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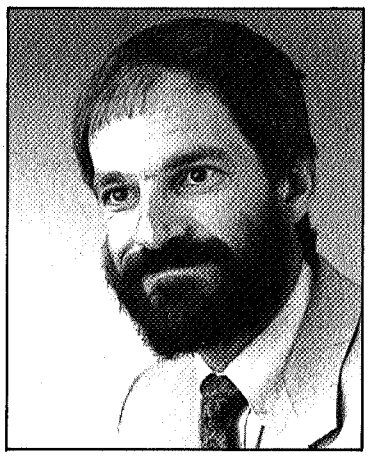
LIPID REVIEW

Dietary Management of the Hyperlipidaemic Patient



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Dietary treatment is necessary in the management of all forms of primary hyperlipidaemia, either as the sole approach or, in a minority of cases, in combination with drug therapy. Lipid-lowering diets have been developed, the nutrient content, palatability and cost of which makes them suitable for lifelong use. In overweight patients, such a diet is combined with restriction of energy intake until a target body weight is attained, while for patients whose plasma lipid response proves inadequate a more rigorous version of the diet may be introduced. These lipid-lowering diets are appropriate for patients with hypercholesterolaemia and for most hypertriglyceridaemic patients. However, rare forms of hypertriglyceridaemia, particularly the chylomicronaemia syndrome ("Type I" hyperlipoproteinaemia) and severe familial hypertriglyceridaemia ("Type V"), may require a different diet, characterized by very low fat content.

A few general points may be made concerning dietary management. The general lipid-lowering diet (either in isocaloric or in weight-reducing form) is similar, in all important respects, to the diet widely recommended by authoritative bodies for general use by populations with high incidence of coronary heart disease [1–3]; as such, it is no more nor less than a healthy eating pattern, designed to help reduce the risk of many common diseases, including CHD. For the individual care of hyperlipidaemic patients dietary instruction is best provided by a professional dietitian, whose skills are necessary to ensure the nutritional adequacy of the diet, to individualize the diet to the patient's taste, energy needs and specific metabolic disorder, and to promote compliance. In an imperfect world, access to trained dietitians is not always possible. It may then be appropriate for general dietary guidelines to be provided by the physician, who should be able to offer qualitative advice to mildly hyperlipidaemic patients. In this situation the physician has an indispensible role in motivating the patient to comply with the diet and to explain the reasons for its use, but if an adequate plasma lipid response is not observed referral to a dietitian becomes mandatory. An isocaloric diet sheet for patients, prepared to assist the physician in providing such guidelines, is featured in this issue.

Nutritional change is seldom attained in a single session of instruction. Several months should be allowed for learning the diet, which involves altering habits and preferences, cooking techniques and food purchasing. Some authorities on behaviour modification advocate stepwise changes in eating pattern, emphasising in turn meat and fish, dairy products and other food groups. Trends in plasma lipid levels can only be discerned from serial measurements and repeated assessment and supplementary counselling will often enhance the plasma lipid response.

Nutrients influencing plasma lipid levels

Plasma lipid levels are influenced by several nutritional factors. The most important single dietary cause of

In next month's issue

"Drug Treatment of Hypercholesterolaemia"

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elevated plasma cholesterol is a high intake of saturated fatty acids with a carbon chain length of 12–16 [4,5]. These are present in meats, dairy products prepared from whole milk, certain vegetable fats such as coconut fat (used in artificial cream and in coffee whiteners) and hydrogenated fats such as hard margarines. Hydrogenation converts *cis*-unsaturated fatty acids into biologically inactive *trans*-fatty acids and saturated fatty acids, potentially reversing the lipid-lowering effect of the *cis*-unsaturated acids. Hydrogenated (hardened) plant oils are widely used for deep-fat frying and for production of margarines, baked goods and convenience foods. The labelling of food products as "containing vegetable fats or oils" can therefore be misleading. Substitution of dietary saturated fats by an increased intake of n-6 polyunsaturated fatty acids (the term refers to the position of the double bonds in the carbon chain), particularly linoleic acid derived from seed oils such as sunflower oil, reduces plasma cholesterol and triglyceride levels by reducing low density and very low density lipoproteins [5]. When only modest amounts of such oils are included in the diet effects on high density lipoprotein-cholesterol (HDL-cholesterol) are usually slight or absent. Plasma cholesterol levels are also reduced when these oils are substituted for dietary carbohydrate [4] and in that circumstance HDL-cholesterol may increase [6].

