

Comparison of the effect of dietary fat restriction with that of energy restriction on human lipid metabolism¹⁻³

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ABSTRACT

Background: Dietary fat and energy have been implicated as factors controlling circulating total and LDL-cholesterol concentrations. Whether these factors work independently or synergistically in regulating human cholesterol metabolism remains to be fully elucidated.

Objective: The objective was to determine whether the effects of fat restriction on circulating lipid concentrations and synthesis differ from those of energy restriction in hypercholesterolemic subjects fed controlled diets.

Design: Eleven men (LDL > 3.6 mmol/L) participated in a randomized crossover study. Subjects consumed 4 prepared diets, each for 4 wk and separated by 6 wk, that contained either typical amounts of fat and energy (TF), low amounts of fat but adequate energy (LF), low amounts of fat and energy through carbohydrate restriction (LFE), or typical amounts of fat and low energy through carbohydrate restriction (LE).

Results: Body weights declined ($P < 0.001$) after the LE and LFE diets. Total cholesterol concentrations were not significantly different between the diets. LDL cholesterol was lower ($P < 0.05$) after the LF and LFE diets (8.2% and 8.0%, respectively) than after the TF diet. The LE diet increased HDL cholesterol (46.8%) and decreased triacylglycerols (22.7%), whereas the LF diet increased triacylglycerols (23.6%), relative to the TF diet. LDL:HDL decreased after the LE and LFE diets ($P < 0.05$). Cholesterol fractional synthesis rates after the LF, LE, and LFE diets were lower (35.2%, 27.7%, and 25.5%, respectively; $P < 0.05$) relative to the TF diet.

Conclusion: Reductions in both dietary fat and energy may modify LDL cholesterol by lowering cholesterol biosynthesis; however, the increase in HDL cholesterol and the suppression of triacylglycerol concentrations and LDL:HDL suggests that favorable plasma lipid profiles were also achieved through energy restriction alone. *Am J Clin Nutr* 2001;73:262-7.

KEY WORDS Energy restriction, fat, cholesterol, biosynthesis, lipoprotein, weight loss, men

INTRODUCTION

Dietary fat has been strongly implicated as a factor contributing to elevated circulating total and LDL-cholesterol concentrations. In population studies, countries with lower fat intakes have lower plasma lipid concentrations and lower rates of heart disease than do countries with higher fat intakes (1). The current consensus calls

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for reductions in consumption of both total (2) and saturated (2-5) fat. The current recommendations of the National Cholesterol Education Panel call for stepwise reductions in fat intake proportional to the desired extent of cholesterol lowering for a given individual (2). Most recommendations suggest replacement of dietary fat with complex carbohydrates (2, 5), which are not only nutrient dense but also enhance intakes of other potential cholesterol-lowering agents, including fiber, saponins, and phytosterols (6, 7). However, replacement of dietary fat with complex carbohydrates results in decreased energy intakes unless more food is consumed to compensate for the differences in energy density. Such energy compensation does not typically occur. Indeed, in experimental settings in which very-low-fat diets are consumed, not only do energy intakes and body weights decrease (8, 9), but circulating lipid concentrations and the severity of atherogenic lesions also decline (10, 11). Moreover, in cultures reporting lower fat intakes and decreased rates of heart disease, energy intakes and obesity rates are commensurately low (1, 12). It is unclear whether the mechanism by which consumption of a low-fat diet reduces circulating lipid concentrations is the substitution of fat with carbohydrate or the consumption of a less energy-dense diet, which provides less energy.

This issue was addressed in part in a study that examined the influence of a low-fat, weight-maintenance diet and a low-fat, low-energy diet on plasma lipid profiles (13). In mildly hypercholesterolemic subjects fed baseline (typical amounts of fat and energy), low-fat, and low-fat, low-energy diets, plasma lipid concentrations decreased only in those who consumed the low-fat, low-energy diet, which resulted in weight loss (13). These data indicate that energy restriction is an important determinant of circulating cholesterol concentrations. However, both fat and cholesterol intakes were lower with the low-fat, low-energy diet than with the low-fat, weight-maintenance diet; therefore, it is

