Obese Men With Type IIB Hyperlipidemia Are Insulin Resistant

Pauli Karhapanä, Erkki Voutilainen, Mari Malkki, Markku Laakso

By using the euglycemic clamp technique and indirect calorimetry, we determined the degree of insulin resistance in 12 obese (body mass index >27.0 kg/m²), normotensive patients with type IIB hyperlipidemia (HLIIB) (total cholesterol ≥6.5 mmol/L and total triglycerides ≥2.0 mmol/L) and 17 control subjects (total cholesterol ≤6.1 mmol/L and total triglycerides <1.8 mmol/L) who were carefully matched for sex, age, and obesity. Fasting plasma insulin was higher in HLIIB patients than in control subjects (18.4±4.6 versus 8.9±1.2 mU/L, respectively; P=.010). The rates of whole-body glucose uptake were significantly lower in HLIIB patients than in control subjects during the last hour of the clamp (42.2±3.9 versus 54.6±2.8 μmol/kg per minute, respectively; P=.013). Glucose oxidation during the last 30 minutes of the euglycemic clamp was lower in HLIIB patients than in control subjects (14.6±0.9 versus 19.0±1.3 μmol/kg per minute, respectively; P=.017). Nonoxidative glucose disposal during the last 30 minutes of the euglycemic clamp was also lower in HLIIB patients than in control subjects, but the difference was not statistically significant (27.6±3.3 versus 35.8±2.8 μmol/kg per minute, respectively; P=.069). Lipid oxidation during the clamp was completely suppressed in control subjects (-0.24±0.44 μmol/kg per minute) but was significantly less suppressed in the HLIIB patients (0.94±0.29 μmol/kg per minute, P=.024). Our study shows for the first time that obese patients with type IIB hyperlipidemia are insulin resistant and that this insulin resistance affects both oxidative and nonoxidative glucose metabolism.

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KEY WORDS • type IIB hyperlipidemia • insulin resistance • insulin

Familial combined hyperlipidemia, characterized by multiple and variable lipoprotein phenotypes, is the most common type of familial hyperlipidemia. It was originally defined as the presence of elevated total cholesterol and/or triglyceride levels, but more recently also by the presence of elevated levels of apolipoprotein (apo) B, small very-low-density lipoprotein (VLDL), and small, dense low-density lipoprotein (LDL) particles. Patients with this lipid disorder are at an increased risk for premature coronary heart disease (CHD). Furthermore, the degree of hypertriglyceridemia seems to modify this risk so that patients with high triglyceride and apoB levels are at higher risk for CHD than those with normal triglyceride levels. The mechanisms behind the association of familial combined hyperlipidemia and premature CHD have remained largely unexplained but could be related to the elevation of LDL cholesterol (LDL-C), triglycerides, and apoB.

High levels of VLDL triglycerides and low levels of high-density lipoprotein cholesterol (HDL-C) have been associated with insulin resistance as measured by the euglycemic clamp technique. In contrast, high levels of LDL-C without simultaneous changes in other lipoproteins are not associated with insulin resistance. Since endogenous hypertriglyceridemia is associated with insulin resistance, it could be expected that at least some of the patients with type IIB hyperlipidemia (HLIIB) are insulin resistant. In support of this possibility is the finding that hypertensive subjects with HLIIB are hyperinsulinemic, although the presence of hypertension, an insulin-resistant state itself, may have confounded these results. The degree of insulin resistance in normotensive patients with HLIIB has not been previously directly measured. Therefore, we investigated whether obese men with combined hyperlipidemia were more insulin resistant than matched normolipidemic control subjects.