When embarking on a lipid-lowering diet it is usual to advise a substantial reduction in saturated fat intake, e.g. from 18% of dietary energy to 8–10%, along with a modest supplementation of n-6 polyunsaturated fat, e.g. from 3–5% to 6–10% of dietary energy. Energy balance is maintained, in patients of acceptable body weight, by increasing intake of foods providing complex carbohydrate (legumes and beans, bread, rice, pasta, potatoes).

While the safety of increased polyunsaturated fat use has been questioned, the suggested increase of dietary n-6 polyunsaturated fats undoubtedly enhances the lipid-lowering effect of the diet. Dietary trials of coronary heart disease prevention have included increased use of n-6 polyunsaturates, and have shown significant reductions in coronary disease without significant increases in non-cardiovascular disease [7]. Similarly, the marked increase in the use of such oils by the U.S. population has been accompanied by, and may have contributed to, a demonstrable fall in average plasma cholesterol and a 40% reduction in coronary mortality in recent decades, also without increasing mortality from common forms of cancer [8]. International comparisons show a strong association of breast and colon cancer mortality with per capita consumption of total fat but not with that of polyunsaturated fat. Habitual patterns of fat intake are reflected by the composition of adipose tissue and of plasma phospholipids, which have been studied in patients with coronary heart disease. An inverse relation has repeatedly been shown between coronary disease and the consumption of linoleic acid [9].

Other dietary fatty acids have recently been under scrutiny for their effects on plasma lipid metabolism. The n-3 polyunsaturated fatty acids present in fish oils markedly reduce elevated triglyceride levels when fed at intakes of 15–30 g oil per day [10]. Such a high intake is not achieved by consumption even of fatty fish, but normal intakes of fish such as mackerel or salmon do produce some lowering of plasma triglyceride levels.

In principle, replacement of saturated by n-3 polyunsaturated fatty acids will lower total cholesterol. However, the amount of n-3 polyunsaturated fatty acids that can be provided by normal foodstuffs is negligible when compared with the dietary availability of linoleic acid. Low density lipoprotein (LDL) levels tend to increase when hypertriglyceridaemic patients are treated with n-3 fatty acids [11] and, unlike linoleic acid, consumption of the n-3 fatty acids is not inversely correlated with CHD incidence [9].

The effect on plasma cholesterol of the monounsaturated fatty acid oleic acid has usually been regarded as "neutral", which is to say it has little effect on plasma cholesterol when substituted for carbohydrate [4,12]. However, when used in a western diet, olive oil, the principal natural dietary source of oleic acid, will tend to replace saturated fats such as butter or cooking fats rather than carbohydrates, so that plasma cholesterol will fall in line with the reduced intake of saturated fats. Under specific experimental conditions it has also recently been found to reduce plasma cholesterol when it replaces carbohydrate, leading to levels similar to those produced by linoleic acid [13]. Important though these studies are, it is premature to apply them in clinical practice pending their confirmation and extension. However, it is clear that moderate use of olive oil is entirely compatible with a lipid-lowering diet and is in conformity with the high intakes characteristic of Mediterranean countries in which coronary disease death rates are low. Since animal fats contain oleic acid and saturated fatty acids in somewhat similar amounts, restriction of the latter will decrease oleic acid intake; inclusion of olive oil in a lipid-lowering diet will tend to redress this loss of oleic acid.

Despite occasional controversy, there is abundant evidence that high dietary cholesterol intake increases plasma cholesterol, this increase affecting most lipoprotein classes. The average effect is not a large one, but there is variation of response among normal individuals [14,15]. The hypercholesterolaemic response may be decreased when cholesterol is fed together with polyunsaturated fats. In a recent study on ambulant normal subjects receiving a diet restricted in saturated fat and supplemented with polyunsaturated fat, plasma cholesterol was only slightly affected by changing the intake of eggs from 7 per week to 2 per week [16]. Despite this, restriction of dietary cholesterol probably should be part of a lipid-lowering diet, partly because such a restriction reinforces the restriction of saturated fat intake and partly because dietary cholesterol not only influences plasma levels of LDL-cholesterol but also raises plasma levels of intermediate density lipoprotein. Both of these classes of lipoprotein are believed to be atherogenic [17].

