

# Effect of low-fat diets on plasma high-density lipoprotein concentrations<sup>1-3</sup>

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**ABSTRACT** Low concentrations of HDLs in plasma are a strong predictor of risk for coronary as well as other cardiovascular diseases. There is increasing evidence that this relation is causal and that interventions that change HDL concentrations also change risk. One such intervention is exchanging fat and carbohydrate. In controlled trials, low-fat, high-carbohydrate diets decrease HDL concentrations. The effect is strongest when carbohydrates replace saturated fatty acids, but is also seen when carbohydrates replace mono- and polyunsaturated fatty acids. The effect is seen in both short- and long-term trials and therefore appears to be permanent. This finding is supported by epidemiologic studies in which populations eating low-fat, high-carbohydrate diets were shown to have low HDL concentrations. Weight losses with consumption of low-fat diets could theoretically counter effects on HDL, but in published trials weight losses have been modest and insufficient to offset the decrease in HDL concentrations induced by carbohydrates. Thus, replacement of saturated fat by carbohydrates adversely affects plasma HDL concentrations; replacement of saturated fat by unsaturated fatty acids deserves consideration as an alternative. *Am J Clin Nutr* 1998;67(suppl):573S-6S.

**KEY WORDS** Review, dietary carbohydrate, dietary fat, high-density lipoprotein, HDL, lipid-lowering drugs, low-density lipoprotein, LDL, plasma triacylglycerol, coronary heart disease, ischemic heart disease, body weight, human studies

## INTRODUCTION

In 1961 a distinguished group of investigators from the Rockefeller Institute led by Ahrens published a paper titled "Carbohydrate-induced and fat-induced lipemia" (1). According to these authors, numerous publications dating back to the preinsulin era showed that low-fat, high-carbohydrate diets increase serum lipids (ie, triacylglycerol), but that despite this "the phenomenon of carbohydrate-induced lipemia is still not commonly appreciated." Ahrens et al went on to discuss the difference between fat-induced lipemia, which is a postprandial phenomenon caused by chylomicrons, and the carbohydrate-induced rise in fasting triacylglycerols caused by lipoproteins with a Svedberg flotation unit ( $S_f$ ) of 20-400, what we would now call VLDLs.

Thus, the effect of low-fat, high-carbohydrate diets on fasting triacylglycerols has been appreciated for almost 40 y and is still being reported in metabolic trials (2). The reciprocal effect of a low-fat diet on HDL concentrations, however, has long been

ignored, possibly because the importance of HDL concentrations in atherosclerosis has taken some time to be established.

## HDL CONCENTRATIONS AND ISCHEMIC HEART DISEASE

The inverse relation between HDL concentrations and ischemic heart disease was discovered in the early 1950s independently by Barr et al (3) and Nikkilä (4), but these discoveries remained dormant until they were revived by Miller and Miller (5) in a seminal paper in 1975. Since that time, the evidence for a relation between HDL concentrations and atherosclerotic diseases has continued to accumulate (6). A cause-and-effect relation has still not been established beyond reasonable doubt, but the results of recent drug trials strongly suggest that manipulation of HDL concentrations does change the progression of atherosclerosis and the incidence of cardiovascular disease.

The first observations made on the effect of drugs on HDL and cardiovascular diseases concerned antiepileptic drugs. Chronic ingestion of the antiepileptic medicine phenytoin, which powerfully elevates HDL concentrations, was found to be associated with markedly lower rates of ischemic heart disease mortality (7). The first evidence from controlled clinical drug trials was obtained in studies of cholestyramine and gemfibrozil. Post hoc analyses of these trials, designed largely to study effects of LDL reduction, suggested that drug-induced changes in HDL concentrations affected the risk of coronary disease independently of effects on LDL concentrations; a reduction in ischemic heart disease incidence was seen in proportion to the drug-induced increase in HDL concentration (8). The Scandinavian Simvastatin Survival Study showed that the HDL-raising effect of  $\beta$ -hydroxy- $\beta$ -methylglutaryl-CoA reductase inhibitors also contributes to the favorable effect of statins on ischemic heart disease incidence (9). The reverse effect was seen in a Swedish trial of probucol, an antioxidant that lowers both LDL and HDL concentrations. In this study, inclusion of probucol in the treatment regimen unexpectedly caused more rather than less atherosclerosis of the femoral artery as determined by angiography. This

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result could be explained by the effect of the drug on HDL; probucol-induced decreases in HDL concentrations were significantly correlated with decreases in lumen volume of the femoral artery (10) and thus with enhanced atherosclerosis.