Methods

Subjects

Male patients with HLIIB were selected from the Lipid Clinic of the Kuopio University Hospital and from population-based studies. The diagnosis of HLIIB was based on the following laboratory determinations: constant elevation of serum total cholesterol ≥6.5 mmol/L and total triglycerides ≥2.0 mmol/L at least twice, in spite of dietary advice, in measurements taken 4 weeks apart. Eight HLIIB patients had hypolipidemic drug treatment, which was discontinued at least 1 month before the oral glucose tolerance test and euglycemic clamp study were performed. Only patients and control subjects who were obese (body mass index [BMI] ≥27.0 kg/m²) were included in our study. All subjects were sedentary. Before the study the patients were advised to reduce the intake of total and saturated fats and to increase the use of unsaturated fats and complex carbohydrates according to the American...
TABLE 1. Characteristics of the Study Groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control Subjects</th>
<th>Type IIB Hyperlipidemia Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of men</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Age, y</td>
<td>51±3</td>
<td>50±2</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>88±2</td>
<td>91±3</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.8±0.4</td>
<td>29.4±0.5</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.99±0.01</td>
<td>1.00±0.01</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>132±3</td>
<td>132±4</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>85±2</td>
<td>88±2</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5.36±0.22</td>
<td>7.42±0.21†</td>
</tr>
<tr>
<td>LDL</td>
<td>3.45±0.19</td>
<td>4.14±0.45</td>
</tr>
<tr>
<td>HDL</td>
<td>1.38±0.06</td>
<td>1.05±0.06†</td>
</tr>
<tr>
<td>VLDL</td>
<td>0.52±0.06</td>
<td>2.24±0.47‡</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1.16±0.08</td>
<td>4.56±0.97‡</td>
</tr>
<tr>
<td>LDL</td>
<td>0.29±0.02</td>
<td>0.57±0.05‡</td>
</tr>
<tr>
<td>HDL</td>
<td>0.18±0.01</td>
<td>0.28±0.05†</td>
</tr>
<tr>
<td>VLDL</td>
<td>0.69±0.06</td>
<td>3.70±0.91‡</td>
</tr>
<tr>
<td>ApoA₁, g/L</td>
<td>1.44±0.04</td>
<td>1.36±0.04</td>
</tr>
<tr>
<td>ApoB, g/L</td>
<td>0.87±0.05</td>
<td>1.55±0.07‡</td>
</tr>
<tr>
<td>(0.37-1.09)</td>
<td>(1.04-1.77)</td>
<td></td>
</tr>
<tr>
<td>LDL-C/apoB ratio</td>
<td>3.96±0.09</td>
<td>2.75±0.34‡</td>
</tr>
</tbody>
</table>

 αP<0.01. †P<0.001.

BMI indicates body mass index; BP, blood pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein; VLDL, very low-density lipoprotein; Apo, apolipoprotein; LDL-C, LDL cholesterol. ApoB range is given in parentheses.

Heart Association Step 1 diet. This diet was also given to subjects when they were admitted to the hospital for metabolic studies.

Male control subjects of corresponding age and obesity were healthy volunteers living in the Kuopio area. Every control subject had serum total cholesterol level <6.1 mmol/L and total triglyceride level <1.8 mmol/L. None of the patients or control subjects had any chronic disease, any drug treatment that could influence carbohydrate metabolism, any abnormality in the oral glucose tolerance test (impaired glucose tolerance or diabetes according to the criteria of the World Health Organization), or hypertension (use of antihypertensive drugs). None of the patients or control subjects had any chronic disease, any drug treatment that could influence carbohydrate metabolism, any abnormality in the oral glucose tolerance test (impaired glucose tolerance or diabetes according to the criteria of the World Health Organization), or hypertension (use of antihypertensive drugs).

Table 1 shows the characteristics of HLIIB patients and their corresponding control subjects. The patients and control subjects were comparable with respect to age, weight, BMI, and blood pressure readings. Total, HDL, and VLDL cholesterol were significantly higher in patients with HLIIB, whereas LDL-C was similar in patients and control subjects. Total, HDL, LDL, and VLDL triglycerides and apoB were higher and the LDL-C/apoB ratio was lower in HLIIB patients than in control subjects. Only one patient with HLIIB had a lower apoB level than the subjects with the highest apoB levels in the control group.

Study Protocol

The subjects were admitted to the metabolic ward for 2 days. On day 1, an oral glucose tolerance test (75 g glucose in 10% solution) was performed, and samples for blood glucose and plasma insulin were drawn at 0, 1, and 2 hours to exclude impaired glucose tolerance or diabetes. On day 2 the euglycemic clamp study and indirect calorimetry were performed.

Informed consent was obtained from all subjects after the purpose and potential risks of the study were explained to them. The protocol was approved by the Ethics Committee of the University of Kuopio.

