Ethnic differences in lipid metabolism in two groups of obese South African women

C. Punyadeera,* M-T. van der Merwe,† N. J. Crowther,[1,]* M. Toman,* G. P. Schlaphoff,§ and I. P. Gray*

Department of Chemical Pathology,* South African Institute for Medical Research, University of the Witwatersrand Faculty of Health Sciences, 7 York Road, Parktown 2193, Johannesburg, South Africa and Departments of Endocrinology† and Nuclear Medicine,§ Johannesburg General Hospital, Parktown 2193, Johannesburg, South Africa

Abstract There is a higher prevalence of ischemic heart disease (IHD) in South African white than black women. The objective of this study was to determine biochemical explanations for this prevalence. The study group contained 15 obese black women (OBW) and 14 obese white women (OWW), all premenopausal, who were examined after an overnight fast. Anthropometric measurements and blood concentrations of glucose, non-esterified fatty acids (NEFAs), catecholamines, plasminogen activator inhibitor-1, C-peptide, proinsulin, lipograms, cortisol, growth hormone, and post-heparin lipoprotein lipase activity were measured during an oral glucose tolerance test (OGTT). Body composition was measured using bioelectrical impedance analysis, and subcutaneous and visceral fat mass were assessed with CT-scans. Visceral fat area was higher in OWW (139.7 ± 10.7 cm^2) than in OBW (72.3 ± 3.9 cm^2) ($P < 0.01$), as were fasting and 3 h triglyceride concentrations ($P < 0.05$ for all). OWW also had higher NEFA levels than OBW at 3 and 4 h compared with OBW ($P < 0.05$ for both). Fasting cortisol (266 ± 24 vs. 197 ± 19 nmol/l; $P < 0.05$) was higher in OWW than in OBW. These data demonstrate that OWW have higher visceral fat mass than OBW, which may lead to a more atherogenic fasting and postprandial lipid profile. The higher cortisol levels of the OWW may promote visceral fat deposition.—Punyadeera, C., M-T. van der Merwe, N. J. Crowther, M. Toman, G. P. Schlaphoff, and I. P. Gray. **Ethnic differences in lipid metabolism in two groups of obese South African women.** ***J. Lipid Res.*** **2001.** 42: **760–767.**

Supplementary key words cortisol • fasting and postprandial triglyceride levels • lipoprotein lipase • non-esterified fatty acids • visceral abdominal adiposity

Obesity (body mass index >30 kg/m^2), has a prevalence on the order of 59% in urban black women and 24% in urban white women between the ages of 45–54 years (1). Urban black women, who have a westernized diet and lifestyle, present with more hypertension (30% vs. 15%) and a higher prevalence of type 2 diabetes (7% vs. 3.6%) than do white women (2–4), but have a lower mortality due to ischemic heart disease (IHD) (5–7). The most recent epidemiological study has shown that the incidence of death from IHD within the female population of South Africa is 8 per 100,000 for blacks and 55 per 100,000 for whites (7); however, it is not known if this is also the case for the obese subgroups in each of these two populations. Previous research has also demonstrated a less atherogenic fasting lipid profile in the South African black, as compared with the white, population (8).

The aim of the present investigation was, therefore, to study the lipid profile of the prolonged post-glucose phase and to measure biochemical and anthropometric variables that may contribute to the higher prevalence of IHD in the white population. Plasminogen activator inhibitor-1 (PAI-1), visceral fat mass, and fasting and post-glucose lipograms were analyzed together with hormonal factors that are known to affect lipid metabolism, i.e., insulin, growth hormone, cortisol, adrenaline, and noradrenaline during an oral glucose tolerance test (OGTT).

