Effect of Weight Loss on Postprandial Lipemia and Low-Density Lipoprotein Receptor Binding in Overweight Men

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Obestity is associated with a range of metabolic abnormalities including fasting and postprandial dyslipidemia, both of which may contribute to increased atherosclerotic risk. Male obese subjects have a decreased level of low-density lipoprotein (LDL) receptor binding in mononuclear cells, the level of which reflects binding in the liver, compared with lean controls. In this study, we investigated whether the implementation of a weight loss regimen in viscerally obese subjects improves LDL receptor binding level. We examined apolipoprotein B_{48} (apo B_{48}) and retinyl palmitate (RP) metabolism following an oral fat challenge to determine whether weight loss improves postprandial dyslipidemia in viscerally obese subjects. Male obese, mildly dyslipidemic, and insulin-resistant subjects were randomly assigned to either a weight loss (n = 12) or control weight maintenance (n = 10) group. In response to weight loss of 10 kg, insulin sensitivity improved as evidenced by decreased fasting insulin and homeostatic model assessment (HOMA) score. In addition, LDL receptor binding in mononuclear cells increased significantly by 27.5% and LDL-cholesterol was significantly reduced. However, despite the increased LDL receptor levels, fasting apo B_{48} levels did not fall. Postprandially, the area under the curve (AUC) for RP was significantly reduced after weight loss, but the incremental and total AUCs for apo B_{48} were not altered. Apo B_{48} is an unequivocal marker of chylomicron particle number; hence, the reduction in RP metabolism achieved with weight reduction may reflect decreased lipid incorporation into nascent chylomicrons or improved hydrolysis of triglyceride-rich chylomicrons resulting from a decreased competition with hepatic lipoproteins for lipoprotein lipase. Our findings suggest that the improvement in LDL receptor binding following weight reduction of 10 kg in insulin-resistant male obese subjects is insufficient to reduce the elevated chylomicron remnant levels.

AN INCREASED atherosclerotic risk is often associated with obesity, a condition that is becoming more prevalent in society. There are a range of metabolic abnormalities associated with obesity, including dyslipidemia, insulin resistance, and hypertension. The obese state is generally also associated with a low high-density lipoprotein (HDL)-cholesterol level and an increased proportion of small, dense low-density lipoprotein (LDL) particles, thought to be involved in the development of atherosclerosis.[1]

One aspect of the dyslipidemic phenotype includes impaired postprandial lipid metabolism and accumulating evidence supports a role for chylomicron remnants in atherosclerosis.[2-4] An elevated concentration of chylomicron remnants postprandially and in the fasting state may explain the increased atherogenic risk in otherwise normolipemic obese subjects. An increase in plasma chylomicron concentration could occur as a consequence of increased production in the intestine, decreased lipolysis, and/or decreased clearance of remnant particles by the liver. Insulin is known to critically regulate the metabolism of hepatic B_{100}-containing lipoproteins.[5,6] It is likely that insulin also significantly influences the kinetics of chylomicrons, due to the similarity of their metabolic pathways. However, the relationship between insulin and chylomicron biogenesis and clearance is poorly understood in insulin-resistant subjects. As insulin-resistant obese individuals exhibit raised fasting apolipoprotein B_{48} (apo B_{48}) levels, we hypothesized that insulin may be involved in the metabolism of chylomicron particles.[7] Insulin is a potent stimulator of the LDL receptor[8,9]; however, we have previously observed that LDL receptor binding is depressed in insulin-resistant obese subjects.[7] Hepatic clearance of chylomicron particles can occur via a number of mechanisms including endocytosis following binding to either the LDL receptor or the LDL receptor–related protein (LRP). The relative importance of each of these pathways for chylomicron clearance, however, remains to be fully determined. There is growing evidence to suggest that removal of chylomicron remnants via the LDL receptor using apo E as a ligand is the major route of clearance from circulation.[10] Indeed, subjects with homozygous familial hypercholesterolemia exhibit postprandial dyslipidemia and raised chylomicron remnant levels and studies in animal models with defective LDL receptor further substantiate the role of LDL receptor in chylomicron remnant clearance.[11,12] In addition, a recent study by Sposito et al found that in subjects with coronary artery disease (CAD) there is a correlation between their concentration of LDL particles and the rate of clearance of chylomicron-like emulsion particles.[13] On the basis of this evidence we propose that reduced hepatic chylomicron remnant uptake in viscerally obese subjects may, in part, be responsible for the raised levels of these lipoproteins in the fasting and postprandial state. Indeed, we previously found that fasting apo B_{48} concentration was elevated in the obese state, and following a lipid load there is an increased incremental areas under the curve (AUCs) for apo B_{48} and retinyl palmitate (RP) compared to lean controls.[7]