Some, but not all, forms of dietary fibre directly reduce plasma cholesterol levels. Soluble, gel-forming "fibres" such as pectins and gums, present in fruit, vegetables and oats, have a moderate cholesterol lowering effect, while wheat fibre is ineffective. Wholewheat bread and other natural high-fibre foods may, however, provide more satiety and have lower energy density than highly refined cereal products and so help to prevent overeating. Such foods also tend to substitute for foods rich in fat, and may therefore have an indirect effect in lowering plasma cholesterol.

Energy balance has complex effects on plasma lipid metabolism, a positive balance increasing production of very low density lipoprotein (VLDL), and probably of LDL. A *sustained* reduction of weight in overweight hyperlipidaemic persons often leads to a lasting reduction of triglyceride and cholesterol levels and may elevate initially low HDL levels; however, even minor subsequent weight gain in such patients may lead to partial relapse of plasma lipid levels.

Very importantly, most or all of the effects of individual nutrients on cholesterol and triglyceride levels are additive [18], permitting their combination into a therapeutic diet of considerable effectiveness. Hence, it is unnecessary to impose large changes in the intakes of individual nutrients, since moderate changes in each have additive effects on lipoprotein metabolism. Accordingly, the changes in conventional eating patterns may be kept to a minimum and need be no burden to the patient. In one long-term study on ambulant hyperlipidaemic patients a mean plasma cholesterol reduction of 22% was achieved [19]. Figure 1 shows a typical example of the effect of such dietary changes in a young man with mildly elevated serum lipids.

The nutrient composition of a standard lipid-lowering diet is shown in Table 1. In some patients in whom this diet fails to achieve an acceptable reduction in plasma cholesterol, a more stringent version of the diet, also shown in Table 1, is sometimes effective. It should be noted that the dietary changes listed have the potential to lessen coronary heart disease risk through mechanisms unrelated to plasma lipid concentrations. An increase in the ratio of polyunsaturated fatty acids (of the n-3 and n-6 series) to saturated fatty acids influences haemostatic mechanisms, tending to lessen thrombotic tendency; in part this is mediated by effects on prostaglandin production. Blood pressure also tends to be lowered by such diets, even in the absence of weight loss. Very importantly, obesity may be brought under control by dietary changes.