Euglycemic Clamp

The degree of insulin resistance was evaluated with the euglycemic clamp technique. At 8 AM, after a 12-hour overnight fast, an intravenous catheter was placed in an antecubital vein for the infusion of insulin and 20% glucose. Another cannula for blood sampling was inserted in a wrist vein and surrounded by a heated box (70°C). After baseline blood drawing and measurement of gas exchange (see "Indirect Calorimetry"), a priming dose of insulin (Velosulin Human, Novo-Nordisk, Gentofte, Denmark) was administered during the initial 10 minutes in a logarithmically decreasing manner to acutely raise serum insulin to the desired level, where it was maintained by a continuous insulin infusion of 80 mU/m² per minute. Blood glucose was clamped at 5.0 mmol/L for the next 180 minutes by the infusion of 20% glucose at varying rates according to blood glucose measurements performed at 5-minute intervals. The data were calculated for each 20-minute interval.

Indirect Calorimetry

Indirect calorimetry was performed with a computerized flow-through canopy gas analyzer system (Delta-trac, Datex, Helsinki, Finland) as previously described. This device has a precision of 2.5% for oxygen consumption and 1.0% for carbon dioxide production. On the day of the experiment, gas exchange (oxygen consumption and carbon dioxide production) was measured for 30 minutes after a 12-hour fast before and during the last 30 minutes of the euglycemic clamp. The first 10 minutes of each set of data was discarded, and the mean value of the remaining 20 minutes was used in calculations. Protein, glucose and lipid oxidation rates, and energy expenditure were calculated according to Ferrannini. The rate of nonoxidative glucose disposal during the euglycemic clamp was estimated by subtracting the carbohydrate oxidation rate (as determined by indirect calorimetry) from the glucose infusion rate (as determined by the euglycemic clamp).

Analytical Methods

Blood glucose in the fasting state and during glucose clamp studies was measured by the glucose oxidase method (Glucose Auto & Stat HGA-1120 analyzer, Daiichi Co, Kyoto, Japan). For the determination of plasma insulin, blood was collected in EDTA-containing tubes. After centrifugation, the plasma was stored at -20°C until the analysis. Plasma insulin concentration was determined by radioimmunoassay (Phadeseph Insulin RIA 100, Pharmacia Diagnostics AB, Uppsala, Sweden).
Sweden. Serum lipids and lipoproteins were determined from fresh serum samples drawn after a 12-hour overnight fast. Lipoprotein fractionation was performed by the use of ultracentrifugation and selective precipitation28 as previously described.14 Cholesterol and triglyceride levels from whole serum and from lipoprotein fractions and plasma lactate were assayed by automated enzymatic methods (Boehringer-Mannheim, Mannheim, FRG). ApoB and apoA, concentrations were determined by a commercial immunoturbidometric method (Kone Instruments, Espoo, Finland). Serum free fatty acids (FFAs) were determined by an enzymatic method of Wako Chemicals GmbH, Neuss, FRG. Serum potassium was measured by flame photometry. Nonprotein urinary nitrogen was measured by an automated Kjeldahl method.29

Data Analysis
All calculations were performed using the spss/pc+ program (SPSS Inc, Chicago, Ill). Data are presented as mean±SEM. The nonparametric Mann-Whitney U test was used to compare the two groups. Correlations were calculated by the Spearman method.

Results
Fig 1 depicts glucose and insulin responses to an oral glucose load in patients and control subjects. Fasting plasma glucose (5.1±0.2 versus 5.7±0.1 mmol/L, respectively; not significant [NS]) did not differ significantly between the groups, whereas fasting plasma insulin was higher in HLIIIB patients than in control subjects (18.4±4.6 versus 8.9±1.2 mU/L, respectively; P=.010). In addition, 1-hour and 2-hour plasma glucose levels after a glucose load were similar in patients and control subjects (1 hour, 7.9±0.6 versus 8.0±0.7 mmol/L, respectively; NS; 2 hours, 5.2±0.5 versus 5.2±0.3 mmol/L, respectively; NS). Plasma insulin responses at 1 and 2 hours were higher in patients than in control subjects, but the differences were not statistically significant (1 hour, 156±40 versus 83±13 mU/L, respectively; NS; 2 hours, 82±20 versus 36±8 mU/L, respectively; P=.057).

