Will a High-Carbohydrate, Low-Fat Diet Lower Plasma Lipids and Lipoproteins Without Producing Hypertriglyceridemia?

Daniel Ullmann, William E. Connor, Lauren F. Hatcher, Sonja L. Connor, and Donna P. Flavell

A sudden increase in dietary carbohydrate invariably increases the plasma levels of very low density lipoprotein (VLDL) and triglyceride. The present studies were designed to test the hypothesis that dietary carbohydrate-induced hypertriglyceridemia need not occur. In the first study we fed gradually increasing amounts of carbohydrate and gradually decreasing amounts of fat to eight subjects. The usual American diet (40% fat, 45% carbohydrate, and 15% protein) was followed in sequence by four diets in a phased regimen, the carbohydrate increasing by 5% of total calories and the fat content decreasing by 5% for each dietary period. In the last dietary period (phase 4), 20% of the energy was in the form of fat and 65% in the form of carbohydrates; the cholesterol content was 100 mg/day. Throughout the study, plasma triglyceride and VLDL triglyceride levels did not change significantly. The plasma total and low density lipoprotein (LDL) cholesterol levels were greatly reduced, by 15% and 22%, respectively (p=0.004). Plasma high density lipoprotein (HDL) cholesterol levels decreased concomitantly. In the second study, after a washout period six of the subjects were initially fed the phase 4 high-carbohydrate diet for a 10-day period. The plasma triglyceride concentration increased over baseline levels by 47%, and VLDL triglyceride levels increased by 73%. We conclude that although a sudden increase in dietary carbohydrate increases the plasma triglyceride level, patients gradually introduced to a high-carbohydrate, low-fat diet may achieve a significant reduction of plasma total and LDL cholesterol without developing carbohydrate-induced hypertriglyceridemia.

Coronary heart disease in Western populations has surged from a minimal public health concern at the turn of the century to the leading cause of mortality. Cross-cultural studies have documented a strong positive association between dietary fat intake and both the prevalence and incidence of this disease, manifested by myocardial infarction and sudden death. Coronary heart disease in the United States is related to elevated plasma levels of cholesterol and low density lipoprotein (LDL), which usually result from consumption of excessive amounts of dietary saturated fat and cholesterol. Accordingly, there has been general agreement in the scientific community that the primary dietary change required to reduce cardiovascular risk would be a decrease in the intake of total fat, saturated fat, and cholesterol. To replace the fat calories as fat intake is reduced, it is then necessary to increase carbohydrate intake because protein intake remains at 15% of total calories. Currently, the average carbohydrate intake by Americans is 45% of total calories. In contrast, current dietary recommendations for individuals with hyperlipidemia and even for those with diabetes are diets with carbohydrate contents of as much as 65% of total calories, with the emphasis on complex carbohydrates from natural sources. These recommendations are consistent with the high-carbohydrate and low-fat intakes of populations having a low incidence of coronary heart disease. Because past studies have shown that suddenly increasing dietary carbohydrate can produce delete-
rious effects in normal,12 hyperlipidemic,13 and diabetic14 individuals, there is no universal agreement that the American diet should be higher in carbohydrate. Some undesired effects of a high-carbohydrate diet include hypertriglyceridemia, postprandial hyperglycemia, hyperinsulinemia, and a decrease of high density lipoprotein (HDL) levels.15 Because prospective studies have shown that all four of these risk factors are associated with an increased incidence of cardiovascular mortality,16-19 it has been argued that replacement of fat with carbohydrate may not be totally benign. However, most studies of the “carbohydrate induction” of hypertriglyceridemia have suddenly increased the amount of dietary carbohydrate, and most have been quite short in duration.12-15,20 Under different conditions, hypertriglyceridemia after a change to a higher carbohydrate intake may not always occur or persist. Previously, we demonstrated that a marked decrease in the concentration of plasma cholesterol without hypertriglyceridemia could occur in patients with insulin-dependent diabetes mellitus 1 year after initiation of a low-fat, high-carbohydrate diet.21 The present studies were designed to test the hypothesis that carbohydrate-induced hypertriglyceridemia need not occur due to a high-carbohydrate diet that was gradually phased in over time.