MATERIAL AND METHODS

Subjects

The study group consisted of 48 premenopausal South African women residing in the greater Johannesburg area selected according to various criteria, which included age, body mass index (BMI), premenopausal status, socioeconomic background, and absence of any metabolic disorders. Of these 48, 29 were obese women (15 black and 14 white). The subjects were defined as obese, i.e., BMI >30, using the WHO criteria (9), and were studied during the first 10 days of the follicular phase of the menstrual cycle. All the subjects had normal liver and kidney function and parity of fewer than 5, and were not on oral contra-

Abbreviations: PAI-1, plasminogen activator inhibitor; HSL, hormone sensitive lipase; LPL, lipoprotein lipase; HDL, high density lipoprotein; LDL, low density lipoprotein; OBW, obese black women; OWW, obese white women.

[1] To whom correspondence should be addressed.
e-mail: 158njcro@chiron.wits.ac.za

Downloaded from www.jlr.org by guest, on June 14, 2012

ceptives. The subjects with metabolic or endocrine disorders were excluded from the study. Subjects were asked to refrain from smoking and vigorous exercise for 48 h prior to the onset of the study. None of the subjects were on any medication known to affect lipid metabolism.

This study protocol was approved by the University of Witwatersrand, Faculty of Health Sciences Human Ethics Committee, and each subject gave written consent. Ten obese women (5 black and 5 white) were also enrolled in a study for the determination of lipoprotein lipase (LPL) activity, and were selected according to the criteria discussed above.

Study protocol

After a 10–12- h overnight fast, the subjects were weighed and their height measured. Lean mass (kg;%) and fat mass (kg;%) were measured using a Bodystat 1500 bioelectrical impedance analyser (The Bodystat Ltd., Douglas, UK) (10). The bioimpedance equations used were based on the South African population as a whole [Fat free mass (kg) = $aH^2/z + bH^2/wt + cH + d$ age + e: H (height); wt (body mass); z (whole body impedance); a, b, c, d, and e are regression coefficients, validated by the Dunn Nutritional Centre, University of Cambridge, UK]. For accurate results the subjects did not drink for 4 h prior to the test, did not consume alcohol for 24 h prior to the test, nor partake in vigorous exercise for 48 h prior to the test. Waist-to-hip ratio (WHR) was measured by taking waist circumference as the midpoint between the lower rib margin and the iliac crest, and hip circumference as the widest circumference of the buttock.

CT scan measurements

A five-level CT scan was performed using computerized axial tomography (CT scan, Philips SR 7000, Netherlands). The scan parameters were 1) 10-mm slice thickness; 2) 120 kV; 3) 250 mA; 4) 2 s; and 5) 34–480-mm field of view, depending on the size of the subject. Photographic images were taken in the resting expiration. Subcutaneous adiposity was measured using a five-level CT scan ranging from the diaphragm, umbilicus, L4-5 lumbar disc, widest diameter of the pelvis, and mid-thigh (the total distance from the iliac crest to the acetabulum and from the acetabulum to the knee joint, divided by 2). The first scanogram included the diaphragm, the umbilicus (marked with a metal coin), iliac crest, and symphysis pubis, with a maximal length of 500 mm from the umbilicus. The second scanogram extended from the symphysis pubis to the knees. The widest parasagittal diameter was measured at the level of L4-5. The fat areas were calculated with a region of interest seeding program on a Philips Gyroview workstation (fat values between −30 and −130 HU were chosen). Subcutaneous and visceral fat areas were calculated separately, and the anatomical boundaries were as described previously (11, 12). Abdominal visceral fat was measured at the top three levels (10). The anthropometric measurements, clinical characteristics and body composition measurements appear in **Table 1**.

OGTT

With the subject in the supine position, a polyethylene catheter was inserted intravenously into the forearm, which was covered in a heating blanket to ensure sampling of arterialized venous blood (13). Normal saline (20 ml) was used to maintain patency of the iv catheter. Blood samples were taken at time intervals as documented in **Table 2**, and in all subjects the fasting sample was taken at 7:30 AM (±15 min). A standardized glucose load of 75 g (SARCHEM, Johannesburg, South Africa) in 200 ml of water was given to the subjects over a 2-min period. The blood samples for catecholamines were placed on ice instantly and were centrifuged within 10 min. All samples were centrifuged at 4°C, and the supernatants frozen and stored at −70°C until analysis as a single batch. A bolus of 5,000 units of heparin was injected 3 h after the glucose load, and samples were collected into heparinized tubes immediately before and 10 min after heparin administration to determine LPL activity.