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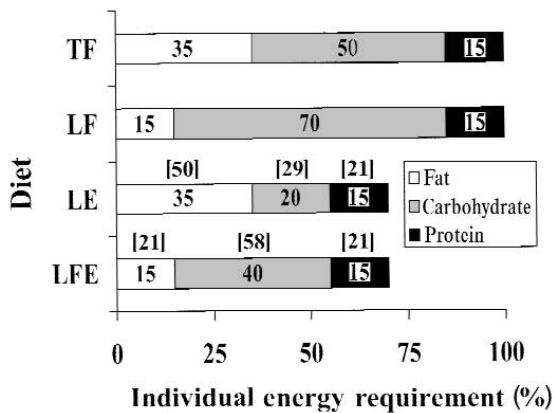


FIGURE 1. Weight-maintenance energy requirements of fat, carbohydrate, and protein with the 4 diets. Values in brackets are percentages of energy delivered. Diets: TF, typical fat and energy contents; LF, low fat and adequate energy contents; LE, typical fat and low energy contents as a result of carbohydrate restriction; LFE, low fat and low energy contents as a result of carbohydrate restriction.

difficult to ascertain whether the cholesterol-lowering advantage of weight loss with a low-fat diet is due to a reduction in fat or to a reduction in energy.

Therefore, the present study was designed to evaluate whether the effects of energy restriction are distinct from those of reduced-fat, reduced-cholesterol intakes in their capacity to modify circulating lipid concentrations and cholesterol biosynthesis in hyperlipidemic subjects. The goal was accomplished by using a dietary design in which equal quantities of fat were consumed but in which energy intakes were changed by modifications in carbohydrate intakes.

SUBJECTS AND METHODS

Subjects

Healthy nonobese men aged 40–60 y ($\bar{x} \pm SD$: 51.5 ± 2 y) were screened for circulating fasting LDL-cholesterol and triacylglycerol concentrations (>3.6 and 1.7 – 3.4 mmol/L, respectively). The subjects selected for the study reported that at least one immediate family member had heart disease. Only subjects with a body fat content between 16% and 30%, assessed by using bioelectrical impedance analysis, were considered eligible for study. All procedures were approved by the Ethical Review Committee of McGill University and all subjects provided informed consent.

Diets

Subjects consumed each of 4 separate diets according to a randomized crossover design. Diets contained 1) typical amounts of fat (35% of weight-maintenance energy requirements) and adequate amounts of energy relative to individual requirements [typical fat and energy; TF (control)], 2) low amounts of fat (15% of weight-maintenance energy requirements, replaced by carbohydrate) and adequate amounts of energy relative to individual requirements (low fat; LF), 3) low amounts of fat (15% of weight-maintenance energy requirements replaced by carbohydrate) and reduced amounts of energy (30% restriction relative to individual requirement) achieved through reduction of the carbohydrate content (low fat and low energy; LFE), and 4) typical amounts of fat (35% of weight-maintenance energy requirements) but reduced

(30% restriction relative to individual requirement) amounts of energy achieved through reduction of the carbohydrate content (low energy; LE). Dietary periods were separated by washout intervals of 6 wk. The LF and LFE diets provided the same amount of all nutrients, except energy, from purified carbohydrate. Removal of 30% of energy from carbohydrate in the LFE and LE diets was calculated to result in a net weight loss of 0.65 kg/wk in an individual consuming 11.7 MJ/d. All diets were formulated to contain 15% of weight-maintenance energy requirements as protein. With this design, intakes of all macro- and micronutrients, except for carbohydrate, were maintained in the LF and LFE diets (Figure 1). The TF diet contained 31.4%, 40%, and 28.6% of total fat as saturated, monounsaturated, and polyunsaturated fatty acids as a blend of butter and corn oil-, olive oil-, and canola oil-based margarines, respectively (Table 1). Other diets contained the same ratio of fatty acids as did the TF diet. The energy requirements of the subjects were established by multiplying an estimate of the resting metabolic rate (14) by an appropriate activity factor (15). Diets were provided as 3 equal-sized meals each day. Subjects consumed breakfast and supper daily at the Mary Emily Clinical Nutrition Research Unit of McGill University under supervision. Many subjects also consumed lunch in the center, although this meal could be eaten outside the center. The TF diet was fed first to ensure that the allocated energy level for each subject was capable of maintaining energy and weight balances. The LF, LFE, and LE diets were provided subsequently in a random order. Subjects were weighed daily before breakfast.

Before breakfast on days 28 and 29 of each diet, blood was obtained for measurement of total cholesterol, LDL-cholesterol, HDL-cholesterol, and total triacylglycerol concentrations. Plasma was separated from blood samples after centrifugation at $520 \times g$ for 20 min and stored at -80°C . Additionally, on day 28 of each dietary phase, subjects were given 0.7 g $\text{D}_2\text{O}/\text{kg}$ estimated body water orally after the fasting blood sample was obtained. Cholesterol biosynthesis was determined over 24 h as the difference in deuterium enrichment in free cholesterol in plasma taken on days 28 and 29. Subjects consumed drinking water labeled with deuterium oxide over this 24-h period to maintain deuterium enrichment in body water at plateau.