**Methods**

**Subjects**

These studies were conducted at the Clinical Research Center at the Oregon Health Sciences University. Informed consent was obtained in accordance with institutional policy, and the protocol was approved by the Human Research Committee. The study group comprised eight healthy nondiabetic adult individuals (two women and six men). Patients were recruited from the Lipid Clinic at the Oregon Health Sciences University. Their ages, weights, body mass indexes, and plasma lipid levels on entry are shown in Table 1. Their mean age was 51 years (range, 36-63 years). Their body weights and body mass indexes averaged 85 kg and 29.5, respectively, which indicated mild overweight. On entry into the study, while patients 1, 2, 3, 4, 6, and 8 had elevated plasma cholesterol concentrations (>220 mg/dl), patients 2, 5, 6, 7, and 8 had elevated triglyceride levels (>200 mg/dl). Thus, on average these patients were mildly hypertriglyceridemic, with an average plasma triglyceride level of 254 mg/dl. None had symptoms of cardiac failure, a history of a recent myocardial infarction, or disease of the gastrointestinal tract, kidneys, or endocrine system, and none were taking any medications known to affect plasma lipids.

**Study Protocol**

Our null hypothesis was that dietary carbohydrate-induced hypertriglyceridemia would not occur, provided that the carbohydrate content of the diet was increased gradually as the fat content was decreased. The studies were designed to test these effects of a high-carbohydrate, low-fat diet on the plasma concentrations of triglyceride, cholesterol, and lipoproteins. There were two components to the study. In the first component, the dietary carbohydrate was phased in gradually as the fat content was reduced. In the second component, we ascertained that the patients would actually become hypertriglyceridemic in response to a short-term high-carbohydrate-diet challenge without the gradual phased approach.

**Study 1: Phased Carbohydrate Diet**

In study 1 we measured plasma lipids and lipoproteins when the dietary carbohydrate intake was phased in gradually as fat was reduced. With eight patients, this study has a statistical power of 0.80 to detect a plasma triglyceride change of 75 mg/dl, which reflects an approximate 1.5 standard deviation shift of the mean, when a significance value of 0.05 or less is used (two-tailed test). All patients were sequentially fed five diets designed to maintain body weight: the typical American diet (40% fat, 45% carbohydrate, and 15% protein) and four diets that were each 5% lower in fat and 5% higher in carbohydrate than the preceding diet. The final diet (phase 4) contained 65% of calories as carbohydrate and 20% of calories as fat. The dietary

### Table 1. Clinical Characteristics of Study Subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (yr)/sex</th>
<th>Body weight (kg)</th>
<th>Body mass index*</th>
<th>Entry lipoprotein values (mg/dl)†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td></td>
<td></td>
<td>Total cholesterol</td>
</tr>
<tr>
<td>1</td>
<td>51/M</td>
<td>81.2</td>
<td>31.3</td>
<td>279</td>
</tr>
<tr>
<td>2</td>
<td>44/M</td>
<td>86.9</td>
<td>30.1</td>
<td>232</td>
</tr>
<tr>
<td>3</td>
<td>51/M</td>
<td>88.8</td>
<td>28.7</td>
<td>260</td>
</tr>
<tr>
<td>4</td>
<td>63/M</td>
<td>67.2</td>
<td>24.2</td>
<td>240</td>
</tr>
<tr>
<td>5</td>
<td>36/M</td>
<td>96.0</td>
<td>33.9</td>
<td>140</td>
</tr>
<tr>
<td>6</td>
<td>44/M</td>
<td>98.7</td>
<td>32.2</td>
<td>255</td>
</tr>
<tr>
<td>7</td>
<td>51/M</td>
<td>98.7</td>
<td>31.9</td>
<td>191</td>
</tr>
<tr>
<td>8</td>
<td>60/F</td>
<td>61.6</td>
<td>24.1</td>
<td>226</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>51±9</td>
<td>84.9±14.1</td>
<td>29.5±3.7</td>
<td>228±44</td>
</tr>
</tbody>
</table>