The link between HDL and atherosclerosis was strengthened by the publication of the Bezafibrate Coronary Atherosclerosis Intervention study (11). Unlike the drugs mentioned above, bezafibrate does not affect LDL concentrations: median percentage changes in LDL differed by only 1.3% between the bezafibrate group and the control group. In contrast, HDL concentrations rose by 8% and triacylglycerol concentrations fell by 23% in the treated compared with the placebo group. Progression of coronary sclerosis was markedly slower in the intervention group, as was the cumulative coronary event rate. Again, this does not constitute final evidence that changing HDL concentrations changes the rate of progression of atherosclerosis; the authors themselves did not rule out any mechanism but mentioned a possible relation with the lowering of triacylglycerol and fibrinogen concentrations with bezafibrate treatment (11). However, the assumption that HDL is causally involved in atherosclerosis and cardiovascular disease does provide a single explanation for much epidemiologic and intervention data.

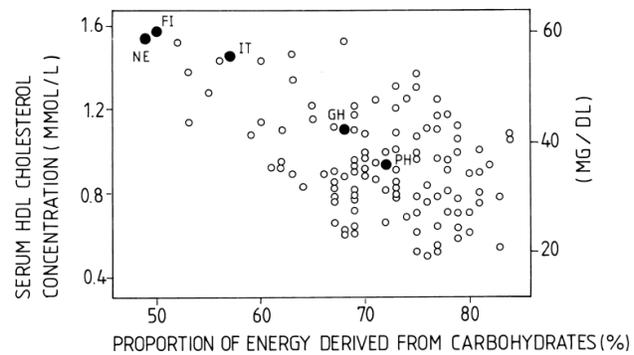
### FAT, CARBOHYDRATES, AND HDL CONCENTRATIONS

High-carbohydrate diets produce higher fasting triacylglycerol and lower plasma cholesterol concentrations than do high-fat diets (2). Most of the decrease in cholesterol is due to decreases in LDL, but part is also due to decreases in HDL concentrations. Lowering of HDL concentrations by a high-carbohydrate diet was reported by Levy et al (12) as early as 1966 and has been a consistent finding in dietary trials ever since. Combined data from 27 well-controlled trials encompassing 682 subjects showed that HDL cholesterol fell by 0.012 mmol/L (0.5 mg/dL) for every 1% of energy from saturated fatty acids that was replaced by carbohydrates. Meta-analyses conducted by Hegsted et al (13) and Yu et al (14) led to similar conclusions. The effect of carbohydrates on HDL concentrations is not restricted to sugars but is also found with diets high in complex carbohydrates (15, 16).

Treatments in feeding trials often last only a few weeks, and it has been suggested that the effects seen on HDL and triacylglycerol concentrations are transient and would disappear if treatment was continued long enough [(17), but *see* reference 18 for detailed data on that study]. However, several metabolic trials have studied changes in HDL concentrations as a function of fat and carbohydrate intakes for periods from 3 mo up to 1 y and they show that the decrease in HDL persists (18–21). Epidemiologic studies also show that chronic intake of a high-carbohydrate diet is associated with lower concentrations of HDL, both for free-living individuals eating self-selected diets (22, 23) and for population means (24–26). The effect is most clearly seen in young boys, where it is less confounded by differences in alcohol intake, cigarette use, physical activity, and obesity than in adults (**Figure 1**). The combined experimental and epidemiologic data suggest that every 10% of energy from fat that is replaced by carbohydrates lowers HDL concentrations by 0.1 mmol/L (2, 27).