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The increased atherosclerotic risk associated with the insulin-resistant state may in part be a consequence of impaired hepatic uptake of chylomicron remnants via the LDL receptor.

Weight loss has been recognized as an important means of improving insulin sensitivity and reducing the risk of cardiovascular disease.[5,14-16] However, the effect of weight reduction on the LDL receptor is less well understood. The aims of this study were to determine whether increased insulin sensitivity as a result of weight loss is associated with an improvement in LDL receptor binding and consequently whether this translates to an improvement in postprandial lipemia.

MATERIALS AND METHODS

Subjects

Twenty-two male obese subjects aged less than 50 years were recruited from the general community. Subjects were randomized to either a weight loss (n = 12) or weight maintenance (n = 10) group. All subjects underwent a medical examination. Exclusion criteria included smoking within 2 years, liver or endocrine dysfunction, malabsorption syndrome, anemia, hypothyroidism, apo E2/E2 genotype, and the use of lipid-lowering or hypertensive agents. Diabetes was excluded based on fasting plasma glucose being less than 7 mmol/L and a normal response to an oral glucose challenge. Subjects with total plasma cholesterol greater than 6 mmol/L or LDL-cholesterol greater than 4 mmol/L were excluded to avoid the potential confounder of genetic hyperlipidemia. Informed consent was obtained for all subjects. All procedures were approved by the Ethics Committee, Royal Perth Hospital and conformed to the Helsinki Declaration.

Dietary Intervention

Subjects were asked to continue their usual diet, alcohol, and exercise routine for 4 weeks before being randomly assigned to either a weight loss or weight maintenance group. Subjects were encouraged to maintain their usual lifestyle during the 16 weeks of the intervention. Subjects randomized to the weight loss group were given dietary advice to reduce their energy intake, aiming to achieve a weight loss of approximately 8 kg during the first 12 weeks followed by a further 4 weeks during which weight was stabilized. Weight maintenance subjects were periodically monitored to ensure total energy intake remained constant over the 16-week period. The dietary intake of subjects in the weight loss group was monitored fortnightly by way of a 3-day diet record (2 weekdays and 1 weekend) and weight was measured weekly. The subjects that were randomized to the weight maintenance group were weighed every 2 weeks and their dietary intake monitored monthly. Subjects in the weight maintenance group were also offered weight loss advice at the end of the study. Alcohol intake and physical activity were monitored every 2 weeks by way of 7-day retrospective diaries. Weight was measured using an electronic scale while the subject was wearing only light clothing and no shoes. Height was measured with a stadiometer.

Anthropometric Measurements

Body weight, height, and waist and hip circumferences were measured following standardized procedures and using a single trained observer.

Postprandial Lipoprotein Assessment

Oral fat load. Subjects fasted for 14 hours prior to consuming a fat load consisting of 100 mL of cream (fat content, 47% wt/wt) and RP (900 U/kg body weight) flavored with 1 g of chocolate powder. On the day preceding the study, subjects abstained from alcohol and the evening meal was low in fat (<20 g fat). Venous blood samples were collected into tubes containing EDTA just before the meal and at 2-hour intervals up to 10 hours, via a Teflon catheter inserted into the antecubital vein. Subjects remained in a semi-recumbent position during the study, were allowed bathroom access, and were provided with water at all times.

Blood samples were centrifuged at approximately 2,000 × *g* for 10 minutes. Plasma was collected for determination of apo B_{48}, RP, lipids, and insulin. Aliquots of plasma awaiting analysis were stored at −80°C.