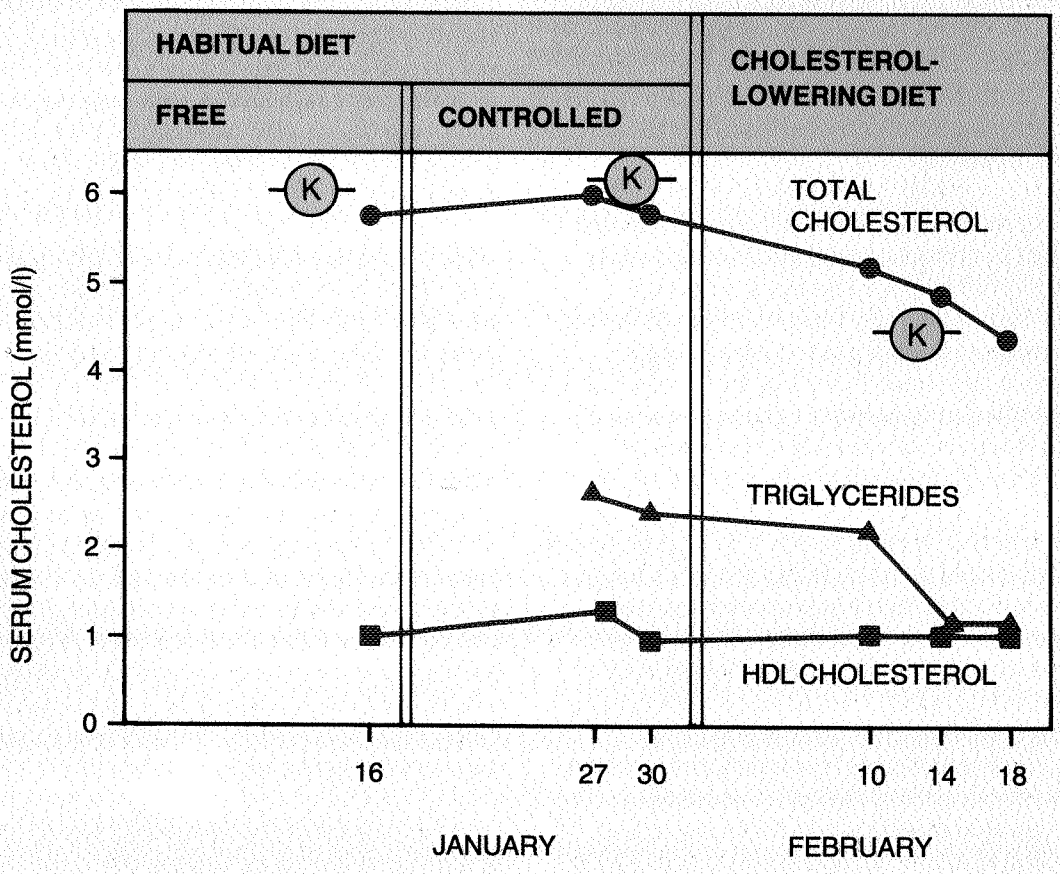

Figure 1. Time course of serum total and HDL cholesterol and triglycerides in a 35-year-old man when eating his habitual diet – either free-living ("FREE") or under the control of a dietician ("CONTROLLED") – and when following prescribed dietary guidelines. "-(K)-" indicates the serum cholesterol levels predicted by Keys' formula for the diet eaten [4,5].

	Standard diet for hypercholesterolaemia and endogenous hyper-triglyceridaemia	Diet for resistant hyper-cholesterolaemia	Diet for the chylomicronaemia syndrome
Protein, % total food energy	12	15	20
Carbohydrate, % total food energy	60	64	60
Saturated fatty acids, % total food energy	10	7	6
Monounsaturated fatty acids, % total food energy	10	7	6
Polyunsaturated fatty acids, % total food energy	8	7	4
Fibre, g/day * +	35	45	35
Cholesterol, mg/day +	<250	<150	<250
Medium chain triglyceride, %			4

+ At an energy intake of 10 MJ (2400) kcal) per day; use proportionally more or less if energy intake differs.
* At least 50% of the fibre to be provided by vegetables, legumes, fruits and oats.

Table 1. Nutrient composition of isocaloric lipid-lowering diets

The high risk of CHD in obesity appears to be due in part to its association with hyperlipidaemia and with low levels of HDL-cholesterol, with glucose intolerance and with hypertension. These risk factors are usually ameliorated by weight reduction. In addition, obesity, especially of truncal distribution, is a risk factor in its own right [20]. Unfortunately, obesity is highly resistant to treatment and perseverance on the part of the doctor and dietitian is required.

In many patients, even moderate degrees of weight reduction result in reductions of plasma lipid levels. However, the preferred goal of weight reducing schedules is to achieve a body weight in the middle of the desirable range; the body mass index (weight/height^2) is then in the range 22–23 kg/m^2. As well as the direct benefits of treating obesity, responsiveness to lipid-lowering drugs is enhanced by treatment of overweight.

The desirable rate of weight loss is 0.5–1 kg per week. To help commit the patient to a programme of weight control it is often helpful for the doctor and patient jointly to agree to a target body weight. Exercise appropriate to the age, cardiorespiratory status and level of fitness of the patient should be undertaken on several days each week. Crash diets and special preparations are of little value, because the weight lost is easily regained when the patient resumes his usual diet. Of much greater benefit is a modest, sustained reduction in caloric intake that provides retraining in eating habits for life.

Practical aspects of dietary treatment of hyperlipidaemia

The lipid-lowering diet is recommended for indefinite use; it may be reduced in energy content in the overweight patient. It includes several components:

- Increased consumption of foods providing complex carbohydrate and soluble forms of fibre; these include cereal products (bread, pasta, oats-based breakfast cereals), root vegetables such as potatoes, legumes and leafy vegetables, rice and fruit. A doubling of total fibre and a three-fold increase in soluble fibre intake is desirable.