### HIGH-CARBOHYDRATE DIETS AND BODY WEIGHT

One reason low-fat diets have such appeal is that they are thought to prevent weight gain. Adult populations or population



**FIGURE 1.** Relation between serum HDL cholesterol concentration and the proportion of energy from carbohydrates in groups of  $\approx 120$  healthy boys aged 8 and 9 y from five countries with widely different fat and carbohydrate intakes. Diets were assessed by 7-d individual records and evaluated by using laboratory analyses of local foods. Filled circles are mean values for  $\approx 120$  boys from each country; open circles are individual values for boys from the Philippines. NE, Netherlands; FI, Finland; IT, southern Italy; GH, Ghana; PH, the Philippines. Reproduced from reference 24 with permission.

groups that subsist on low-fat diets are often lean, and this may cancel out the effect of such diets on HDL. Knuiman et al (24, 28) reported that persons following a macrobiotic diet had HDL concentrations similar to those of their omnivorous countrymen despite consuming a diet low in fat and high in carbohydrates; in multivariate analysis these high HDL concentrations could largely be explained by the extremely low body mass index of the macrobiotic subjects.

The same effect of low-fat diets should not be expected in the general public, however. In the eye of the public, *fat* has become synonymous with *calories*, and it is thought that a food low in fat cannot be fattening. There is some truth in this if one considers low-fat foods as a shorthand notation for vegetables, fruit, and pulses. However, that is not the official definition of a low-fat food: a low-fat food is a food low in components that are soluble in hexane or other organic solvents. Such a food can still be high in sugars, starch, and protein, all of which contribute plenty of energy. The typical low-fat items available on supermarket shelves today are not the seaweed and brown rice favored by macrobiotics; on the contrary, the food industry provides many foods that are low in fat but often not low in energy and that are as appetizing as their high-fat analogues. These foods are legitimately called low-fat foods, but are not the fruit, vegetables, and unrefined high-fiber foods that scientists had in mind when they recommended a low-fat diet. There is no evidence that these modern low-fat products produce substantial long-term weight losses.

Some biochemical models of macronutrient metabolism (29) predict that low-fat diets should induce weight loss even if their nominal energy content is not low, and some (30), although not all (31), short-term experiments support this view. This implies that weight is not just a matter of energy intake but that there is a specific benefit in eliminating energy from fat from the diet. However, the acid test of such theories is long-term controlled trials of high-carbohydrate, low-fat diets, and the outcomes of these trials in terms of weight loss have been disappointing (32). Such trials have produced decreases in body weight of from 0.4 to 2.6 kg relative to weight changes in control subjects (21, 33–36). However, much larger decreases are needed to affect HDL con-

centrations (37); indeed, HDL concentrations have consistently fallen in subjects eating low-fat diets despite decreases in body mass index (19, 21). Thus, the absence of widespread obesity in poor populations is probably not explained simply by the number of triacylglycerol molecules in the foods consumed by these populations; the limited availability of attractive foods plus the need for hard physical labor are a more likely explanation.

### UNSATURATED OILS AS AN ALTERNATIVE

There is widespread agreement that saturated fatty acid intake should be decreased so as to decrease the risk of ischemic heart disease. The question then arises as to which nutrient should take the place of saturated fatty acid. To this author, at least, drastic increases in carbohydrate intake appear less than desirable. Decreasing saturated fat intake will produce some decrease in total fat intake, because replacement of high-fat dairy products and meats by their low-fat counterparts will decrease fat intake. However, there is no reason the intake of unsaturated oils and products made with them should be limited; such oils have been tested in controlled clinical trials and have produced favorable effects on ischemic heart disease as well as on total mortality (38, 39). A diet containing  $\leq 35\%$  of energy from fat, low in saturated fatty acids, and high in a variety of *cis*-unsaturated fatty acids, might provide the optimum for the reduction of ischemic heart disease risk.

### CONCLUSION

The pros and cons of diets high in carbohydrates compared with diets high in unsaturated fats have still not been completely worked out; they involve considerations beyond coronary risk and it may take another 40 y before all the effects of high-carbohydrate diets have been clarified. However, the lowering of HDL concentrations by low-fat, high-carbohydrate diets constitutes a distinct disadvantage that can no longer be ignored. 

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