Measurement of lipid concentrations

Plasma total cholesterol, HDL-cholesterol, and triacylglycerol concentrations were measured in quadruplicate at each time

TABLE 1

Composition of energy in the 4 diets¹

Dietary energy composition	Weight-maintenance diets		Low-energy diets	
	TF	LF	LFE	LE
Protein (% of energy)	15	15	21	21
Carbohydrate (% of energy)	50	70	58	29
Fat (% of energy)	35	15	21	50
Saturated (% of energy)	11	4.7	6.6	15.7
Monounsaturated (% of energy)	14	6.0	8.4	20.0
Polyunsaturated (% of energy)	10	4.3	6.0	14.3
Total energy intake relative to individual requirement	100	100	70	70

¹Diets: TF, typical fat and energy contents; LF, low fat and adequate energy contents; LE, typical fat and low energy contents as a result of carbohydrate restriction; LFE, low fat and low energy contents as a result of carbohydrate restriction.

TABLE 2
Body weights of subjects participating in the 4 diet groups¹

	Diet group			
	LF (n = 11)	LE (n = 11)	LFE (n = 11)	TF (n = 11)
Weight (kg)				
Day 0	78.0 ± 2.4	78.1 ± 2.2	79.2 ± 2.5	79.6 ± 2.7
Day 28	77.3 ± 2.3	74.5 ± 2.0	76.0 ± 2.2	78.4 ± 2.5
Decline	0.7 ± 0.3 ^a	3.6 ± 0.4 ^b	3.2 ± 0.5 ^b	1.2 ± 0.3 ^a

¹ $\bar{x} \pm \text{SEM}$. Values with different superscript letters are significantly different, $P < 0.05$. Subjects were aged 51.5 ± 2 y with a height of 173 ± 2 cm. Diets: TF, typical fat and energy contents; LF, low fat and adequate energy contents; LE, typical fat and low energy contents as a result of carbohydrate restriction; LFE, low fat and low energy contents as a result of carbohydrate restriction.

point with a VP Autoanalyzer and commercial enzymatic kits (Abbott Laboratories, North Chicago, IL). HDL-cholesterol concentrations were determined after precipitation of non-apolipoprotein B lipoproteins with dextran sulfate–magnesium chloride (16). LDL-cholesterol concentrations were calculated according to the method of Friedewald et al (17). CVs for replicate analyses of total cholesterol, HDL cholesterol, and triacylglycerol were 1.6%, 2.8%, and 3.2%, respectively. The mean value on days 28 and day 29 was taken as the endpoint lipid concentration for each diet.

Deuterium incorporation measurement of cholesterol synthesis

Cholesterol biosynthesis was measured as the rate of incorporation of deuterium from body water into erythrocyte free cholesterol. To determine erythrocyte cholesterol deuterium enrichment, total lipids were extracted from red blood cells and chromatographed by using thin-layer chromatography as described previously (18). Free cholesterol was identified against authentic internal cochromatographed standards, eluted from silica, and placed together with 0.6 g cupric oxide and a 2-cm length of silver wire into high-temperature glass combustion tubes. These tubes were evacuated of gas at <2.6 Pa (20 mtorr) and sealed before combustion at 550°C for 4 h. The resultant combustion water and separate samples of plasma water were vacuum distilled into vycor tubes containing 60 mg Zn (Biogeochemical Laboratories, Indiana University, Bloomington, IN). These tubes were reduced at 550°C over 30 min and the hydrogen gas

evolved analyzed for deuterium content by isotope ratio mass spectrometry (model 903D; VG Micromass, Cheshire, United Kingdom). Samples were analyzed in triplicate.

Cholesterol synthesis was determined as the fractional synthesis rate of the rapid turnover pool, as calculated previously (18–23). In addition, the absolute rates of synthesis (ASR) were determined by multiplication of cholesterol fractional synthesis rate (FSR) by an arithmetic estimate of cholesterol pool size (18, 20):

$$\text{ASR (g/d)} = \text{FSR (pool/d)} \times M_1 \text{ pool} \quad (1)$$

$$M_1 \text{ pool} = 0.278 \times \text{body wt (kg)} + 1.3764 \\ \times \text{total cholesterol (mmol/L)} \\ - 2.40 \times \text{TGF} \quad (2)$$

where TGF (triacylglycerol factor) is a variable that is equal to 1, 2, or 3, depending on the plasma triacylglycerol concentration (<2.267 , 2.267 – 3.401 , or >3.401 mmol/L, respectively).