Biochemical methods

Plasma levels of glucose (normal range: fasting 3–6 mmol/l) were analyzed by a commercially available enzymatic colorimetric method, GOD-PAP (Boehringer, Mannheim, Germany); NEFA (normal range: fasting 100–600 μmol/l) was assayed using an enzymatic colorimetric method (Boehringer); glycerol (normal range: fasting 32–187 μmol/l) was analyzed by automating an existing Boehringer Mannheim food assay kit to run on BM/Hitachi autoanalyser 917; catecholamines (normal range: fasting adrenaline 560-2,636 pmol/l and fasting noradrenaline <366 pmol/l) were measured using a standard high performance liquid chromatography technique (instruments and chemicals; Chromsystems, Munich, Germany). Serum triglyceride levels (normal value: fasting <2 mmol/l), total cholesterol (normal value: fasting <5.2 mmol/l), and high density lipoprotein (HDL) (normal levels for women: fasting >0.9 mmol/l) were measured using enzymatic assay kits (Boehringer). The low density lipoprotein (LDL) levels were calculated (14) at fasting

TABLE 1. Anthropometric data for the four groups of women

Variables	Obese White (n = 14)	Obese Black (n = 15)
Age (years)	42.8 ± 2.5 (40.5)	45.5 ± 2.2 (44)
Weight (kg)	99.5 ± 3.1 (95.9)[a]	92.5 ± 2.6 (93.6)
BMI (kg/m^2)	38.5 ± 1.2 (38.6)	36.8 ± 1.1 (37.0)
Waist circumference (cm)	101.5 ± 2.9 (103)[b]	94.8 ± 2.7 (95)
Hip circumference (cm)	123.7 ± 2.6 (121.0)	123.5 ± 2.1 (123.7)
WHR	0.83 ± 0.01 (0.84)[b]	0.77 ± 0.02 (0.77)
Fat (kg)	50.7 ± 2.4 (51.7)[a]	45.8 ± 2.4 (52.8)
Percentage fat (%)	50.3 ± 1.2 (51.1)	50.1 ± 1.7 (46.1)
Lean (kg)	49.6 ± 1.2 (48.9)	45.8 ± 1.3 (45.3)
Percentage lean (%)	49.6 ± 1.3 (48.9)	49.8 ± 1.7 (47.2)
Subcutaneous fat (cm^2)[c]	549.0 ± 42.6 (475.7)	512.4 ± 32.0 (499.5)
Visceral fat (cm^2)[c]	139.7 ± 10.7 (128.1)[b]	72.3 ± 3.9 (70.6)

Mean values ± SEM; median values are given in parentheses. BMI, body mass index; WHR, waist-to-hip ratio.
[a] $P < 0.05$ OWW versus OBW;
[b] $P < 0.01$ OWW versus OBW.
[c] Fat area measured in 9 OWW and 10 OBW.

Downloaded from www.jlr.org by guest, on June 14, 2012

TABLE 2. Study design

Analytes	Time (min)					
	0	30	60	120	180	240
Glucose	Yes	Yes	Yes	Yes	Yes	—
Insulin	Yes	Yes	Yes	Yes	Yes	—
Proinsulin	Yes	Yes	Yes	Yes	Yes	—
C-peptide	Yes	Yes	Yes	Yes	Yes	—
Cortisol	Yes	Yes	Yes	Yes	Yes	—
Growth hormone	Yes	Yes	Yes	Yes	Yes	—
Lipogram	Yes	—	—	—	Yes	Yes[a]
PAI-1	Yes	—	—	—	—	—
LPL	—	—	—	—	Yes	—
Adrenaline	Yes	—	—	—	Yes	—
Noradrenaline	Yes	—	—	—	Yes	—
NEFA	Yes	Yes	Yes	Yes	Yes	Yes[a]

