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Dietary Treatment to prevent cardiovascular disease PART II: Effects on hyperlipidemia

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Patterns of cardiovascular disease (CVD) worldwide, epidemiology in the US, and clinical studies of diet, leave no doubt that high rates of coronary heart disease (CHD) and stroke are caused by poor nutrition (ie, too much food and too many harmful foods), as well as the erosion of an active lifestyle. In the Mediterranean countries and in Japan, where traditional lifestyles are maintained, CHD is far lower than in the urban areas of the Mediterranean or in northern Europe and the US (Figure 1).¹ Concerned about CVD? The fact is – we are giving it to ourselves! The first part of this 2-part series, presented in the August issue of *Cardiology Rounds*, examined the role of diet and sodium restriction in cardiovascular disease. This second part examines the issue of diet and its effect on hyperlipidemia.

Despite the tremendous success of drug therapy for hyperlipidemia, national guidelines specify dietary therapy as the first step for primary prevention, and for dietary modifications to be employed, concomitantly with drugs, for secondary prevention. The effects of dietary treatment to reduce low-density lipoprotein (LDL) cholesterol are at least additive to the effects of pharmacological treatment. Weight loss accentuates the dietary effects, particularly raising high-density lipoprotein (HDL) cholesterol and lowering triglycerides (TG). Diet and weight loss may reduce or even eliminate the need for drug therapy, depending on the degree of adherence and intrinsic individual biological responsiveness.

Effects of diet on blood lipids.

Dietary fats that raise the blood cholesterol are saturated fats, trans-unsaturated fats from partially hydrogenated vegetable oils, and cholesterol itself. All scientifically-based diet therapies advocate reducing the intake of these fats. In this context, various leaders in the field recommend both low-fat high-carbohydrate diets, and high-unsaturated fat diets.

Low-fat diets

Low-fat diets reduce LDL cholesterol because saturated fat, trans-unsaturated fats, and cholesterol are all reduced and replaced with carbohydrate.² Many individual studies, as well as meta-analyses, show that this approach modestly reduces LDL cholesterol by 5%-10%. Not only are saturated fats reduced, but monounsaturated and polyunsaturated fats are also reduced.



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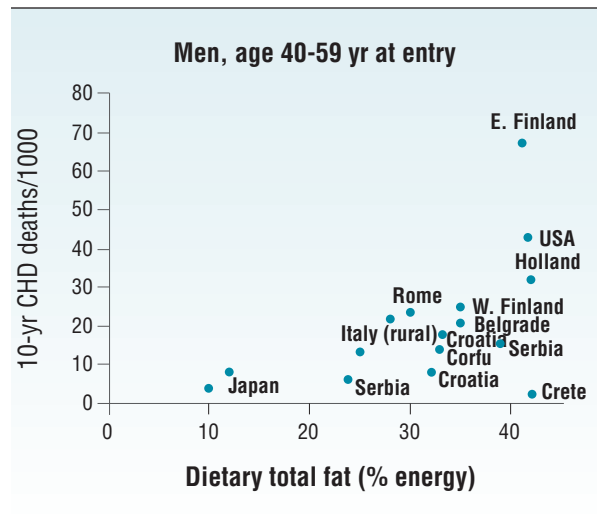
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Figure 1: Seven-countries study: Dietary total fat and 10-year CHD death rate, 1958-1974¹



Extremely low-fat diets can be deficient in essential fatty acids, and advocates such as Ornish, recommend a supplement of polyunsaturated oil capsules. Long-term adherence is also a challenge with low-fat diets.

Reducing saturated fat intake reduces LDL cholesterol, but it also reduces HDL cholesterol by the same percentage, so that the LDL/HDL ratio does not generally fall.² Moreover, triglycerides increase as carbohydrate increases,² particularly in patients with hypertriglyceridemia. Replacement of saturated fat with carbohydrate generally results in an 8% and 10% reduction in LDL and HDL, respectively, and as mentioned, an increase in triglycerides (Table 1).