Statistics

Results are expressed as means \pm SEMs. Normal distribution of data were tested by using SAS software, version 6.03 (24). The effect of diet on plasma lipid concentrations, determined as the average of values obtained on days 28 and 29, was determined by using a crossover analysis of variance model (24). Effects of diet on cholesterol FSR and ASR were also determined by analysis of variance. When diet effects were significant, Duncan's new multiple-range post hoc test was used to compare differences between diets.

RESULTS

The body weights of subjects participating in the trial are presented in **Table 2**. Subjects' body weights were influenced by diet ($P < 0.0001$). Body weight decreased ($P < 0.001$) with the LE and LFE diets (by 3.6 ± 0.4 and 3.2 ± 0.5 kg, respectively); however, weight loss across diets with adequate energy contents was not significant (0.7 ± 0.3 and 1.2 ± 0.3 kg in the LF and TF diet groups, respectively).

Plasma lipid concentrations after each dietary treatment are presented in **Table 3**. Effects of diet on circulating total cholesterol concentrations were not significant between any of the diet groups. Diet had a significant effect on circulating LDL-cholesterol concentrations. The LF and LFE diets lowered LDL-cholesterol

TABLE 3
Plasma lipid concentrations in the 4 diet groups¹

Plasma lipid	Diet group			
	LF (n = 11)	LE (n = 11)	LFE (n = 11)	TF (n = 11)
Total cholesterol (mmol/L)	6.43 ± 0.47	6.31 ± 0.47	6.34 ± 0.53	6.48 ± 0.54
Change relative to control (%)	−0.8	−2.6	−2.2	
HDL cholesterol (mmol/L)	0.81 ± 0.04 ^b	0.94 ± 0.08 ^a	0.87 ± 0.06 ^b	0.64 ± 0.07 ^c
Change relative to control (%)	26.6	46.8	35.9	
LDL cholesterol (mmol/L)	4.49 ± 0.44 ^b	4.65 ± 0.41 ^{ab}	4.50 ± 0.51 ^b	4.89 ± 0.52 ^a
Change relative to control (%)	−8.2	−4.9	−8.0	
LDL:HDL	6.03.44 ^b	5.43 ± 0.41 ^c	5.58 ± 0.51 ^c	9.16 ± 0.52 ^a
Change relative to control (%)	−34.2	−40.7	−39.1	
Triacylglycerol (mmol/L)	2.51 ± 0.29 ^a	1.57 ± 0.16 ^c	2.12 ± 0.17 ^b	2.03 ± 0.25 ^b
Change relative to control (%)	23.6	−22.7	4.4	

¹ $\bar{x} \pm \text{SEM}$ of values on days 28 and 29. Values with different superscript letters are significantly different, $P < 0.05$. Diets: TF, typical fat and energy contents; LF, low fat and adequate energy contents; LE, typical fat and low energy contents as a result of carbohydrate restriction; LFE, low fat and low energy contents as a result of carbohydrate restriction.

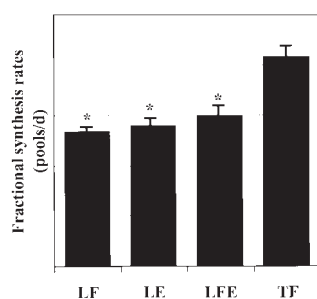


FIGURE 2. Mean (\pm SE) fractional synthesis rates of cholesterol in response to fat- and energy-manipulated diets in hypercholesterolemic subjects. *Significantly different from the TF (control) diet, $P < 0.05$. Diets: TF, typical fat and energy contents; LF, low fat and adequate energy contents; LE, typical fat and low energy contents as a result of carbohydrate restriction; LFE, low fat and low energy contents as a result of carbohydrate restriction.

concentrations (by 8.2% and 8.0%, respectively) relative to the TF diet. HDL-cholesterol concentrations at the end of each treatment were influenced ($P < 0.01$) by diet. HDL-cholesterol concentrations were significantly lower after the TF diet than after the LF, LE, and LFE diets. The HDL-cholesterol concentration was significantly higher after the LE diet than after the other 3 diets. LDL:HDL declined after the LF, LE, and LFE diets (by 34.2%, 40.7%, and 39.1%, respectively) relative to the TF diet. This ratio was significantly lower after the LE and LFE diets than after the LF diet, but there was no significant difference between the LE and LFE diets.