Yes, blood was collected and assayed at that time point; —, no blood collected; NEFA, non-esterified fatty acid.
[a] Plasma samples were collected from 9 OWW and 10 OBW.

and at 3 and 4 h postprandially. Insulin (normal range: fasting 10–73 pmol/l) concentrations in the serum were determined by an enzyme-amplified immunoassay (Mercodia, Upsala, Sweden). C-peptide concentrations (normal range: fasting 0.3–1.32 nmol/l) were determined by chemiluminescent enzyme immunoassay (Chiron Diagnostics, Emeryville, CA). The lower limit of detection for the C-peptide assay was 0.99 nmol/l. Proinsulin (normal range: fasting 1.30–2.78 pmol/l) was measured using a two-site immunoradiometric assay (15). The lower limit of detection for proinsulin was 1 pmol/l. A commercially available assay kit (ACS: 180; Chiron diagnostics, Boston, MA) was used to measure the cortisol levels (normal range: fasting 200–650 nmol/l) in serum samples and growth hormone (normal range: 1–10 mIU/l) was measured by enzyme immunometric assay using an IMMULITE assay kit (Diagnostic Product Corporation, Los Angeles, CA). For determining LPL activity (normal range: 53–361 ng/ml), a MARKIT-F-LPL kit (Dainippon Pharmaceutical Co. Ltd., Oska, Japan) was used. PAI-1 (normal value: 45 ± 33 ng/ml) concentrations in the fasted samples were measured using a COALIZA method (Chromogenix, Amsterdam, Netherlands). The intra- and interassay coefficients of variation (CV) for the assays were as follows: glucose 0.9% and 1.8%; NEFA <5% for both; glycerol 2.5% and 2.59%; adrenaline 5.0% and 5.7%; noradrenaline 4.5% and 3.9%; LPL <5% for both; plasminogen activator inhibitor-1 5.5% and 7.3%; triglycerides 1.5% and 1.8%; total cholesterol 0.8% and 1.7%; HDL 1.3% and 2.6%; insulin 4% and 3.6%; C-peptide 6.3% and 5.3%; proinsulin <5% for both; cortisol 4.5% and 6.4%; and growth hormone 6.2% and 5.7%, respectively.

Statistical analysis

Data in the text, figures, and tables are presented as means ± SEM, and statistical analysis was carried out using Statistica V5.0 (Statsoft Inc., 1984–1996). One-way analysis of covariance (ANCOVA) was used to measure the differences between the means of biochemical variables (**Figs. 1–3**) for the two obese study groups, adjusting for weight and waist circumference (where appropriate). One-way ANCOVA was also used for the comparison of anthropometric means adjusting for total body fat when analyzing visceral and subcutaneous adipose areas. Partial correlation analyses were used to test whether correlation existed in either of the subgroups and in the full combined group. Differences in correlations between groups were examined using multiple regression analysis, with weight included as a covariate. The appropriate slope and intercept terms of the regression models were compared between the groups, and a significance level of $P < 0.05$ was used in all statistical analyses. Cortisol and growth hormone data were nonsymmetrically distributed and were therefore log-transformed for regression analysis. Total glucose, insulin, cortisol, growth hormone, and NEFA during the 3-h OGTT were calculated by measuring area under the curve (AUC) using the trapezoid rule (16).

The number of subjects in each study group was sufficient to detect statistically and clinically significant differences in the metabolic variables under investigation.

RESULTS

Anthropometric measurements

Age, BMI, waist circumference, hip circumference, body fat (%), lean body mass (kg), and amount of subcutaneous abdominal fat were similar in both obese subject groups (see Table 1). The amount of visceral fat mass and WHR were significantly higher in OWW than in OBW ($P < 0.01$).