Apolipoprotein B_{48} Determination

Apo B_{48} was quantitated using a Western blotting/enhanced chemiluminescence procedure as previously described.[17] Complete recovery of chylomicrons and hydrolyzed remnants requires isolation by ultracentrifugation at a density of less than 1.063 g/mL (576,000 g/h, Beckman SW41 rotor). Apolipoproteins from lipoprotein isolates were separated on a 5% to 20% sodium dodecyl sulfate (SDS) polyacrylamide gel and transferred to polyvinylidine fluoride (PVDF) membranes. The membranes were incubated with an antibody to apo B (DAKO A/S, Glostrup, Denmark), and protein visualized using anti-rabbit IgG (horse radish peroxidase [HRP]-conjugated) (Amersham, Little Chalfont, UK) and enhanced chemiluminescence reagent (Amersham, UK). Membranes were exposed to blue-light film (Amersham, UK) and developed in an AGFA-Gevaert Rapidoprint X-Ray Developer (AGFA-Gevaert, Cologne, Germany). Apo B_{48} bands were identified and quantified by densitometry against purified apo B_{48} protein of known mass. The mean intra- and interassay coefficients of variance for apo B_{48} were each less than 4%.

Quantitation of Retinyl Palmitate

RP was extracted immediately after sample isolation, with appropriate precautions for exposure to light. RP was quantitated by high-performance liquid chromatography (HPLC) on a reverse-phase C18 column (Hewlett Packard, Waldbrunn, Germany) using methanol as the mobile phase.[12] Quantitation was based on the retention time and area response of purified RP and retinyl acetate was used as an internal standard. The coefficient of variation for RP determination by HPLC was 2.4%.

Postprandial Assessment

Postprandial metabolism was quantified by calculating the AUC for plasma triglycerides, apo B_{48}, and RP. For triglyceride and apo B_{48}, the incremental AUC (IAUC) was estimated as the difference between the area defined below the baseline concentration and the AUC for plasma between 0 and 10 hours. The IAUC represents the increase in area after the response of the fat load above fasting concentrations, whereas AUC reflects total plasma concentrations of these measures over time.

Measurement of LDL Receptor Activity in Human Monocytes

Measurement of LDL receptor activity in human monocytes was done according to the method of Roach et al.[18] Briefly, on the day of the postprandial challenge, monocytes were isolated from whole blood using a Ficoll separation method and frozen at −80°C in a background solution of 20% (vol/vol) sucrose. LDL-gold was bound to the monocytes and total and nonspecific binding determined by measuring the absorbance of the bound gold when fixed with a silver stain enhancer (Amersham IntenseSE BL) using a Cobas Mira Autoanalyzer (Roche, Nutley, NJ).

Lipids and Insulin and Lathosterol Assays

Plasma triglyceride (Waco Pure Chemical, Osaka, Japan) and cholesterol (Trace Scientific, Melbourne, Australia) were determined by enzymatic colorimetric kits. Plasma insulin was measured using an

Table 1. Subject Characteristics and Nutritional Data Before and After Intervention

	Weight Maintenance		Weight Loss	
	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention
Age (yr)	52.2 ± 1.6		52.2 ± 1.6	
Wt (kg)	112.0 ± 7.2	111.6 ± 7.3	108.9 ± 3.3	98.9 ± 3.2‡‖
BMI (kg/m^2)	35.6 ± 1.9	35.4 ± 1.9	34.4 ± 0.8	30.9 ± 0.7‡‖
Waist (cm)	120.2 ± 7.4	119.2 ± 8.1	117 ± 2.1	110.4 ± 2.3†
WHR	1.02 ± 0.01	1.02 ± 0.01	1.02 ± 0.01	1.00 ± 0.01*
Pulse (bpm)	69.8 ± 3.0	68.1 ± 3.1	68.9 ± 2.0	62.0 ± 2.4*
Sys BP (mm Hg)	139.4 ± 7.6	142.3 ± 6.3	136.8 ± 5.0	124.1 ± 3.7†§
Dia BP (mm Hg)	78.9 ± 3.6	81.3 ± 3.3	78.2 ± 3.0	73.1 ± 2.8*
EI (kJ/d)	7896 ± 1061	6857 ± 850	6480 ± 566	5448 ± 514†

NOTE. Values are means ± SE.