Changes in circulating triacylglycerol concentrations varied as a function of diet ($P < 0.01$). The highest and lowest triacylglycerol concentrations were seen after the LF and LE diets, respectively, and were significantly different from those after the other diets. The LF diet increased (23.6%) whereas the LE diet decreased (22.7%) triacylglycerol concentrations relative to the TF diet.

The influence of diet on cholesterol biosynthesis is shown in **Figure 2**. On day 29, the mean FSR was significantly greater ($P < 0.01$) after the TF diet (0.0822 ± 0.0077 pools/d) than after the LF (0.0533 ± 0.0054 pools/d), LE (0.0594 ± 0.0078 pools/d), and LFE (0.0612 ± 0.0053 pools/d) diets. The FSR was 35.2%, 27.7%, and 25.5% lower, respectively, after the LF, LE, and LFE diets relative to the TF diet. FSR values across the LF, LE, and LFE diets did not differ significantly. The effects of diet on the ASR were similar to the effects on the FSR. The mean ASR after the TF diet (0.77 ± 0.09 g/d) was significantly higher than that after the LF (0.50 ± 0.05 g/d), LE (0.54 ± 0.09 g/d), and LFE (0.56 ± 0.05 g/d) diets. In other words, the ASR decreased significantly after consumption of the diets low in fat or energy or low in both fat and energy.

DISCUSSION

Despite the observation that circulating lipid concentrations decreased after weight loss, the responsible mechanism remains obscure, largely because low-fat diets are almost invariably less energy dense and provide lower energy intakes relative to non-low-fat diets. The present results showed that in hyperlipidemic subjects, the consumption of diets low in fat (LF) and low in both fat and energy (LFE) resulted in an identical reduction in

LDL-cholesterol concentrations relative to the TF (control) diet. However, the LE diet alone failed to produce any reduction in LDL cholesterol. The LFE diet lowered plasma LDL cholesterol but did not alter plasma triacylglycerol, whereas the LF diet lowered LDL cholesterol yet significantly elevated triacylglycerol and, compared with the LE and LFE diets, suppressed HDL-cholesterol concentrations. On the basis of these findings, the LFE diet appears to be more desirable than the LF diet. However, the LE diet lowered triacylglycerol and elevated HDL cholesterol to an even greater extent relative to the LFE diet, although its effect on LDL cholesterol was not as great as that modified by the other 2 fat-restricted diets.

In addition, LDL:HDL was the most favorable after the LE diet. These results show the importance of discriminating between plasma lipid profile-modifying mechanisms attributable to reductions in fat intake and those due to lower energy intakes that often result with a transition to a low-fat diet in a clinical setting. In an active weight-loss trial, Noakes and Clifton (25) showed that LDL-cholesterol concentrations decreased after diets low in saturated fatty acids, regardless of the energy source, whereas concentrations did not decrease after an energy-restricted diet (16.8% of total energy) high in saturated fatty acids. Our findings were similar, ie, the dietary ratio of fatty acids and the total energy provided by diets as saturated fatty acids played crucial roles in the modulation of LDL-cholesterol concentrations.

Contrary to the findings of Lichtenstein et al (13), who observed that a low-fat diet had a positive influence on plasma LDL cholesterol only when accompanied by weight loss resulting from consumption of an energy-restricted diet, the present study showed that LDL-cholesterol and total cholesterol concentrations were similar after the LF diet (no weight loss observed) and after the LFE diet (weight loss was observed). Nelson et al (26), who studied the effects of weight-maintenance diets differing only in the percentage of energy delivered as fat, showed that compared with a high-fat diet, a low-fat diet that provided the same amount of energy did not result in changes in total cholesterol but did result in elevated triacylglycerol concentrations. In combination, these results suggest that manipulation of dietary energy with accompanying weight loss has a greater beneficial effect on the plasma lipid profile than does manipulation of dietary fat without weight loss. Data from the present study showed that LDL-cholesterol concentrations decreased and triacylglycerol concentrations increased after the LF diet. In contrast, HDL cholesterol increased and triacylglycerol concentrations decreased after the LE diet. Indeed, the increase in triacylglycerol associated with consumption of the LF diet should be viewed as potentially detrimental, given the role of postprandial triacylglycerol in the atherosclerotic process (27). In contrast, although the LFE diet positively modified LDL and HDL cholesterol relative to the TF diet, it is clear that the greater HDL cholesterol-raising effect of the LE diet (in combination with a reduction in triacylglycerol and a favorable LDL:HDL) render the LE diet the most desirable of those tested in the present study. The HDL-cholesterol-raising ability of weight-loss diets was shown previously (28).