*Body mass index is the weight in kilograms divided by the square of the height in meters.
†To convert cholesterol and triglycerides to mmol/l, divide by 3.87 and 88.5, respectively.
Diets was fed in study 2. The composition of the five vent any body weight fluctuations. Boothby-Berkson nomogram, incorporating addi-

<table>
<thead>
<tr>
<th>TABLE 2. Composition of the Phased-Carbohydrate Diets*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Composition</strong></td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Carbohydrate (% of total calories)</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Complex</td>
</tr>
<tr>
<td>Simple sugars (sucrose, glucose, fructose, and galactose)</td>
</tr>
<tr>
<td>Total fat (% of total calories)</td>
</tr>
<tr>
<td>Saturated</td>
</tr>
<tr>
<td>Polysaturated</td>
</tr>
<tr>
<td>Monounsaturated</td>
</tr>
<tr>
<td>P to S ratio</td>
</tr>
<tr>
<td>Cholesterol (mg/1,000 kcal)</td>
</tr>
<tr>
<td>CSI (per 1,000 kcal)†</td>
</tr>
</tbody>
</table>

P, polynsaturated; S, saturated.
*Protein is 15% of total calories in each diet.
†Cholesterol–saturated fat index = (1.01 × g saturated fat) + (0.05 mg cholesterol).

periods had a duration of 10 days each, in accordance with previous evidence that the rise in the plasma triglyceride level from a high-carbohydrate diet is largely completed within 10 days.20

Study 2: Carbohydrate Induction

Study 2 was designed to document the physiological response of carbohydrate-induced hypertriglyceridermia that occurs when the amount of dietary carbohydrate is suddenly increased. The phase 4 diet (65% carbohydrate, 20% fat, and 15% protein) was fed acutely to six subjects (subjects 1, 2, 3, 4, 7, and 8) for a 10-day period after a washout period of at least 6 weeks. The values obtained were compared with the control American diet values, which were also the bases for comparisons in study 1.

Throughout the study, body weight was measured daily, with the subject clothed and shoeless, on a beam-type balance scale calibrated with standard weights.

Diets

The research diets were prepared at the Clinical Research Center and were composed of typical mixed foods. The diets were eucaloric for each patient to keep body weight constant. The energy expenditure for each patient was estimated by the Boothby-Berkson nomogram, incorporating additional calories as needed to adjust for physical activity. The patients were instructed to keep energy expenditure from physical activity constant to prevent any body weight fluctuations.

The five experimental diets were fed sequentially for 10 days each in study 1. Only one diet (phase 4) was fed in study 2. The composition of the five different eucaloric diets is presented in Table 2. The initial diet was planned to simulate the composition of the usual American diet.9 It provided 40% of the total energy as fat (15% saturated, 6% polyunsaturated, and 19% monounsaturated fatty acids) and 45% as carbohydrate (17% complex and 28% simple carbohydrates). The four subsequent diets had a gradual increase in carbohydrate content to 65% in phase 4, the last dietary period. The phase 4 diet contributed 20% of the energy as fat (5% saturated, 8% polyunsaturated, and 7% monounsaturated fatty acids) and 65% of energy as carbohydrate (40% complex and 25% simple carbohydrate). The diets ranged from 179 to 36 mg cholesterol per 1,000 kcal, respectively. The phase 4 diet was thus low in fat, saturated fat, and cholesterol. The association between coronary atherosclerosis and dietary cholesterol and saturated fat can be denoted by the choles-

Biochemical Analysis

Blood samples were collected into tubes containing 0.1% EDTA, after a 14-hour fast, on days 4, 7, and 10 when each dietary period was completed. The plasma specimens were analyzed for total cholesterol, triglyceride, and lipoprotein concentrations. The laboratory procedures for the plasma lipid and lipoprotein determinations were in compliance with the standardization and surveillance programs of the Centers for Disease Control Laboratory in Atlanta, Ga., according to procedures established by the Lipid Research Clinics of the National Heart, Lung, and Blood Institute.35 Plasma total cholesterol and tri-
glyceride concentrations were measured fluorometrically with an AutoAnalyzer II (Technicon Instruments Corp., Tarrytown, N.Y.). Plasma HDL cholesterol was measured enzymatically after precipitation of the apolipoprotein (apo) B-containing lipoproteins by heparin-MnCl₂. The very low density lipoprotein (VLDL) fraction was separated by ultracentrifugal flotation (d<1.006 g/ml) to yield a supranatant containing VLDL. LDL cholesterol was determined by difference, that is, cholesterol in the infranatant fraction after ultracentrifugation (HDL plus LDL) minus HDL cholesterol equals LDL cholesterol.