Abbreviations: Wt, weight; WHR, waist-to-hip ratio; Sys BP, systolic blood pressure; Dia BP, diastolic blood pressure; EI, energy intake; Prot, protein; Carb, carbohydrate.

Statistical differences between pre- and post-intervention values are indicated by *$P < .05$, †$P < .01$, ‡$P < .001$, whereas changes after weight loss that are statistically different to those observed in the weight maintenance group are indicated by §$P < .05$, ¶$P < .01$, ‖$P < .001$.

enzyme-linked immunosorbent assay (ELISA) kit (Dako Diagnostics, Kyoto, Japan). Plasma lathosterol concentration was assayed by a modification of the method of Mori et al using gas chromatography/mass spectrometry (GCMS).[19]

Measurement of Insulin-Resistant State

Estimation of the subjects' state of insulin resistance was by calculation of a homeostatic model assessment (HOMA) score, defined as the product of fasting insulin concentration (mU/L) and fasting glucose concentration (mmol/L) divided by 22.5.[20]

Statistical Analysis

Statistical analysis was by parameteric methods using SPSS for Windows (SPSS Inc, Chicago, IL). Comparison of within-group effects before and after intervention were performed by paired *t* test analysis. Comparison between the weight reduction and weight maintenance groups for changes in lipid parameters and areas under the postprandial curves as a result of the intervention were performed using univariate analysis of variance.

RESULTS

Subject Characteristics

The characteristics of the weight reduction and weight maintenance groups are shown in Table 1. There was no significant difference between the 2 groups at baseline with respect to age, weight, body mass index (BMI), fat mass, waist circumference, waist to hip ratio (W:H ratio), pulse, and systolic and diastolic blood pressure (Table 1). In addition, there was no difference in the dietary intake between both groups prior to the intervention period (Table 1). At baseline there was no difference in fasting triglyceride, total cholesterol, HDL-cholesterol, LDL-cholesterol, glucose, insulin, or apo B_{48} levels between the groups (Table 2). Furthermore, insulin resistance (as measured by the HOMA score) and postprandial metabolism (as measured by the incremental area under the postprandial triglyceride, and apo B_{48} curves, and area under the postprandial RP curve) were not different between groups prior to intervention (Fig 1). A correlation between waist circumference and HOMA ($r = 0.593$, $P < .01$), was found and also BMI was found to correlate with HOMA ($r = 0.567$, $P < .01$).

Implementation of Dietary Modification

During the dietary intervention period subjects in the weight loss group lost on average 10 kg. During this time they reduced energy intake by 16% compared to the pre-intervention period ($P < .01$). The weight maintenance group exhibited no signif-

Table 2. Effects of Weight Loss Intervention on Fasting Lipid/Lipoprotein Levels and Postprandial Metabolism

	Weight Maintenance		Weight Loss	
	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention
TG (mmol/L)	2.3 ± 0.3	2.0 ± 0.3	1.8 ± 0.4	1.5 ± 0.1
TC (mmol/L)	5.4 ± 0.3	5.5 ± 0.4	5.1 ± 0.2	4.5 ± 0.2*
HDL-C (mmol/L)	1.1 ± 0.01	1.1 ± 0.08	1.1 ± 0.01	1.0 ± 0.01
LDL-C (mmol/L)	3.3 ± 0.3	3.4 ± 0.4	3.3 ± 0.2	2.8 ± 0.3*
Gluc (mmol/L)	4.5 ± 0.3	5.0 ± 0.1	4.9 ± 0.3	5.1 ± 0.24
Insulin (IU/L)	13.8 ± 3.3	15.5 ± 4.0	15.0 ± 2.5	8.1 ± 1.0*¶
HOMA score	2.6 ± 0.8	3.4 ± 1.1	3.2 ± 0.5	1.8 ± 0.3*¶
Apo B_{48} (μ/mL)	14.4 ± 1.6	17.8 ± 4.9	24.3 ± 5.1	14.9 ± 3.2
Lathosterol (μmol/L)	10.2 ± 2.3	7.3 ± 1.3	8.2 ± 1.5	6.4 ± 1.5

NOTE. Values are means ± SE.