Energy restriction has multiple effects on mammalian lipid metabolism. Fasting is associated with a reduction in cholesterol synthesis in animals (29, 30) and humans (21, 22, 31). In humans, an abrupt inhibition of cholesterol synthesis occurs after a 24-h fast (21, 22), with concurrent decreases in insulin and glucose-dependent insulinotropic polypeptide concentrations (32).


Negative energy balance, with constant fat intake, also affects other aspects of lipid metabolism. In rats, triacylglycerol fatty acid (33, 34) and cholesterol (34) metabolism respond differently to energy deficits than to changes in dietary fat. The present data showed that low energy intakes associated with weight loss did not influence total or LDL-cholesterol concentrations; however, the overall lipoprotein profile was positively altered through favorable changes in HDL-cholesterol and triacylglycerol concentrations. Why LDL-cholesterol concentrations did not decline significantly with the LE diet, despite the reduction in cholesterol synthesis, is not clear; it might have been because of a high consumption of saturated fatty acids (25). Di Buono et al (35) reported declines in both LDL-cholesterol and cholesterol synthesis after weight loss in mildly hypercholesterolemic, overweight men. However, in the present study, fat provided 50% of energy in the LE diet (Figure 1).

Why cholesterologenesis decreased during the LF diet, during which time carbohydrate intakes increased and subjects maintained body weights, is also unclear. The presence of polyunsaturated fat in the diet has been associated with enhanced biosynthesis of cholesterol in hyperlipidemic individuals (23). It can be speculated that during energy balance, the suppression of cholesterologenesis by removal of fat outweighs any stimulation of synthesis by an increase in the carbohydrate content. However, as energy balance becomes negative, synthesis rates decrease regardless of dietary fat intakes.

The positive effect of the LE diet on the plasma lipid profile and on cholesterol synthesis in the present study is important in the context of dietary recommendations for improved cardiovascular health. Current recommendations call for reduced-fat diets, with less emphasis on energy restriction (2–5). However, the present findings suggest that energy restriction rather than fat restriction results in a lipid profile as favorable as that seen after the LFE diet. Because both total cholesterol and triacylglycerol concentrations were shown to be independent risk factors for cardiovascular disease (36–38), the disparate effect of low-energy compared with low-fat diets on these blood lipid indexes is extremely important. Dietary guidelines advising reductions in fat intake to decrease the risk of cardiovascular disease may have to be reconsidered, with the focus perhaps redirected toward reductions in energy intake for those individuals with excess body weight.

Manipulation of energy density may provide a means for reducing intakes of both energy and fat. Rolls et al (39) showed that energy intake depends on energy density but not on the fat content of portioned food, which is consistent with the findings of the present study, ie, diets with a low energy density favorably suppressed lipid concentrations through energy restriction. A focus on energy restriction also addresses the issue of obesity, both as a health concern and in relation to its status as an independent risk factor for cardiovascular disease (40–42). Energy restriction below energy requirements, as in the present study, is a means of reducing body weight. It is obvious that reductions in body weight result from reductions in total energy intake, increases in energy expenditure, or both. Controversial findings exist concerning the effects of dietary fat reductions on body weight loss. Willett (43) reported that a reduction in dietary fat is not always a successful approach for weight loss in the obese. Indeed, reductions in dietary fat appear to be associated with an increase, rather than with a decrease, in the percentage of the population that is overweight (43). In contrast, Bray and Popkin (44) argued that dietary fat does play a role in the development of obe-

sity. Furthermore, Noakes and Clifton (25) showed that reductions in dietary energy through fat or carbohydrate restriction have the same effect on body weight loss. Therefore, energy-reduced diets, through balanced restriction of carbohydrate and fat, affect several independent risk factors for heart disease, such as total cholesterol, triacylglycerol, and obesity, perhaps in a manner different from that of a constant low-fat energy intake. As stated by Grundy (45), consequences of dietary fat intakes cannot focus solely on body weight but must examine the overall metabolic action of the diets. However, when low-fat diets result in weight loss in subjects who are not attempting to suppress their total energy intakes, such diets should be viewed as favorable because weight loss is almost invariably linked to an improvement in health status.