During the euglycemic clamp studies the blood glucose level was 5.1±0.1 mmol/L in HLIIIB patients and 5.1±0.1 mmol/L in control subjects, with a coefficient of variation <4% during the last 2 hours of the clamp. The steady-state insulin levels during the clamp were 186±8 mU/L in control subjects and 214±12 mU/L in HLIIIB patients (NS).

As shown in Fig 2, the rates of whole-body glucose uptake were significantly lower in HLIIIB patients than in control subjects during the last hour of the clamp (42.2±3.9 versus 54.6±2.8 mmol/kg per minute, respectively; P=.013). The rates of whole-body glucose uptake did not correlate significantly with fasting FFA levels or systolic blood pressure either in the patients (correlations -.59 and .04, respectively) or in the control subjects (correlations -.12 and -.32, respectively). To avoid the possible confounding effect of smoking, the rates of whole-body glucose uptake were also compared in nonsmokers. In nonsmokers the rates of whole-body uptake were also significantly lower in patients (n=9) than in control subjects (n=14) (38.9±4.1 versus 55.3±3.3 mmol/kg per minute, respectively; P=.006).

Table 2 summarizes the results of indirect calorimetry measurements. In the fasting state the rates of glucose and lipid oxidation, the respiratory quotient, and energy expenditure did not differ between the patient and control groups. Glucose oxidation during the last 30 minutes of the euglycemic clamp was lower in HLIIIB patients than in control subjects (P=.017; Table 2 and Fig 2). Nonoxidative glucose disposal during the last 30 minutes of the euglycemic clamp was also lower in HLIIIB patients than in control subjects, but the difference was not statistically significant. Lipid oxidation
Table 2. Indirect Calorimetry Measurements of the Study Groups in the Fasting State and During Euglycemic Clamp

<table>
<thead>
<tr>
<th>Condition</th>
<th>Control Subjects</th>
<th>Type IIB Hyperlipidemia Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory quotient</td>
<td>0.85±0.01</td>
<td>0.83±0.01</td>
</tr>
<tr>
<td>Oxidative glucose disposal</td>
<td>7.9±0.7</td>
<td>6.8±0.6</td>
</tr>
<tr>
<td>Lipid oxidation</td>
<td>2.8±0.3</td>
<td>3.2±1.2</td>
</tr>
<tr>
<td>Energy expenditure</td>
<td>1204±26</td>
<td>1235±33</td>
</tr>
<tr>
<td>(kcal/min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Euglycemic clamp</td>
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<td></td>
</tr>
<tr>
<td>Respiratory quotient</td>
<td>0.97±0.02</td>
<td>0.92±0.01*</td>
</tr>
<tr>
<td>Oxidative glucose disposal</td>
<td>19.0±1.3</td>
<td>14.6±0.9*</td>
</tr>
<tr>
<td>Nonoxidative glucose disposal</td>
<td>35.8±2.8</td>
<td>27.6±3.3</td>
</tr>
<tr>
<td>Lipid oxidation</td>
<td>-0.24±0.44</td>
<td>0.94±0.29*</td>
</tr>
<tr>
<td>Energy expenditure</td>
<td>1344±0.06</td>
<td>1324±31</td>
</tr>
<tr>
<td>(kcal/min)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Measurements are given as micromoles per kilogram per minute. *P<.05.

Discussion

The aim of our study was to investigate the degree of insulin resistance in obese men with HLIIB and corresponding normolipidemic control subjects who were carefully matched for age, sex, and the degree of obesity. Although previous studies show that endogenous hypertriglyceridemia is associated with insulin resistance, our finding of insulin resistance in HLIIB subjects has not been previously reported. The reduction in the rates of whole-body glucose uptake in HLIIB patients was due to the decrease in glucose oxidation, but nonoxidative glucose disposal (glycogen synthesis, lipid synthesis, and anaerobic glycolysis) was also reduced, although the latter change was not statistically significant. Furthermore, our study showed that the suppression of lipid oxidation by insulin was impaired during the euglycemic hyperinsulinemic clamp in HLIIB patients. In contrast, potassium disposal in these patients was normal.