Abbreviations: TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; Gluc, glucose; HOMA, homeostatic model assessment score; Apo B_{48}, apolipoprotein B_{48}.

Statistical differences between pre- and post-intervention values are indicated by *$P < .05$, †$P < .01$, ‡$P < .001$, whereas changes after weight loss that are statistically different to those observed in the weight maintenance group are indicated by §$P < .05$, ¶$P < .01$, ‖$P < .001$.

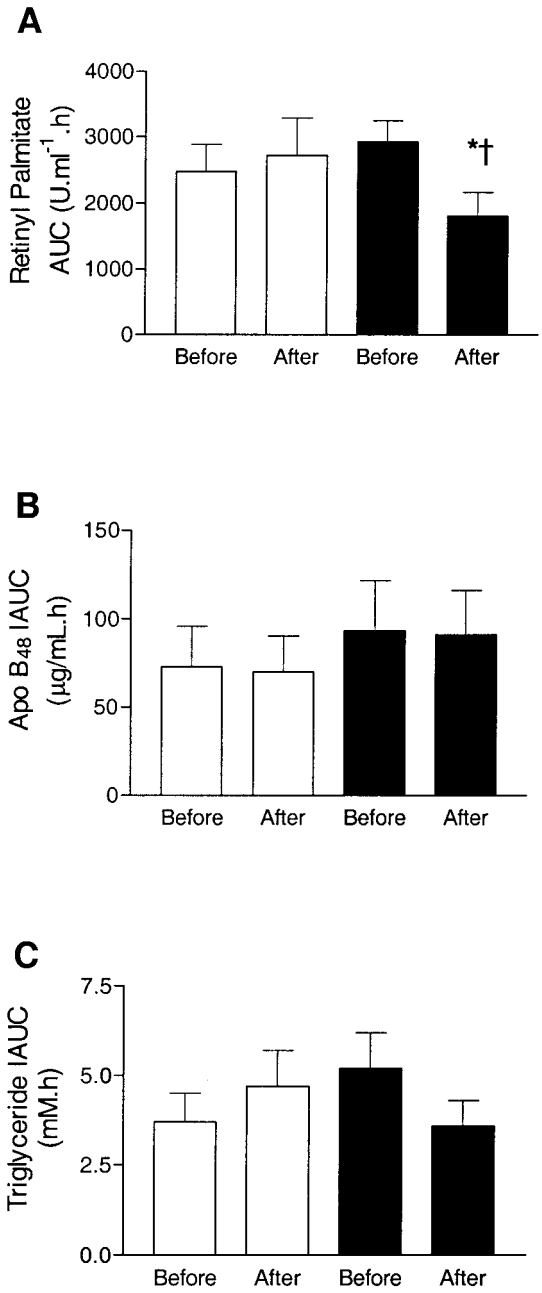

Fig 1. Postprandial measure of lipid metabolism before and after intervention. Shown are means ± SE for RP AUC (A), apo B_{48} IAUC (B), and triglyceride IAUC (C) before and after the intervention period in the maintenance group (□) and weight loss group (■). Statistically significant differences between pre- and post-intervention values are indicated by *$P < .05$, whereas changes after weight loss that are statistically different to those observed in the weight maintenance group are indicated by †$P < .05$.

icant change in caloric intake during the intervention period compared to their pre-intervention diet. There was no change in the reported physical activity in either group before and during the dietary intervention period.

Changes in Anthropometric/Cardiovascular Output Measures

Subjects in the weight reduction group exhibited significant decreases in weight and BMI following intervention compared to the weight maintenance group. Also a significant decrease, albeit modest, in both W:H ratio and waist circumference was observed in the weight reduction group.

An improved cardiovascular output profile was observed after weight loss with significant decreases in pulse rate and both systolic and diastolic blood pressures, although only the change in systolic blood pressure was different compared to maintenance group.

Changes in Insulin Sensitivity

A significant improvement in insulin sensitivity was observed following weight loss, with a decrease in both fasting insulin levels and HOMA score, although fasting glucose levels did not change.