In summary, the effects of low-fat diets on the lipid profile are:

- Reduction of total cholesterol concentration
- Reduction of LDL cholesterol concentration
- Reduction of HDL cholesterol concentration
- No effect on the LDL/HDL cholesterol ratio
- Increase in triglycerides

Moderate unsaturated fat diets

Many leaders in the CVD prevention field recommend an alternative approach to diet that increases unsaturated fats rather than carbohydrates to replace saturated fat. The total fat intake is unchanged or even increased. Saturated fat is replaced with unsaturated fats from unhydrogenated liquid vegetable oils, (eg, canola, olive, sunflower, safflower, peanut, soybean), or from nuts. In lowering LDL levels, unsaturated fatty acids, either monounsaturated or

Table 1: Dietary fats and blood cholesterol²
Replacement of saturated fat (10% of total daily calories) with carbohydrate or unsaturated fat

	LDL-C	HDL-C	LDL/HDL	TG
CARB	- 8%	-10%	+2%	+14%
MONO	- 10%	-3%	- 6%	+2%
POLY	- 12%	-4%	- 8%	-2%

Monounsaturated (mono) oils: Olive, Canola, Nuts
Polyunsaturated (poly) oils: Corn, Soy, Sunflower, Safflower

polyunsaturated have slightly more effect than carbohydrates.²

The substitution of one type of fat for another has little effect on HDL or triglycerides. Thus, in contrast to low-fat diets, high-unsaturated fat diets do not lower HDL or raise triglycerides, and the LDL to HDL cholesterol ratio has a more favorable decrease (Table 1).

In summary, the effects of high-unsaturated fat diets on the lipid profile are:

- Reduction of total cholesterol concentration
- Reduction of LDL cholesterol concentration
- Little or no effect on HDL cholesterol concentration
- Reduction in the LDL to HDL cholesterol ratio
- Little or no effect on triglycerides

Choosing between a low-fat or moderate-unsaturated fat diet

All those working in this field agree that reducing LDL cholesterol is good. However, not all experts believe that the effect of low-fat diets on HDL and triglycerides is harmful. Some refer to populations that have low coronary disease rates where they have not only low LDL concentrations, but also low HDL concentrations. However, such populations also have regular physical activity, a lack of obesity, and low rates of diabetes. These factors could counteract any adverse effect of low HDL. Finally, advocates of the low-fat diet state that high-unsaturated fat diets cause weight gain. This topic will be addressed subsequently.

Clinical trials and epidemiological evidence on dietary fat and carbohydrates

Randomized trials definitively show the benefits of polyunsaturated fats. In the 1960s and 1970s, standard

Table 2: Randomized clinical trials of polyunsaturated vegetable oils

	N	Yrs	% Fat	Cholesterol	CVD
Finnish Hospital	676	6	34	-15%	-43%*
Oslo	412	5	39	-14%	-25%*
MRC Soy Oil	393	4	46	-15%	-12%
Los Angeles (Dayton)	846	8	39	-13%	-34%*

* P<0.05

dietary therapy used polyunsaturated vegetable oil to lower cholesterol. Hypercholesterolemic patients would still shot glasses of corn oil. Three³⁻⁵ out of four⁶ randomized trials showed significant benefits on coronary rates (Table 2). In addition to lowering LDL, polyunsaturated fats may reduce the vascular inflammatory response. These fats may also limit the propensity of LDL particles to bind to vascular cells and deposit their cholesterol in the vascular intima. In monkeys, consumption of polyunsaturated fats from vegetable oils actually caused regression of coronary atherosclerosis.⁷ Polyunsaturated fats also have anti-arrhythmic actions.⁸ Thus, there is much evidence for the use of polyunsaturated oils to replace saturated fats in order to prevent coronary disease.

Monounsaturated fat has a less direct relationship to coronary disease prevention than polyunsaturated fat. Epidemiology studies show modest reductions of CHD with monounsaturated fat that are of borderline statistical significance.⁹ There has never been a clinical trial that specifically increased monounsaturated fats to prevent CHD. However, monounsaturated fats decrease LDL and preserve HDL and TG levels as much as polyunsaturated fats. Monounsaturated oils, particularly olive oil, have been an integral part of the centuries-old traditional Mediterranean Diet, which is associated with very low coronary disease rates (Figure 1).¹ Finally, alpha-linolenic acid, a polyunsaturated fat in soybean oil, rapeseed (“Canola”) oil, and some vegetable products, is strongly protective against CHD in epidemiological studies. There are reasons then, to advocate an increased intake of unsaturated oils from a variety of sources, both monounsaturated and polyunsaturated. On the other hand, trans-fatty acids, present in many margarines and shortenings in the United States and ubiquitous in bread, baked goods, and fried foods, can raise LDL and lower HDL, and have been associated with increased coronary risk.⁹

Table 3: Clinical trials of fish oil after myocardial infarction

<ul style="list-style-type: none"> • GISSI (<i>Lancet</i> 1999;354:447) <ul style="list-style-type: none"> – 1 g/d n-3 PUFA for 3.5 years – 5666 fish oil, 5658 control – CVD Death reduced by 30% • DART (<i>Burr et al. Lancet</i> 1989;ii:757) <ul style="list-style-type: none"> – 1015 fish oil, 1015 control – 0.3 g/d n-3 PUFA for 2 years – IHD death reduced by 33% • Non-fatal CVD <i>not</i> reduced