In study 1 in addition to lipid and lipoprotein analyses, plasma apos A-I, B, C-III, and E were also assessed in fasting blood samples collected at baseline and at the end of phase 4. The quantitative determinations of apolipoproteins were performed by electroimmunoassay procedures at the Oklahoma Medical Research Foundation. 26

Statistical Analysis

Means and standard errors of the mean were calculated for all variables at the end of each of the 10-day dietary periods. Baseline plasma lipid and lipoprotein values were compared with the mean of the lipid and lipoprotein values in each dietary period by repeated-measures analysis of variance (ANOVA) calculated according to the general linear model procedure of SAS. 27 When the ANOVA was significant (p<0.05), contrasts were used to compare differences between the control and the different dietary periods of interest with the use of Bonferroni's corrected paired t tests. 27 We report both the probability values for the ANOVA as well as the corrected probability values for comparisons with the control diet. Exact probability values are reported. Apolipoprotein data analyses were performed by comparing the apolipoprotein values at baseline with their respective levels at the completion of the study, or phase 4, by use of two-tailed paired t tests. Two-tailed paired t tests were also used to analyze the effects of the high-carbohydrate diet during the acute challenge.

Results

Study 1

All patients consumed only the food provided to them. Adherence to the dietary intervention was excellent, and the high-carbohydrate, low-fat diets did not cause side effects in any patient. Body weights did not change during the different dietary periods. At entry, these patients had an average body weight of 84.9±14 kg. On completion of the study, their average body weight remained unchanged (85.0±14 kg). Individual responses to each dietary period for levels of plasma cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, and VLDL triglyceride are presented in Figures 1 and 2. Mean levels of plasma lipids and lipoproteins and the ratios of total and LDL cholesterol to HDL cholesterol are shown in Table 3.

Compared with the values during consumption of the control lower-carbohydrate diet (45%), the plasma levels of triglyceride did not change significantly during the high-carbohydrate diet at any time point (Table 3). The even more sensitive VLDL triglyceride levels also remained unchanged. The plasma triglyceride levels were 213 mg/dl during the
control diet and 230 mg/dl after the phase 4 high-carbohydrate diets (p=0.70). VLDL triglyceride reflected a similar pattern: 147 mg/dl while patients were on the control diet and 157 mg/dl after the high-carbohydrate diet (p=0.92). Furthermore, no significant differences were noted in the plasma levels of VLDL cholesterol.

When the plasma cholesterol levels during phases 1 and 2 were compared with the levels during the low-carbohydrate period (45%), no significant change was noted for the first two dietary periods. However, by the end of phase 3 (60% carbohydrate), plasma cholesterol levels decreased from 232 to 209 mg/dl (p=0.04), and phase 4 of the high-carbohydrate diet further reduced the plasma total cholesterol from 232 to 198 mg/dl, a 15% decline (p=0.0036). Significant changes occurred in LDL cholesterol levels in all dietary periods compared with baseline. LDL cholesterol decreased from 161 to 144 mg/dl (phase 1) to 141 mg/dl (phase 2), to 134 mg/dl (phase 3), and to 126 mg/dl at the end of the study, a 22% reduction (p=0.001).

HDL cholesterol decreased from 43 to 36 mg/dl at the completion of the study, or phase 4 (16%). However, after adjustment for post hoc comparisons, this decrease was not statistically significant. No significant difference occurred in the ratios of total or LDL cholesterol to HDL cholesterol.