Changes in Lipid Concentrations

Fasting triglyceride levels decreased by 17.5% in response to weight loss, although the difference did not reach significance. The fasting triglyceride level prior to intervention significantly predicted the extent of decrease in fasting triglyceride after weight loss ($r = 0.94$, $P < .01$). Total cholesterol levels also decreased after weight loss, although not compared to the maintenance group. The decline in total cholesterol levels following weight loss paralleled a significant decrease in LDL-cholesterol levels. A significant correlation was observed between the degree of weight loss and the decreases observed in both total cholesterol and LDL-cholesterol levels in the weight loss group ($r = 0.635$, $P < .05$; $r = 0.738$, $P < .01$, respectively). HDL-cholesterol levels were unchanged with weight loss.

Changes in LDL Receptor Binding

We examined LDL receptor binding level in mononuclear cells as a marker for hepatic LDL receptor–mediated particle uptake in order to assess the potential for improved chylomicron clearance following weight loss. Indeed, we detected a significant 27.5% ($P < .05$) increase in the level of LDL receptor binding in mononuclear cells following weight loss, while binding in the weight maintenance group remained unchanged (Fig 2). We did not observe any effect of weight reduction on endogenous cholesterol synthesis as measured by plasma lathosterol concentration (Table 2).

Fasting chylomicron particle number was assessed by measurement of apo B_{48} levels prior to oral fat load assessment. No significant change in fasting apo B_{48} levels was found following intervention; however, there was a trend towards a decrease in apo B48 levels following weight loss (Table 2). Chylomicron metabolism was assessed following an oral fat load using several markers of postprandial lipid metabolism. After weight loss a significantly reduced AUC for RP was observed within the weight loss group, and the decrease was significant compared to the weight maintenance group (Fig 1). Evidence substantiating this finding comes from our observation of a significant correlation within the weight loss group between both the extent of weight loss and the decrease in waist circumference

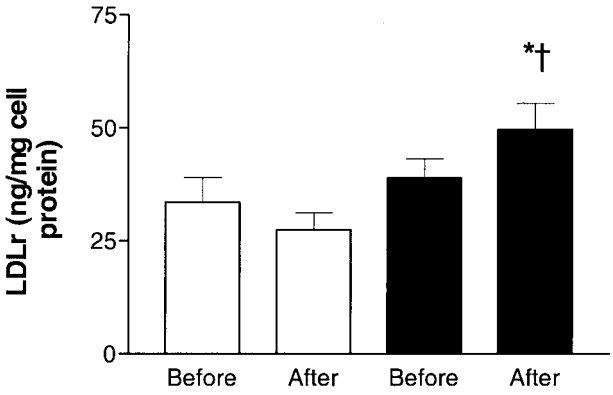

Fig 2. LDL receptor (LDLr) binding in mononuclear cells. Shown are the LDL receptor binding levels from subjects in the weight maintenance group (□) and weight reduction groups (■). Data are means ± SE. Statistically significant differences between pre- and post-intervention values are indicated by *$P < .05$, whereas changes after weight loss that are statistically different to those observed in the weight maintenance group are indicated by †$P < .05$.

and the decrease in area under the postprandial RP curve after intervention ($r = 0.635$, $P < .05$; $r = 0.727$, $P < .01$, respectively).

We observed that modest weight loss did not alter postprandial chylomicron levels in plasma as measured by apo B_{48} IAUC (Fig 1). In addition, the total AUC for apo B_{48}, which reflects total postprandial circulating levels, was not altered by weight loss. Furthermore, we observed no change in postprandial triglyceride metabolism following weight loss, as both the AUC and the IAUC remained unaltered following the fat load (Fig 1).