PUFA = polyunsaturated fatty acids

Fish oil to prevent fatal CHD (Table 3)

The Diet and Reinfarction Trial (DART) tested the effect of an increased intake of fatty fish or fish oil (1.5 g/d) for 2 years in 2033 Welsh men who had had an acute myocardial infarction.¹⁰ This small amount of fatty fish or fish oil significantly reduced total and coronary mortality. Nonfatal myocardial infarction, however, was not affected significantly. These results have recently been reinforced by the GISSI Prevenzione trial, which tested 1 g/d of n-3(omega-3) polyunsaturated fatty acids in 11,324 Italian patients surviving a recent myocardial infarction.¹¹ In both trials, the death rate began to lessen in the fish oil group as early as 3 months after treatment was started. These benefits of fish oil could be from several actions, including the reduction of triglycerides and blood pressure, and a rise in the threshold for cardiac arrhythmias. As a result, it is recommended that patients who have CHD take fish oil capsules (2 per day).

Mediterranean diet to prevent cardiovascular disease

The Lyon Heart Study¹² was a randomized trial in men with MI using a diet that emphasized major aspects of the traditional diet of Crete and other Mediterranean regions.¹ The diet was high in monounsaturated fats, omega-3 polyunsaturated fatty acids, and vegetables and fruits. The Mediterranean diet significantly reduced total mortality, coronary death, and myocardial infarction. The trial of 605 patients was stopped prematurely after only 27 months because of the clear benefits.

In summary, epidemiology and clinical trials indicate:

- Replacing saturated fat with polyunsaturated fatty acids is associated with a reduced risk of coronary disease,

and a lower incidence of cardiovascular disease in randomized trials.

- No randomized trial of a low-fat diet showed a reduction in coronary disease, although no trial has been adequate in design or execution to address this issue.

- The Mediterranean diet reduced death after acute myocardial infarction

Type of carbohydrate

The usual mix of carbohydrates in the Western diet contains many refined polysaccharides such as those in bread and baked goods, as well as sugars in juices and soft drinks. These foods have a high glycemic index, causing glucose and insulin to rise substantially. Other types of carbohydrates that are found in whole grains and vegetables have a lower glycemic index because the digestion and absorption of the glucose is slow. These carbohydrates produce less of a rise in blood glucose and hence insulin. The low glycemic index of grains and vegetables is partially explained by the fiber content of these foods, but also by the intrinsic digestibility of the food. These foods cause less of a rise in plasma triglycerides than the more commonly eaten higher glycemic index carbohydrates. Therefore, some of the concerns about a low-fat diet can be set aside if a patient truly eats low glycemic index foods rather than the ubiquitous low-fat foods that all too often are a major part of low-fat diets.

Dietary effects on weight loss

The progressive increase in overweight and obesity in the US and worldwide is a major cause of concern due to the links with diabetes, hyperlipidemia, hypertension, and cardiovascular disease. Control of hyperlipidemia and hypertension is markedly facilitated by weight loss (see Part I in the August issue of *Cardiology Rounds*). Physicians often experience difficulty with patients in achieving weight loss, and more importantly, in the maintenance of early success. A common situation is for a moderately overweight patient — for example with 30 pounds of excess “paunch” — losing half the extra weight in 3 months, but then regaining it all back after a year.

Table 4: Weight loss and participation on moderate fat vs low fat energy restricted diets¹³

	Body weight or weight loss (pounds)	
	Moderate fat	Low fat
Baseline	198	195
6 months	-11	-11
12 months	-9***	+6(ns)

*** P<0.001

The conventional diet for weight loss is low in fat, which has a rational basis since fat is energy dense compared to carbohydrate. We recently published the results of our trial on alternative dietary approaches to weight loss.¹³ This trial found that a moderate-fat diet, based on the diets of southern Europe and the Mediterranean, allowed for a greater variety of foods that are considered very appetizing compared with a more bland, low-fat diet, and had better long-term success. In this study of 101 overweight men and women, half were instructed to eat a low-fat diet (20% calories from fat) and half to eat a moderate-fat diet (35% calories from fat, mostly monounsaturated fats from peanut butter, nuts, olive and canola oils). After 18 months, only 1 in 5 study participants continued with the low-fat diet, while more than half continued with the moderate-fat diet. Both groups lost an average of 11 pounds in the first 6 months. However, the moderate-fat group maintained significant weight loss for 18 months, whereas the low-fat group actually had a net weight gain (Table 4). After 2 and a half years, the moderate-fat group still maintained this weight reduction. Surprisingly, those on the moderate-fat diet increased their consumption of vegetables and fiber, compared to the low-fat group.

