on total cholesterol and no beneficial effect on HDL:LDL in the only controlled trial to examine it. Dietary change undoubtedly can lower serum cholesterol, as shown by reductions averaging 13% over 1–5 years with rigorous step-3 diets, but these diets have proved unpalatable and are no longer recommended. Step-3 diets are effective and safe, but neither feasible nor tolerable.

The findings for the step-1 diet contrast sharply with assertions in many guidelines and reviews that it will lower serum cholesterol by 10–25% (Shepherd *et al.* 1987; Study Group, European Atherosclerosis Society, 1987; Howard & Brown, 1988; Lewis *et al.* 1989; Thompson, 1989*a*,*b*). Why are perceptions of efficacy so unrealistic? Among the reasons are over-reliance on short-term experiments, controlled studies of rigorous diets in captive populations, and uncontrolled observations. The Oslo study (Hjermann, 1980; Hjermann *et al.* 1981) has understandably been given considerable weight, but with no

recognition that the subjects were highly selected and the diet much more rigorous than the step-1 diet. Evidence from the other controlled trials reviewed here has been ignored, citing instead uncontrolled studies purporting to show efficacy. For example, one study (Reid *et al.* 1984) cited by a Standing Medical Advisory Committee (1990) was held to show efficacy of dietary intervention over 6 years. In this uncontrolled trial serum cholesterol fell from 6·03 to 6·01 mmol/l over 1 year, i.e. a change of 0%. The responses at 6 years (Reid *et al.* 1984) were attained by 'losing' non-responders, a manoeuvre which is inappropriate, as discussed previously. A perception of efficacy is reinforced in everyday practice by regression to the mean, which may produce a cholesterol fall of 5% between two visits without any intervention (Hjermann, 1980; Multiple Risk Factor Intervention Trial Research Group, 1982). This is the likely explanation of larger responses to diet in some uncontrolled trials (Jones *et al.* 1982).

Current guidelines for managing hyperlipidaemia are entirely misleading. Given a mean response to diet of 2%, less than 1% of people with an initial cholesterol concentration higher than 6·5 mmol/l would be expected to attain the target serum cholesterol of 5·2 mmol/l. Doctors and their patients are being boxed into an impossible corner, and the consequences are not difficult to predict. Doctors will have two options: to leave the raised cholesterol concentration uncorrected or prescribe lipid-lowering drugs. As has been pointed out the 'cholesterol numbers' dominate medical consultations (Tunstall-Pedoe, 1989), and widespread use of lipid-lowering agents is the likely outcome. Considering the high prevalence of high cholesterol concentrations in the British population this is an unattractive proposition (Anonymous, 1988). Doctors need to formulate their policy for screening, recognizing that the diet recommended has little impact on serum cholesterol and that screening followed by an ineffective diet may force the use of lipid-lowering drugs.

The central issue with lipid-lowering drugs is the relationship between benefit and risk. Outcome trials of lipid-lowering drugs have shown a significant reduction in non-fatal coronary events, a small reduction in coronary mortality, but a substantial and significant increase in non-coronary mortality. This increase in non-coronary mortality is probably related to the drugs used rather than cholesterol reduction *per se* (Davey Smith *et al.* 1993). Its net effect is to increase total mortality when lipid-lowering drugs are used in subjects at relatively low coronary risk, e.g. for primary prevention. When the risk of coronary mortality is very high the benefit of cholesterol reduction outweighs the adverse effects of drug therapy, and total mortality is reduced by treatment. The crossover point at which benefit exceeds risk is a coronary mortality of 3% per year (Davey Smith *et al.* 1993). Below this level of risk, lipid-lowering drugs do more harm than good; above it the benefit exceeds risk. To put the 3% per year risk of coronary death in context, a middle-aged man without vascular disease who smokes cigarettes, has mild hypertension, and has total cholesterol >6·2 mmol/l has a risk of coronary death of only 0·4% per year (Stamler *et al.* 1986). A man with cardiovascular disease and a serum cholesterol above 6·2 mmol/l has a risk of coronary death of 1·8% per year (Pekkanen *et al.* 1990). Lipid-lowering drugs should be used very rarely for primary prevention, and indeed should not be used routinely for secondary prevention. Their use should be restricted to secondary prevention in patients with cardiovascular disease who have, in addition, an above-average coronary risk. Knowledge of the serum cholesterol is not essential to identify high-risk subjects (Shaper *et al.* 1986).

Brett (1989) has discussed the ethical aspects of dietary intervention when unequivocal

proof of benefit is lacking. He considered such dietary advice ethical provided there was hope of benefit and the diet was harmless. Considering these criteria, little benefit can be expected from step-1 diet used for intervention in individuals; perhaps a 5% reduction in coronary events. The ethics of seeking out healthy individuals, measuring cholesterol, and offering intervention of such limited efficacy needs to be reconsidered. Guidelines for detection and management of raised cholesterol should be revised to incorporate a more realistic estimate of the response to diet.

Other diets discussed such as the 'Mediterranean diet' and the role of antioxidants deserve further study, but their effects if any on coronary events remain to be confirmed. Current guidelines for screening and treating hyperlipidaemia have as their cornerstone a diet which has been proven repeatedly to have extremely limited efficacy, and we should not fall into the same trap again. Advice to the public or doctors on changes in diet should be based on evidence from sound long-term randomized prospective trials, and the measures advised should be feasible, effective and safe.

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