Glucose concentrations

The mean (± SEM) fasting and postprandial glucose levels are shown in Fig. 1A. No differences were noted between the two groups. The total glucose level ($AUC_{0-180min}$; expressed in mol/l × min) in OBW (1.24 ± 0.03) was not different from that in OWW (1.33 ± 0.06).

Insulin concentrations

Obese black and white women had similar insulin levels throughout the entire study (Fig. 1B). No differences in total insulin ($AUC_{0-180min}$) were documented between OBW (84.8 ± 12.0) and OWW (88.2 ± 12.0 nmol/l × min).

C-peptide concentrations

The 60-min C-peptide level was higher in OWW than in OBW (Fig. 1C), and total C-peptide ($AUC_{0-180min}$) (555 ± 43 vs. 443 ± 39 nmol/l × min; $P < 0.05$) was also higher in OWW than in OBW.

Downloaded from www.jlr.org by guest, on June 14, 2012

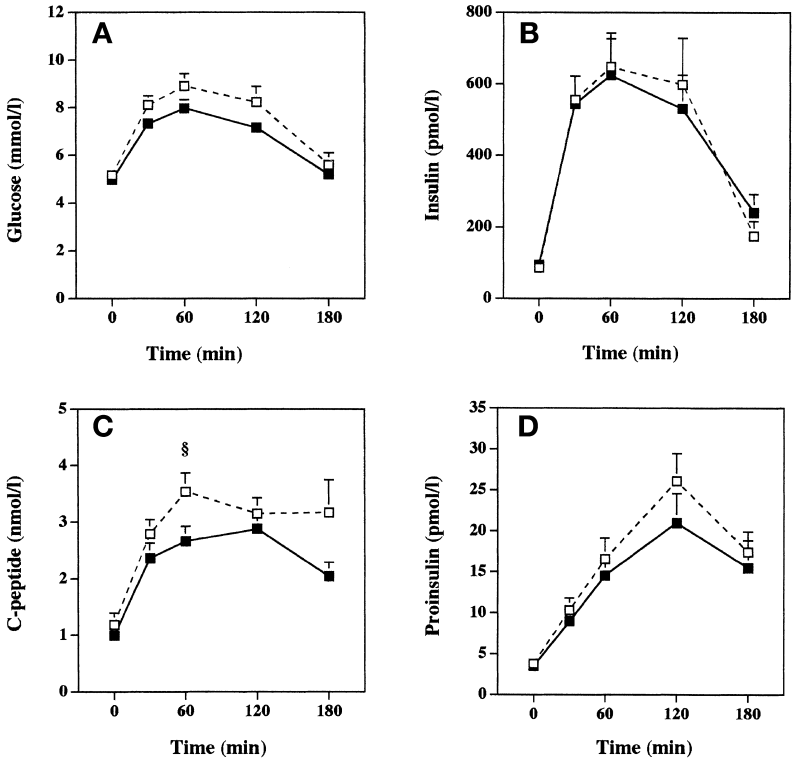

Fig. 1. Plasma levels of glucose (A) and serum levels of insulin (B), C-peptide (C), and proinsulin (D) in ■ obese black and □ obese white women; $^{\S}P < 0.05$ for obese black versus obese white women.

Serum proinsulin concentrations

No interethnic differences were noted in total (3.20 ± 0.40 for OWW and 2.70 ± 0.40 nmol/l × min for OBW) or fasting (Fig. 1D) proinsulin levels between the two groups.

Fasting and post-glucose lipid profile

The OWW had significantly higher fasting total cholesterol, triglyceride, and LDL than did OBW ($P < 0.05$ for all) (**Table 3**). Triglyceride at 3 h (1.51 ± 0.19 mmol/l vs. 0.83 ± 0.13 mmol/l) ($P < 0.01$) and at 4 h (1.73 ± 0.27 vs. 0.89 ± 0.18 mmol/l) ($P < 0.01$) were higher in OWW than in OBW (Table 3). The 3- and 4-h triglyceride levels correlated positively with visceral fat mass independent of age and weight in obese women ($r = 0.54$, n = 19, $P < 0.05$).