Although the high-carbohydrate diet did not produce significant differences in plasma concentrations of apolipoproteins (Table 4) between the control and the final dietary period, the apolipoprotein concentrations of A-I, A-II, and B tended to decrease. Those decreases were concurrent with the significant declines in HDL and LDL cholesterol levels.

Study 2

The effects of a sudden increase in dietary carbohydrate for each patient are depicted in Table 5 and Figure 3. Body weights did not change during this dietary period. During the acute challenge of the high-carbohydrate diet (phase 4) to six of the subjects (subjects 1, 2, 3, 4, 7, and 8), total triglyceride concentration increased significantly, from 204 to 296 mg/dl, a 47% increase. VLDL triglyceride levels increased concurrently, from 137 to 215 mg/dl, a 73% increase.

Although total cholesterol concentrations had not attained a steady state, we observed that while the VLDL cholesterol increased by 46% 10 days after this high-carbohydrate challenge, the LDL cholesterol decreased from 174 to 143 mg/dl, an 18% decline (p<0.0001), indicating a shift in the distribution of the plasma cholesterol from LDL to VLDL. HDL cholesterol remained unchanged at the end of this 10-day period.

Discussion

Carbohydrate-induced hypertriglyceridemia was prevented in eight male and female subjects by gradually increasing the dietary carbohydrate intake over time. Typically, when the amount of dietary carbohydrate is suddenly increased, hypertriglyceridemia invariably results within a few days, a fact also documented in the acute challenge (study 2) by the 65% carbohydrate, 20% fat diet of our study. This result indicated the susceptibility of our subjects to the phenomenon of carbohydrate-induced hypertriglyceridemia, a physiological response: the higher the initial plasma triglyceride concentration, the greater the hypertriglyceridemia that ensued. The mechanism of this effect is enhanced synthesis of triglyceride and VLDL by the liver. In addition, a high-carbohydrate diet produces both greater num-
TABLE 3. Plasma Lipid and Lipoprotein Levels* After Different Dietary Phases of the High-Carbohydrate Diets

<table>
<thead>
<tr>
<th>Percent of calories as carbohydrate</th>
<th>Control</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>p values for ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>232±15</td>
<td>223±15</td>
<td>216±15</td>
<td>209±14‡</td>
<td>198±13‡</td>
<td>0.0001</td>
</tr>
<tr>
<td>VLDL*</td>
<td>40±9</td>
<td>43±7</td>
<td>41±6</td>
<td>41±5</td>
<td>42±7</td>
<td>0.9280</td>
</tr>
<tr>
<td>LDL*</td>
<td>161±17</td>
<td>144±16§</td>
<td>141±16§</td>
<td>134±14¶</td>
<td>126±15#</td>
<td>0.0001</td>
</tr>
<tr>
<td>HDL*</td>
<td>43±4</td>
<td>41±3</td>
<td>44±4</td>
<td>42±3</td>
<td>36±3</td>
<td>0.0190</td>
</tr>
<tr>
<td>Total/HDL</td>
<td>5.8±0.7</td>
<td>5.6±0.5</td>
<td>5.1±0.4</td>
<td>5.1±0.2</td>
<td>5.6±0.4</td>
<td>0.2445</td>
</tr>
<tr>
<td>LDL/HDL</td>
<td>4.1±0.7</td>
<td>3.6±0.4</td>
<td>3.3±0.3</td>
<td>3.2±0.3</td>
<td>3.6±0.4</td>
<td>0.0888</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>213±38</td>
<td>232±37</td>
<td>237±30</td>
<td>230±37</td>
<td>230±35</td>
<td>0.7042</td>
</tr>
<tr>
<td>VLDL</td>
<td>147±39</td>
<td>169±42</td>
<td>171±37</td>
<td>171±46</td>
<td>157±37</td>
<td>0.9280</td>
</tr>
</tbody>
</table>

VLDL, very low density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein.

*All values are in mg/dl and are mean±SEM.

Bonferroni corrected paired t tests: ‡p=0.0004, 45% vs. 65% carbohydrate values; §p=0.0108, 45% vs. 50% carbohydrate values; ¶p=0.0376, 45% vs. 55% carbohydrate values; †p=0.0048, 45% vs. 60% carbohydrate values; #p=0.0004, 45% vs. 65% carbohydrate values.