- Decreased use of foods with a high content of saturated fatty acids; these usually contain palmitic acid (which is saturated) and oleic acid (monounsaturated). Intake of saturated fatty acids needs to be approximately halved and should provide less than 10% of food energy, so that total intake of fat decreases from 40% to < 30% of energy. If the ensuing reduction of plasma cholesterol is inadequate, total fat may subsequently be reduced to 20–25% of food energy and that of saturated fatty acids to 5–7%; in some patients this will enhance the reduction of plasma cholesterol. Saturated fatty acids are substantial components of butter, hard margarine, cream, whole milk, full fat cheeses, red meats except for the very lean cuts now becoming available, sausages and processed meats, baked goods, many convenience foods, and shortening. Hence the foods to be restricted may be of vegetable or animal origin.

- A lower intake of cholesterol (250 mg/day) which may be further reduced to 100 mg/day if the initial response is inadequate. Reduced intake of animal foods, intended to restrict intake of saturated fat, will also decrease cholesterol intake; other cholesterol-containing foods that need to be limited are egg yolk, liver and other offal. Complete elimination of eggs and liver is undesirable, however, as they are valuable sources of vitamins and other nutrients.

- Substitution of skimmed and/or low-fat milk and their products for whole milk and high-fat milk products. Milk fat, present in whole milk and yoghurt, cheese, butter and cream, is more hypercholesterolaemic than other animal fats because it is very low in linoleic acid (1–2%) and very high in cholesterol (270 mg/100 g, as opposed to 60–80 mg/100 g in lard, beef fat and tallow). As milk fat provides little in the way of essential nutrients there is no hazard in reducing its intake.

- A greater use of all types of fish, chicken, turkey, veal and game, all of which are low in saturated fatty acids. The moderate use of very lean red meat is allowable. These, together with legumes such as beans and lentils, and low-fat milk products, produce a satisfactory protein intake. Fish contain n-3 polyunsaturated fatty acids that reduce plasma triglyceride. Fish is also a good source of vitamin D and iodine, the intake of which is marginal in many people.

- Introduction of margarines based on unhydrogenated polyunsaturated oils (sunflower or corn oils) as spreads and use of such oils, and/or olive oil, for cooking. The optimal intakes of polyunsaturated fatty acids (particularly linoleic acid) and of fish oil preparations or of oils providing monounsaturated fatty acids, such as olive oil, have yet to be determined. A widely held view is that the ratio of polyunsaturated fatty acids to saturated fatty acids, should increase towards, but should not exceed, 1.0.

Miscellaneous foods

There is no need to deny the moderate use of alcoholic drinks to a patient if his triglycerides are normal. However, alcohol is an important source of calories and many people under-report its use. Sugar as such has no major influence on serum lipids, but it too is a major source of calories. In addition, many sweet foods are also high in saturated fat and cholesterol and low in fibre. A cholesterol-elevating effect of coffee has been reported but the data are too preliminary for clinical application. There is no good evidence that lecithin preparations, gamma linolenic acid, garlic, vitamin E or other vitamin preparations are of value in the treatment of hyperlipidaemia.

A substantial reduction in serum cholesterol (15–25%) and triglyceride (20–40%) can be attained by the diet described, especially when body weight is in, or can be reduced towards, the desirable range. There is some individual variation in response, and for patients with familial hypercholesterolaemia diet is inadequate as the sole therapeutic approach. However, dietary treatment will usually suffice in patients with plasma cholesterol up to 7–7.5 mmol/l (270–289.5 mg/dl) or with mild hypertriglyceridaemia (< 6 mmol/l (< 531 m/dl)).

A rare disorder, the chylomicronaemia syndrome, causes gross hypertriglyceridaemia, which is dealt with by severe reduction (to 10–25% of dietary energy) of the dietary intake of all natural fats. Moderate use of medium chain triglyceride is permitted.

Summary

The preferred approach to management of hyperlipidaemia is dietary modification and in a majority of patients this is sufficient in itself. Dietary manipulation is also a necessary component of the management of patients with disorders requiring drug treatment. The fat-modified, high-fibre diet, with or without initial weight reduction, is thus the mainstay of lipid-lowering therapy. A very low fat diet is used to avert pancreatitis in patients with the chylomicronaemia syndrome.