DISCUSSION

Previously we made the novel observation that in addition to dyslipidemia, obese, insulin-resistant subjects are characterized by reduced LDL receptor binding in mononuclear cells compared to normolipidemic leans.[7] We aimed to further our previous findings by investigating whether the implementation of a weight loss regimen and its associated improvement in insulin sensitivity would lead to an increase in LDL receptor binding in a group of obese mildly insulin-resistant subjects. We observed an improvement in insulin sensitivity as assessed by the HOMA score following weight loss as is commonly observed, particularly if a reduction in visceral adipose tissue is also observed.[16,21,22]

An important finding from this study is that LDL receptor binding in mononuclear cells was increased following weight loss. LDL receptor binding in mononuclear cells closely correlates with hepatic binding; hence, we can infer that weight loss increases the potential for clearance of remnant particles of very-low-density lipoprotein (VLDL) and chylomicrons.[23] We would expect the clearance of both postprandial and hepatically derived lipoproteins following weight loss to be increased as a consequence of increased LDL receptor levels. Decreased LDL-cholesterol levels after weight loss are indeed in keeping with this finding and suggest increased LDL clearance. The improvement in insulin sensitivity may, in part, play a role in the increased LDL receptor binding, presumably by increasing LDL receptor transcription and synthesis.[9] Although we did not observe a correlation between the increase in insulin sensitivity following weight loss and the increased LDL receptor binding in mononuclear cells, it remains possible that the two phenomena are indirectly related via other means.

The hepatic uptake of postprandial and hepatically derived lipoproteins differ in the number of LDL receptors required for their internalization.[24] Weight loss–induced increases in LDL receptor levels therefore would be expected to affect the metabolism of these particles differentially. Chylomicron particles bind the LDL receptor via apo E and require 4 receptors to enable particle uptake and internalization, whereas hepatically derived lipoproteins, which bind via apo B_{100}, require only one receptor. It is likely, therefore, that a greater change in LDL receptor level/binding is required to observe altered chylomicron metabolism than that needed to improve clearance of hepatically derived lipoproteins.

We have used 2 markers to trace postprandial chylomicron metabolism. RP reflects the net result of lipid packaging, secretion, and clearance from circulation, whereas apo B_{48} is an unequivocal marker of chylomicron particle concentration. Although we did not observe a change in postprandial chylomicron levels following weight loss, the effect of weight loss on the RP AUC may be explained by either an attenuation of the lipid delivery to nascent chylomicrons or from increased lipolysis of triglyceride-rich chylomicrons. An increase in triglyceride-rich chylomicron lipolysis may occur in the absence of increased LPL activity, as competition with hepatically derived lipoproteins would be less following weight loss. Indeed, the decrease in postprandial RP levels following weight loss correlated with the extent of weight loss, a finding reported previously.[25] However, despite improvements in LDL receptor levels, postprandial and fasting apo B_{48} levels were not decreased after weight loss. We did not observe a decrease in apo B_{48} area under the postprandial curve (total or incremental) after weight loss; however, fasting apo B_{48} levels tended to decrease. It remains a possibility that a greater effect may have been observed following more extensive weight loss. It is likely therefore that the weight loss–induced increase in LDL receptor binding may play at least a minor role in improved chylomicron metabolism.

Lathosterol levels did not decrease significantly following weight loss in the present study, but has been reported previously[5]; thus, it appears that the observed increase in LDL receptor binding may not be entirely accounted for by increased insulin action on cholesterol biosynthesis,[26] but rather may represent the combined effects of a trend towards a decreased cholesterol biosynthesis and a direct effect of insulin on LDL receptor binding. The observed effects following weight loss in this study are likely to result from a combination of metabolic changes that may be related to insulin sensitivity. However, further improvements in insulin sensitivity may be required to reduce cholesterol biosynthesis significantly.

We have previously reported that hypertriglyceridemia is not a requisite feature of subjects with elevated chylomicron remnant levels (raised apo B_{48}).[7] In this study, sustained weight reduction of 10 kg achieved only a modest reduction in fasting triglyceride concentration. Nonetheless, the observation of a

correlation between the fasting triglyceride level and the change in triglyceride levels after the weight loss period raises the notion that dyslipidemia, as described by elevated fasting triglycerides, is required, at least to some extent, in order to observe an improvement in their levels after weight loss. Similar findings have also been reported recently.[27]

In summary, we have found that moderate weight loss in obese subjects leads to improvements in both insulin sensitivity and LDL receptor binding in mononuclear cells. However, despite increased LDL receptor binding we did not observe a decrease in chylomicron particle number in either the fasting state, or postprandially. The implementation of a more aggressive weight loss regimen or further improvements in insulin sensitivity may therefore be required to decrease plasma chylomicron concentrations to that observed in lean individuals.

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