TABLE 4. Apolipoprotein Changes After a High-Carbohydrate Diet

<table>
<thead>
<tr>
<th>Variable</th>
<th>Entry 65% CHO diet</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apolipoprotein A-I</td>
<td>139±6.0</td>
<td>124±13.4</td>
</tr>
<tr>
<td>Apolipoprotein A-II</td>
<td>57±2.5</td>
<td>49±4.5</td>
</tr>
<tr>
<td>Apolipoprotein B</td>
<td>90±10.5</td>
<td>76±8.1</td>
</tr>
<tr>
<td>Apolipoprotein C-III</td>
<td>14±2.1</td>
<td>14±2.0</td>
</tr>
<tr>
<td>Apolipoprotein E</td>
<td>13±2.1</td>
<td>13±1.4</td>
</tr>
</tbody>
</table>

Values are in mg/dl and are mean±SEM. CHO, carbohydrate.

TABLE 5. Effects of a High-Carbohydrate Diet on Plasma Lipid and Lipoprotein Levels in Study 2 (Acute Challenge)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cholesterol (mg/dl)</th>
<th>Triglycerides (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>VLDL</td>
</tr>
<tr>
<td>Control diet</td>
<td>243±12</td>
<td>39±11</td>
</tr>
<tr>
<td>65% CHO diet</td>
<td>233±13</td>
<td>50±12</td>
</tr>
<tr>
<td>Percent Δ</td>
<td>-4</td>
<td>+46</td>
</tr>
<tr>
<td>p</td>
<td>NS</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Values are in mg/dl and are mean±SEM. VLDL, very low density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein; CHO, carbohydrate; Δ, change.

bers of VLDL particles and larger particles that are relatively richer in triglyceride content.²⁹,³⁰

Using a diet high in carbohydrate content, Melish and colleagues²⁹ reported that the VLDL triglyceride synthetic rate increased; there was, however, no increase in VLDL apo B production rate, and thus, increased rates of secretion of VLDL triglyceride in the setting of constant VLDL apo B secretion must result in nascent VLDL particles with a high ratio of triglyceride to apo B. We routinely used a standard high-carbohydrate diet to induce hypertriglyceridemia. In one of our published studies,²⁰ plasma triglyceride increased even more (85%) in response to a high-carbohydrate formula diet. This response was completely blocked by the concurrent ingestion of ω-3 fatty acids from fish, which inhibit the hepatic synthesis of triglyceride.³¹ In our present study, while the acute feeding of a high-carbohydrate diet produced hypertriglyceridemia, the gradual phased-carbohydrate approach presumably allowed metabolic adaptation to occur without the usual stimulus of a high-carbohydrate intake to enhance VLDL and triglyceride synthesis.²⁰

In a historical context, Ahrens et al²⁸ published their classic article in 1961 demonstrating that subjects with elevated plasma triglyceride levels developed further increases when acutely fed a high-carbohydrate diet. They introduced the concept of "carbohydrate-induced lipemia" and postulated that this was a common phenomenon, "especially in the areas of the world distinguished by caloric abundance and obesity." Antonis and Bersohn³² showed that changing from a low- to a high-carbohydrate diet caused a rise in fasting serum triglyceride concentration, regardless of the type of fat consumed in the preceding regimen. The difference in carbohydrate content between the two diets corresponded to 25% of the total caloric intake. The average concentration of serum triglyceride reached a maximum, about double the starting value, 3-5 weeks after the dietary change. After 32 weeks on the high-carbohydrate diet, most of the subjects had triglyceride levels similar to initial values. A substantial degree of
variability in the individual responses was observed; some of the subjects showed only moderate increases in triglyceride concentration, while others developed marked hypertriglyceridemia. This study supported the concept that carbohydrate-induced hypertriglyceridemia may ultimately be resolved in some subjects. However, Reaven and colleagues found that the elevated plasma triglyceride from a high-carbohydrate diet did not resolve after 6 weeks.