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ANNOTATION

Low Serum Cholesterol Levels and Longevity

A recent report has suggested that low levels of serum cholesterol are associated with increased longevity, at least up to age 50 [1]. This is congruent with international mortality statistics, which reveal greater life expectancies in countries where the dietary intake of saturated fat, and consequently the mean serum cholesterol level, is low [2,3].

The health implications of low serum cholesterol levels have been, with justification, the subject of close scrutiny. The underlying issue is the definition of levels of plasma cholesterol levels requiring therapy and of the target levels to which plasma cholesterol should be reduced by such treatment [4]. Is the desirable level as low as possible (within the realm of therapeutic feasibility)? Or is there an optimal range of serum cholesterol, such that an increased risk of adverse effects exists in those with levels below (or above) this range? Epidemiology, clinical trials and clinical observations all provide information relevant to these issues, and recent longitudinal epidemiological studies have offered important clarification.

Belief in the health benefits of reduced plasma cholesterol has not been universal. Despite a reassuring analysis of earlier trials [5], concern arose at the outcome of the WHO coronary heart disease (CHD) primary prevention trial [6]. Use of the lipid-lowering agent clofibrate was associated with decreased CHD incidence, but also with an increase in total mortality due to remarkably heterogeneous causes. However, the non-specificity of the increase in non-cardiovascular deaths, and the variation in relative frequency of these causes at different follow-up intervals [7], tended to argue against a direct pathogenic role of cholesterol-lowering. Further, another large-scale clofibrate trial revealed no excess of cancer deaths [8]. Despite these inconsistencies, some anxiety as to possible untoward effects of cholesterol reduction persisted.

About one-half of the longitudinal observational studies reviewed up to 1982 have also suggested that cancer mortality, notably death from carcinoma of the colon, occurs more frequently in men with serum cholesterol levels in the lowest quintile, typically with levels below 4.7 mmol/l (180 mg/dl) [9,10]. When data from the largest such studies were pooled, representing a collective experience of more than 60,000 subjects, a similar conclusion was reached for cancers of the colon, cancer of the lung and for overall cancer mortality [11]. However, as in the original study by Rose and Shipley [12], a striking conclusion emerged when the pooled data was examined in detail. This was that the increased cancer rates in subjects with the lowest cholesterol levels were confined to deaths occurring within a short period after the lipid measurement. Cancer deaths occurring later were unrelated to serum cholesterol levels. The investigators concluded that preclinical cancer, present at the time of entry into the study, led to a fall in serum cholesterol, so explaining the apparent inverse relationship. A similar conclusion was recently reported from the largest longitudinal study - 361,662 men screened for entry into the Multiple Risk Factor Intervention Trial (MRFIT) [13]. The mean follow-up period was seven years. The death rate from cancer was greatest in subjects in the lowest decile of serum cholesterol (<4.34 mmol/l (168 mg/dl)). No association between serum cholesterol and cancer mortality was established in the remaining nine deciles; this absence of a "dose-response" relationship has been a feature of such studies. The increased death rate from cancer in patients in the lowest decile of cholesterol distribution was maximum during the first two years of follow-up and then declined progressively at longer time intervals. A further feature of this study was the availability of serial cholesterol measurements on 150 of the MRFIT trial participants who died of cancer, documenting a fall of serum cholesterol during a period of at least two years before death from malignant disease.

Among other recent investigations of this relationship, three may be mentioned. One smaller study [14], in which 12,488 men and women were followed for 10 years, was at variance with the two larger studies summarised above [11,13]; an inverse relation between serum cholesterol and cancer deaths remained evident in men, but not in women, when the interval between entry examination and death exceeded six years. Other, larger, investigations have recently provided somewhat different results. In one, based on 160,135 men and women examined in the Kaiser Permanente Medical Care Program, cancer incidence was increased in those with cholesterol levels in the lowest quintile only during the first two years of follow-up [15]. Site-specific data were reported; of 21 cancers, only two – a cervical cancer and a lymphoma in a man – showed this inverse relation.