We studied our subjects during a period of insulin concentration of ~200 mU/L, which is a high physiological insulin concentration that stimulates glucose uptake in insulin-sensitive tissues to greater than 80% of the maximum response.30 The insulin concentration obtained in our study completely suppresses the liver glucose production in normoglycemic subjects.31,32 Because the patients with HLIIB were more insulin resistant than the corresponding control subjects, the evaluation of liver glucose production during clamp studies is important. Hepatic glucose production was not measured in this study because we recently demonstrated33 that liver glucose production was completely suppressed in 13 highly insulin-resistant nondiabetic patients with HLIIB who underwent a similar degree of hyperinsulinemia as in the present study. Thus, our results suggest that the defect in glucose uptake in obese patients with HLIIB is in peripheral tissues, most likely in skeletal muscle.

Type IIB hyperlipidemia is a heterogeneous disorder, and lipid phenotype may vary among affected patients when lipoprotein measurements are repeated.3 Environmental factors such as obesity, abdominal obesity, smoking, high intake of saturated fats and carbohydrates, and sedentary lifestyle tend to raise cholesterol and triglyceride levels.34-37 In our study, BMI and waist-to-hip ratio were similar in patients and control subjects, suggesting that the difference in insulin resistance between the groups did not depend on obesity or its distribution. Because waist-to-hip ratio cannot fully account for individual differences in adipose tissue distribution, we cannot exclude that the amount of abdominal visceral adipose tissue, a major contributor to disturbances in glucose and lipid metabolism,38 could be different in our study groups. There were three smokers among patients and control subjects. Non-smokers in the patient group were more insulin resistant than nonsmokers in the control group, excluding the possibility that insulin resistance in combined hyperlipidemia patients could depend on smoking. A recent study shows that reasonable fat and carbohydrate intake does not affect insulin sensitivity as measured by the euglycemic clamp technique.34 Thus, given the similar degree of obesity in patients and control subjects, it is presumable that diet alone does not explain the difference in insulin sensitivity between the groups.

In addition to environmental factors, elevations of total cholesterol and triglyceride levels, characteristic findings in our HLIIB patients, can also be due to...
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With respect to rare inheritable syndromes, eg, apoC-II deficiency, our patients were unrelated and did not show any clinical or laboratory evidence of extreme familial dyslipidemias. Because the lipid and lipoprotein levels of relatives of subjects with HLIIB were not measured, the patients cannot be classified as having familial combined hyperlipidemia. However, they had higher plasma apoB levels, lower LDL-C/apoB ratios, and lower HDL-C levels than the control group. The pattern of high triglyceride and high apoB levels is a characteristic finding in familial combined hyperlipidemia, whereas high triglycerides and normal apoB levels are typical for familial hypertriglyceridemia. Consequently, our patients with HLIIB showed lipid and apolipoprotein phenotypes that are typical for familial combined hyperlipidemia.

The metabolic or genetic defects in our HLIIB patients could be related to mechanisms that regulate lipoprotein lipase. Babirak et al describe the heterozygous state for lipoprotein lipase deficiency, and some of these patients have elevated apoB, which makes them clinically similar to patients with familial combined hyperlipidemia. The same authors report that 36% of patients with familial combined hyperlipidemia had reduced lipoprotein lipase activity. In the present study, we did not measure lipase activities, but it is possible that hyperlipidemia was at least partially due to impaired lipolysis of VLDL triglycerides, because our patients exhibited the elevated apoB levels often seen in subjects with low lipoprotein lipase concentrations. Because hyperinsulinemia or insulin resistance may downregulate muscle lipoprotein lipase activity, insulin resistance could affect lipoprotein levels in HLIIB via reduced lipoprotein lipase activity.