Cortisol, catecholamine, and growth hormone concentrations

Fasting cortisol levels were higher in OWW (266 ± 24 nmol/l) than in OBW (197 ± 19 nmol/l; $P < 0.05$) (Fig. 2A), but total AUC levels were not different (43.5 ± 5.9 for OWW and 34.7 ± 2.7 mmol/l × min for OBW).

No differences were noted in growth hormone levels (Fig. 2B), and total AUC levels were also similar (315 ± 69 for OWW and 200 ± 56 mIU/l × min for OBW).

Adrenaline levels at fasting were 222.2 ± 72.7 and 128.0 ± 41.0 pmol/l, and at 3 h were 247.0 ± 89.7 and 225.0 ± 69.0 pmol/l in OWW and OBW, respectively. Noradrenaline levels at fasting were 1,222 ± 215 and 1,398 ± 205 pmol/l, and at 3 h were 1,354 ± 143 and 2,039 ± 757 pmol/l in OWW and OBW, respectively. No significant differences in levels of either catecholamine were noted.

Plasma NEFA concentrations

OWW had higher NEFA at 180 min (99.2 ± 38.9 vs. 21.1 ± 4.8 μmol/l, $P < 0.05$) and 240 min (556.7 ± 71.8 vs. 278.6 ± 65.3 μmol/l, $P < 0.05$) than did OBW (Fig. 3). Total AUC NEFA levels were similar (59.7 ± 8.1 in OWW and 45.7 ± 3.9 mmol/l × min in OBW). Percentage suppression of NEFAs at 30 min of the OGTT from the fasting value was 28.4 ± 9.5% in OWW and –13.5 ± 18.1% in OBW ($P < 0.05$), i.e., there was no suppression in the early post-glucose NEFA levels in the latter group. Total NEFA ($AUC_{0-240min}$) correlated positively with visceral, but not subcutaneous, fat mass, independent of age in the obese women ($r = 0.52$, $P < 0.05$, n = 18).

PAI-1 concentrations

Basal PAI-1 concentrations were as follows: OWW, 50.4 ± 6.0 ng/ml and OBW, 45.2 ± 6.2 ng/ml. No interethnic differences in the levels of PAI-1 were noted.

LPL concentrations

LPL activity was determined at the 240-min time point of an OGTT and 10 min after injecting a bolus of heparin in 5 OBW and 5 OWW. The results were as follows: OWW, 69.5 ± 32.6 ng/ml and OBW, 39.7 ± 9.6 ng/ml (P = ns).

DISCUSSION

Previous studies in South Africa have shown that ischemic heart disease (IHD) is far more prevalent in white than in black women (5–7), despite a high incidence of obesity in both populations (1). The present study was