Fasting plasma triglyceride levels in free-living populations accustomed to receiving 65% or more of their calories from carbohydrates are not profoundly higher than those seen in Western populations. Tarahumara Indians of Mexico consume 75% of their calories as carbohydrate from corn and beans and have mean plasma triglyceride levels of 150 mg/dl and very low plasma cholesterol levels of 133 mg/dl. It is apparent from these studies that diets nutritionally adequate in every respect may contain a very high carbohydrate content and yet result in triglyceride levels similar to those observed in Western populations, but with greatly lower plasma cholesterol levels as in the Tarahumaras.

Another significant advantage of the low-fat, high-carbohydrate diet used in this study would be a great reduction in postprandial triglyceride-rich lipoproteins, which are not measured in fasting plasma; these include chylomicrons and their remnants. Such postprandial particles are certainly considered atherogenic and should be avoided whenever possible. Our phase 4 diet with an energy intake of 2,800 kcal and 20% fat content would contain only 50 g fat. This would clearly generate only half as much postprandial triglyceridemia as would a diet containing 100 g fat, the typical American norm. Even a high-fat diet of monounsaturated fat, which might lower LDL levels, would still generate large amounts of postprandial particles. Fish oil, however, did inhibit postprandial lipemia.

In addition to preventing hypertriglyceridemia in study 1, the concomitant gradual reduction of dietary saturated fat and cholesterol greatly lowered the total and LDL cholesterol levels. On average, plasma total and LDL cholesterol levels were 15% and 22% lower, respectively, after the high-carbohydrate diet when compared with their control baseline diet values. Furthermore, significant changes in mean plasma cholesterol levels were seen even at the completion of phase 3 (60% carbohydrate, 25% fat, and 15% protein). The dietary composition of this phase is similar to the recent recommendation by the National Cholesterol Education Program Expert Panel on Dietary Therapy of Hypercholesterolemia. The Bonferroni adjusted t tests showed that LDL concentrations actually decreased significantly for each phase of the study. Because emphasis has recently been placed on the particular atherogenicity of LDL, an apo B-100–rich lipoprotein, the decreases of LDL levels obtained in this study are especially pertinent. The major benefit of the high-carbohydrate diet was that it was possible to greatly reduce total and saturated fat as well as dietary cholesterol. The biochemical mechanism whereby dietary cholesterol and saturated fat elevate plasma LDL levels is through their effect on the LDL receptor in the liver. These dietary factors downregulate LDL receptor activity by decreasing the synthesis of LDL receptor mRNA.

A convenient way to express the action of dietary cholesterol and saturated fat on the LDL receptor would be through a single number, the cholesterol–saturated fat index developed from regression equations. The cholesterol–saturated fat index is 26 per 1,000 kcal for the American diet and only 7 for the phase 4, 20% fat diet. Consequently, the high-carbohydrate, low-fat diet would permit the expression of maximal LDL receptor activity for the removal of LDL from the plasma. Synthesis of cholesterol in the liver is probably also reduced with less dietary saturated fat.

We cannot exclude the possibility that some mild plasma total and LDL cholesterol lowering seen with the high-carbohydrate diet may have resulted from the soluble fiber, saponins, and other substances in plants, but we judge these effects not to have been great. With regard to dietary fiber effects on plasma triglyceride levels, a high-fiber diet did not lower triglyceride levels when body weight was maintained.

The effects of the high-carbohydrate diet on plasma LDL cholesterol during the acute challenge reflect a downward shift, although the effect of the high-carbohydrate diet may not have been fully appreciated because this dietary period had a duration of 10 days, which is insufficient to attain stability in cholesterol and LDL cholesterol levels. However, stability for plasma triglyceride and VLDL probably occurred because of their shorter turnover time. Even for plasma LDL and total cholesterol, it should be indicated that the phased approach (study 1) did take 40 days, and relative stability of their values had occurred by day 30 of the study.