In the present study, both oxidative and nonoxidative glucose disposal rates were equally reduced (23%) during the euglycemic hyperinsulinemic clamp in obese HLIIB patients, although the latter reduction was not statistically significant. Several possibilities should be considered to explain insulin resistance in our patients. First, in hypertriglyceridemic states, including HLIIB, insulin resistance could be due to high FFA levels, since in vivo experimental human studies show that the elevation of FFA levels inhibits glucose oxidation and nonoxidation. In the present study, fasting FFA concentrations and the suppression of FFA levels during the euglycemic clamp did not differ between the groups, thus excluding this possibility. Supporting this interpretation, however, were the correlations between FFA levels and oxidative glucose disposal, although these were not significant (fasting, \(-23, \text{ NS} \); during clamp, \(-27, \text{ NS} \)). Second, the defect in glucose oxidation could be due to high lipid oxidation, as Randle et al have shown that increased FFA/lipid oxidation leads to decreased glucose oxidation in rat heart and diaphragm. Supporting this hypothesis, several studies demonstrate that glucose oxidation and lipid oxidation are negatively correlated. In our study the inverse correlations between lipid and glucose oxidation rates were both high and statistically significant (fasting, \(-78, \text{ P.<.001} \); during clamp, \(-92, \text{ P.<.001} \)). Furthermore, lipid oxidation during the clamp in our study was significantly higher in HLIIB patients than in control subjects, which suggest that low glucose oxidation rates in HLIIB patients could be due to high lipid oxidation. Third, end products of lipid oxidation (ie, citrate, acetyl-coenzyme A) may inhibit glucose oxidation via inhibition of the enzymes involved in the oxidative metabolism of glucose, particularly pyruvate dehydrogenase. Impaired stimulation of pyruvate dehydrogenase by insulin, independent of the increase in lipid oxidation, could also cause a reduction in oxidative glucose metabolism in these patients.

With respect to nonoxidative glucose disposal, a recent study has shown that glycogen synthesis accounts for almost all nonoxidative glucose metabolism in normal man. Presumably, the reduction in nonoxidative glucose disposal in our HLIIB patients was mainly due to the defect in glycogen synthesis. This notion is further supported by the similar increases in lactate levels during the euglycemic clamp studies in both groups, indicating no defect in anaerobic glycolysis in HLIIB patients. Because the reductions in both oxidative and nonoxidative glucose disposal rates were equal (23%), the possibility that the defect leading to reduced rates of whole-body glucose uptake in HLIIB patients could be located proximal to intracellular metabolism of glucose is not excluded. In this case, insulin resistance could simply reflect reduced glucose entry into muscle tissue in HLIIB patients. One of the mechanisms that agrees with this notion is enhanced lipid oxidation in HLIIB patients via the increase in intracellular acetyl-coenzyme A and citrate concentrations, which could lead to the accumulation of glucose 6-phosphate. This, in turn, could result in decreased glucose transport into skeletal muscle and thus in the reduction of both glucose oxidation and nonoxidation.

Previous studies indicate that insulin resistance is associated with high VLDL concentrations, and hence, theoretically, hypertriglyceridemia per se could cause insulin resistance in HLIIB patients. In our recent study we investigated whether the lowering of triglyceride levels improved insulin sensitivity in 13 highly insulin-resistant nondiabetic men with HLIIB. Although triglyceride levels were reduced significantly by 50%, we could see no improvement in insulin sensitivity. This indicates that insulin resistance in HLIIB is of an inherited nature and does not depend on triglyceride concentration in these patients. This conclusion is supported also by other studies on the effects of bezafibrate or gemfibrozil in nondiabetes and in type II diabetics with hypertriglyceridemia. These studies demonstrate unchanged rates of glucose uptake after significant reductions of triglyceride level.

Our patients and control subjects were equally obese. It is clear from previous studies that obesity alone is associated with insulin resistance. Elevated fasting FFA levels and increased lipid oxidation are reported in obese subjects, which contribute, at least in part, to impaired glucose oxidation and nonoxidation in these subjects. Whatever the mechanisms for impaired insulin-mediated glucose uptake in obesity might be, our results suggested that HLIIB further increased insulin resistance related to obesity alone. Whether insulin resistance in combined hyperlipidemia is restricted to obese patients alone or to the type II phenotype needs further studies.

In conclusion, our results showed that obese patients with HLIIB are more insulin resistant than equally obese control subjects. This reduction in the rate of...
whole-body glucose uptake was equally due to reduced oxidative and nonoxidative glucose disposal, although the latter change was not statistically significant. In addition to giving novel metabolic characteristics for patients with HLIIB, our findings may also help to understand why such patients are at increased risk for CHD. The accelerated atherosclerosis often found in these patients is probably mediated not only by changes in lipid and lipoprotein metabolism, but also by hyperinsulinemia and insulin resistance.

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References


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