The success of a moderate-fat, energy-restricted diet can be attributed to the fact that patients can include favorite foods if they carefully watch portion sizes. For example, they can use full-fat salad dressings, nuts for snacks, and sautéed vegetables and meats.

**Figure 2A: Primary prevention of CVD:
5 attributes to define low-risk¹⁵**

1. Diet in upper 40% of cohort
 Good fat: Low saturated and trans fat, high poly-unsaturated fat, high fish oil
 Good carbohydrates: Low glycemic load, high fiber (whole grains)
 High folate (vegetables, fruit)
2. Not currently smoking
3. Moderate alcoholic beverage drinking
 1 drink every other day to daily
4. Regular Exercise
 1/2 hour daily (e.g. 2 miles/hour walking)
5. Body mass index <25 kg/M² (optimal <21 kg/M²)

**Figure 2B: Primary prevention of CVD:
5 attributes to define low-risk¹⁵**

- Three low-risk attributes:
 Good diet, no smoking, regular exercise
 13% of nurses,
 51% of coronary events and strokes avoided
- Four low-risk attributes:
 Good diet, no smoking, regular exercise, BMI <25
 7% of nurses, 60% of events avoided
- Five low-risk attributes:
 Above, plus moderate alcohol
 3% of nurses, 74% CVD events, 82% coronary events in the population avoided

The overall effect of diet and lifestyle

With full adherence, diet and exercise have a very strong potential for major improvements in risk factors, ie, dyslipidemia, high blood pressure, diabetes, and obesity. For example, my first research project, in strict vegetarians in Boston in the early 1970s, showed very low cholesterol and blood pressure and near absence of overweight problems.¹⁴ However, a more realistic approach is to simultaneously target more modest changes in several aspects of lifestyle. Together, these adjustments would be projected to reduce CHD markedly,¹⁵ even if individual risk factors would

be expected to change only mildly (Figures 2A and 2B).

Dietary guidelines could also be improved in order to be easily understood and to emphasize healthy dietary patterns. Such examples as the Mediterranean and Latin American dietary pyramids, designed by faculty in the Department of Nutrition, Harvard School of Public Health, and the nonprofit Oldways Preservation and Exchange Trust of Boston, among others, were designed with these goals in mind (Figures 3A and 3B).

Figure 3A: The traditional healthy Mediterranean Diet Pyramid

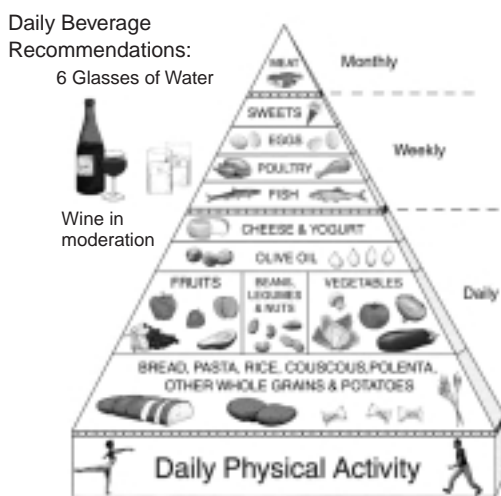


Figure 3B: The traditional healthy Latin American Diet Pyramid



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His research program is a combination of laboratory research on human lipoprotein metabolism, clinical trials in nutrition, and drug therapy in cardiovascular disease. Dr. Sacks is the Chair of the Steering Committee for the recently completed DASH-Sodium trial. This multi-center NHLBI trial studied the effect of dietary patterns and salt intake on blood pressure in persons with mild hypertension or high-normal blood pressure. Dr. Sacks was the Principal Investigator of the Cholesterol and Recurrent Events trial (CARE) that found that pravastatin treatment reduced coronary events and stroke in patients with average cholesterol concentrations.

Dr. Sacks is active in national and international committees and conferences in nutrition and health guidelines. He is member of the American Heart Association Nutrition Committee, the policy making group for nutrition at the AHA. He recently chaired European-American consensus conferences on dietary fat and health. He was a member for 7 years of the Nutrition Study Section, the grant review committee on nutrition for the NIH.

Announcement

We are pleased to announce that Harvard Medical School Department of Continuing Education and the Cardiovascular Division of the Department of Medicine, Brigham and Women's Hospital will provide AMA category I credit beginning with this issue. For those interested, please see the enclosure.

Dr. Sacks has no disclosures to announce related to this program.

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