With the high-carbohydrate diet in study 1, the plasma level of HDL cholesterol had decreased 16% by the end of the study. This is an expected response to a low-fat diet; other metabolic studies have shown similar responses. It appears that the decrease in HDL cholesterol is due in part to the enhanced catabolic rate for apo A-I. Furthermore, in a recent report Katan and associates described the effects in populations consuming a high-carbohydrate diet over a lifetime. They observed lower concentrations of HDL cholesterol, and these lower concentrations were not associated with an increased risk of coronary heart disease because the diets were low in fat and cholesterol content and the resultant plasma LDL cholesterol levels were also low. This concept is further supported by the absence of an inverse association between HDL cholesterol concentration and the risk of coronary heart disease among Tarahumara Indians, Masai vegetarians, and others following low-fat, high-carbohydrate diets.
The HDL changes in study 1 were significant in that a low HDL cholesterol level is commonly regarded as an important risk factor for the development of coronary heart disease. Low HDL concentrations have been noted in all population studies in which the dietary fat content is 20% or less of the total caloric intake. A classic population that has undergone many metabolic studies is the Tarahumara Indians of Chihuahua Province in Mexico. Their plasma total cholesterol levels are 133 mg/dl, LDL cholesterol, 87 mg/dl, and HDL cholesterol concentrations, 25 mg/dl. These HDL levels would certainly be considered atherogenic in the American population. Yet, coronary heart disease in this population as well as in other populations consuming low-fat diets is exceptionally rare because the LDL level is also low. It is inappropriate to assume that diet-induced decreases in HDL cholesterol concentrations carry the same burden of atherosclerosis as do low HDL cholesterol levels in high-fat-diet populations.

In summary, our findings indicate that although a sudden increase in dietary carbohydrate increases the levels of triglyceride, human subjects gradually fed a high-carbohydrate diet that ultimately contains 65% carbohydrate, 20% fat, 15% protein, and 100 mg cholesterol had a profound lowering of plasma total and LDL cholesterol levels without developing hypertriglyceridemia at any time during the 7 weeks of the study. For the future, the effects of diets high in carbohydrate and low in fat need critical evaluation in patients with non-insulin-dependent diabetes mellitus and hypertriglyceridemia. These patients are especially susceptible to coronary disease and should have maximal lowering of plasma LDL cholesterol levels. We suggest that the phase-carbohydrate approach may prevent the usual hypertriglyceridemic effect in these adult-onset diabetic patients. The data of the present study certainly suggest the benefits of the high-carbohydrate diet in human subjects with mild hypertriglyceridemia, who ordinarily would be the most susceptible to dietary induction of further hypertriglyceridemia.

Acknowledgments

We are grateful to the nursing and dietary staff of the Clinical Research Center for patient care and assistance in this study and to Petar Alauopovic, Oklahoma Medical Research Foundation, for determination of apolipoproteins. We are also grateful to the patients who participated in this study for their enthusiasm, interest, and cooperation. The authors wish to thank Gary Miranda for his helpful comments in the preparation of the manuscript, Jann Poersch for typing the manuscript, CharEll Melfi for assistance in designing the figures, and Gary Sexton and David Wilson for assistance in the statistical analysis for this project.

References

17. Pyorala K: Relationship of glucose tolerance and plasma insulin to the incidence of coronary heart disease: Results from two population studies in Finland. Diabetes Care 1979;2:131-141


44. Knuiman JT, West CE, Katan MB, Hautvast GAJ: Total cholesterol and high density lipoprotein cholesterol levels in populations differing in fat and carbohydrate intake. *Atherosclerosis* 1987; 7:612–619


**KEY WORDS**  • carbohydrate-induced hypertriglyceridemia • plasma cholesterol • triglycerides • low density lipoproteins • very low density lipoproteins • low-fat diet • low dietary cholesterol • low saturated fat
Will a high-carbohydrate, low-fat diet lower plasma lipids and lipoproteins without producing hypertriglyceridemia?

D Ullmann, W E Connor, L F Hatcher, S L Connor and D P Flavell

doi: 10.1161/01.ATV.11.4.1059

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://atvb.ahajournals.org/content/11/4/1059

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Arteriosclerosis, Thrombosis, and Vascular Biology can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Arteriosclerosis, Thrombosis, and Vascular Biology is online at:
http://atvb.ahajournals.org//subscriptions/