In summary, the present study showed that, although reductions in dietary fat or in both dietary fat and energy favorably modified lipid concentrations, reductions in dietary energy alone also consistently decreased the risk of cardiovascular disease. 

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REFERENCES

1. Stamler J. Population studies. In: Nutrition, lipids and coronary heart disease. In: Levy RI, Rifkind BM, Dennis BN, Ernst N, eds. New York: Raven Press, 1979:25–88.
2. National Cholesterol Education Program. Summary of the second report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA* 1993;269:3015–23.
3. Mann J. Complex carbohydrates: replacement energy for fat or useful in their own right? *Am J Clin Nutr* 1987;45(suppl):1202–6.
4. Grundy SM, Denke MA. Dietary influences on serum lipids and lipoproteins. *J Lipid Res* 1990;31:1149–72.
5. National Research Council (U.S.) Committee on Diet and Health. Diet and health, implications for reducing chronic disease risk. Washington, DC: National Academy Press, 1989:183.
6. Dougherty RM, Fong AKH, Iacono JM. Nutrient content of the diet when the fat is reduced. *Am J Clin Nutr* 1988;48:970–9.
7. Retzlaff BM, Dowdy AA, Walden CE, et al. Changes in vitamin and mineral intakes and serum concentrations among free-living men on cholesterol-lowering diets: the Dietary Alternatives Study. *Am J Clin Nutr* 1991;53:890–8.
8. Lissner L, Levitsky DA, Strupp BJ, Kalkwarf H, Rao DA. Dietary fat and the regulation of energy intake in human subjects. *Am J Clin Nutr* 1987;46:886–92.
9. Kendall A, Levitsky DA, Strupp BJ, Lissner L. Weight loss on a low-fat diet: consequence of the imprecision of the control of food intake in humans. *Am J Clin Nutr* 1991;53:1124–9.
10. Thuesen L, Henriksen LB, Engby B. One-year experience with a low-fat, low-cholesterol diet in patients with coronary heart disease. *Am J Clin Nutr* 1986;44:212–29.
11. Walford RL, Harris SB, Gunion MW. The calorically restricted low-fat nutrient-dense diet in Biosphere 2 significantly lowers blood glucose, total leukocyte count, cholesterol and blood pressure in humans. *Proc Natl Acad Sci U S A* 1992;89:11533–7.
12. Gordon T, Kagan A, Garcia-Palmieri M, et al. Diet and its relation to coronary heart disease and death in three populations. *Circulation* 1981;63:500–15.
13. Lichtenstein AH, Ausman LM, Carrasco W, Jenner JL, Ordovas JM, Schaefer EJ. Short-term consumption of a low-fat diet beneficially affects plasma lipid concentrations only when accompanied by weight loss. Hypercholesterolemia, low-fat diet, and plasma lipids. *Arterioscler Thromb* 1994;14:1751–60.



14. Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO. A new predictive equation for resting energy expenditure in healthy individuals. *Am J Clin Nutr* 1990;51:241-7.
15. Bell L, Jones PJH, Telch J, Clandinin MT, Pencharz PB. Reduction of energy needs for clinical studies. *Nutr Res* 1985;5:123-30.
16. Warnick GR, Benderson J, Albers JJ. Dextran sulfate-Mg²⁺ precipitation procedure for quantitation of high-density-lipoprotein cholesterol. *Clin Chem* 1982;28:1379-88.
17. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972;18:499-502.
18. Jones PJH, Leitch CA, Li ZC, Connor WE. Human cholesterol synthesis measurement using deuterated water. Theoretical and procedural considerations *Arterioscler Thromb* 1993;13:247-53.
19. Jones PJH, Lichtenstein AH, Schaefer EJ. Interaction of dietary fat saturation and cholesterol level on cholesterol synthesis measured using deuterium incorporation. *J Lipid Res* 1994;35:1093-101.
20. Wong WW, Hachey DL, Clarke LL, Zhang S. Cholesterol synthesis and absorption by ²H₂O and ¹⁸O-cholesterol and hypocholesterolemic effect of soy protein. *J Nutr* 1995;125S:612-8.
21. Jones PJH, Scanu AM, Schoeller DA. Plasma cholesterol synthesis using deuterated water in humans: effect of short-term food restriction. *J Lab Clin Med* 1988;111:627-33.
22. Roe RP, Jones PJH, Frohlich JJ, Schoeller DA. Association between apolipoprotein E phenotype and endogenous cholesterol synthesis as measured by deuterium uptake. *Cardiovasc Res* 1991;25:249-55.
23. Jones PJH, Lichtenstein AH, Schaefer EJ, Namchuk GL. Effect of dietary fat selection on plasma cholesterol synthesis in older, moderately hypercholesterolemic humans. *Arterioscler Thromb* 1994;14:542-8.
24. SAS Institute Inc. SAS procedure guide, version 6.03. Cary, NC: SAS Institute Inc, 1996.
25. Noakes M, Clifton PM. Changes in plasma lipids and other cardiovascular risk factors during 3 energy-restricted diets differing in total fat and fatty acid composition. *Am J Clin Nutr* 2000;71:706-12.
26. Nelson GJ, Schmidt PC, Kelley DS. Low-fat diets do not lower plasma cholesterol levels in healthy men compared to high-fat diets with similar fatty acid composition at constant caloric intake. *Lipids* 1995;30:969-76.
27. Ooi TC, Ooi DS. The atherogenic significance of an elevated plasma triglyceride level. *Crit Rev Clin Lab Sci* 1998;35:489-516.
28. Dattilo AM, Kris-Etherton PM. Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. *Am J Clin Nutr* 1992;56:320-8.
29. Kelley MJ, Story JA. Effect of type of diet and feeding status on modulation of hepatic HMG-CoA reductase in rats. *Lipids* 1985;20:53-5.
30. Turley SD, West CE. Effect of cholesterol and cholestyramine feeding and of fasting on sterol synthesis in the liver, ileum, and lung of the guinea pig. *Lipids* 1976;11:571-7.
31. Neese RA, Faix D, Kletke C, Wu K, Shackleton CHL, Hellerstein MK. Measurement of endogenous synthesis of plasma cholesterol in rats and humans using MIDA. *Am J Physiol* 1993;264:E136-47.
32. Jones PJH, Leitch CA, Pederson RA. Meal-frequency effects on plasma hormone concentrations and cholesterol synthesis in humans. *Am J Clin Nutr* 1993;57:868-74.
33. Jones PJH, Toy BR, Cha MC. Differential fatty acid accretion in heart, liver and adipose tissues of rats fed beef tallow, fish oil, olive oil and safflower oils at three levels of energy intake. *J Nutr* 1995;125:1175-82.
34. Cha MC, Jones PJH. Dietary fat type related changes in tissue cholesterol and fatty acid synthesis are influenced by energy intake level in rats. *J Am Coll Nutr* 1997;16:592-9.
35. Di Buono M, Hannah JS, Katzell LI, Jones PJH. Weight loss through energy restriction suppresses cholesterol biosynthesis in overweight, mildly hypercholesterolemic men. *J Nutr* 1999;129:1545-8.
36. Criqui MH. Triglycerides and cardiovascular disease. A focus on clinical trials. *Eur Heart J* 1998;19:A36-9.
37. Kannel WB, Castelli WP, Gordon T. New perspectives based on the Framingham study. *Ann Intern Med* 1979;90:85-91.
38. The Lipid Research Clinics Program. The Lipid Research Clinics Coronary Primary Prevention Trial results. I. Reduction in incidence of coronary artery disease. *JAMA* 1984;251:351-64.
39. Rolls BJ, Bell EA, Castellanos VH, Chow M, Pelkman CL, Thorwart ML. Energy density but not fat content of foods affected energy intake in lean and obese women. *Am J Clin Nutr* 1999;69:863-71.
40. Bray GA. Health hazards of obesity. *Endocrinol Metab Clin North Am* 1996;25:907-19.
41. Garrison RJ, Higgins MW, Kannel WB. Obesity and coronary heart disease. *Curr Opin Lipidol* 1996;7:199-202.
42. Rabkin SW, Mathewson FA, Hsu PH. Relation of body weight development to development of ischemic heart disease in a cohort of young North American men after a 26 year observation period: The Manitoba Study. *Am J Cardiol* 1977;39:452-8.
43. Willett WC. Is dietary fat a major determinant of body fat? *Am J Clin Nutr* 1998;67(suppl):556S-62S.
44. Bray GA, Popkin BM. Dietary fat intake does affect obesity! *Am J Clin Nutr* 1998;68:1157-73.
45. Grundy SM. How we can optimize dietary composition to combat metabolic complications and decrease obesity. Overview. *Am J Clin Nutr* 1998;67(suppl):497S-9S.