Downloaded from www.jlr.org by guest, on June 14, 2012

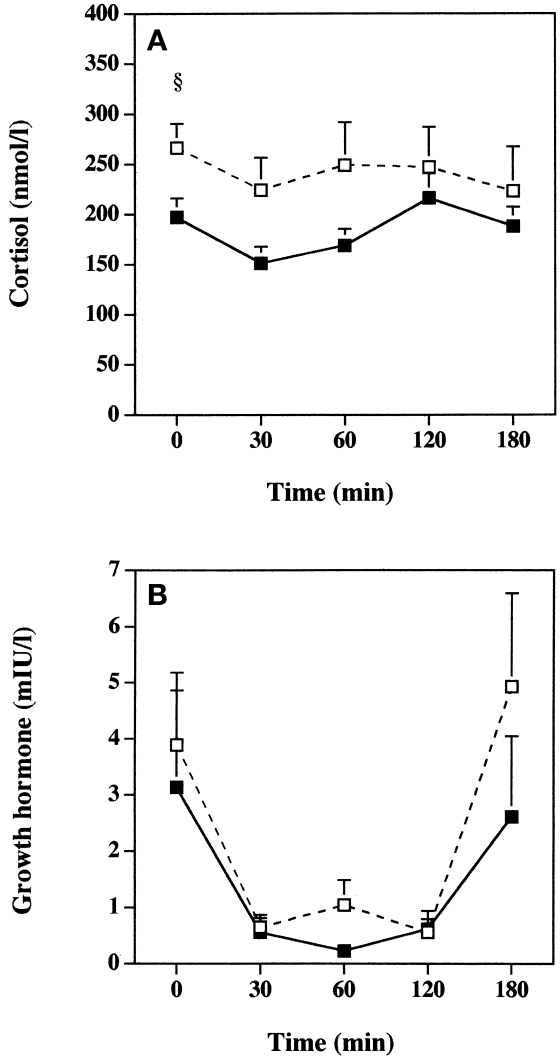

Fig. 2. Serum levels of cortisol (A) and growth hormone (B) in ■ obese black and □ obese white women; $^{\S}P < 0.05$ for obese black versus obese white women.

undertaken to determine possible factors that may protect the black population against IHD, despite the escalating incidence of type 2 diabetes in South Africa (3, 4). Studies have shown that the black population of South Africa has a less atherogenic fasting lipid profile than the white population (8, 17), and the present investigation confirmed this.

The present study shows that visceral fat area and WHR were greater in the obese white population. This was not simply a result of the greater fat mass of the OWW, as a significant interethnic difference was still observed in an ANCOVA correcting for fat mass. Previous studies of OWW and OBW matched for fat mass also demonstrated interethnic differences in visceral fat area (10, 18). This fat depot is more lipolytically active than subcutaneous fat (19, 20) owing to higher β-adrenoreceptor-mediated catecholamine-induced lipolysis and greater resistance to the antilipolytic activity of insulin (21). The greater visceral fat mass may contribute to the poor lipid profile in OWW via the release of NEFAs directly into the portal vein (22). High NEFA levels in the liver increase hepatic very low density lipoprotein output, leading to an increase in plasma triglyceride and cholesterol concentrations (23). High triglycerides in turn cause the production of smaller LDL particles (24) and decrease HDL levels (25, 26). The present study demonstrates a positive correlation between visceral fat mass and post-glucose triglyceride levels. Furthermore, visceral fat mass (19) and C-peptide concentrations (27) have both been positively associated with an increased risk of IHD, and both these factors are higher in OWW than in OBW. However, no interethnic differences in PAI-1 concentrations were observed, and therefore ethnic differences in the prevalence of IHD are unlikely to be related to this peptide.

The NEFA levels during the late post-glucose period were higher in OWW than in OBW. This was not due to catecholamine or growth hormone levels, as these were the same in both populations, confirming a previous study (10). Visceral fat area was greater in OWW than in OBW and it has been shown that in men with a higher visceral fat mass than weight-matched controls, postprandial NEFA levels were higher (28). The present study also showed that NEFA levels correlated with visceral, but not subcutaneous, fat area. The mechanism by which visceral fat, which represents only a small percentage of the total body fat mass (19), may cause high postprandial NEFA concentrations in the general circulation is unclear, although it has been suggested that high visceral fat mass may impair the inhibition of adipose tissue lipolysis (29).

The subcutaneous adipose tissue depot may also be involved in the exaggerated post-glucose NEFA response of the OWW. A recent study has shown that OWW have lower subcutaneous adipose tissue blood flow than do OBW (10). Plasma NEFA uptake by adipose tissue may thus be slower in OWW, and this may also contribute to the elevated late post-glucose NEFA levels.

Fasting cortisol levels were found to be higher in OWW than in OBW. This is unlikely to be due to differences in sampling times, as the fasting blood samples were taken at

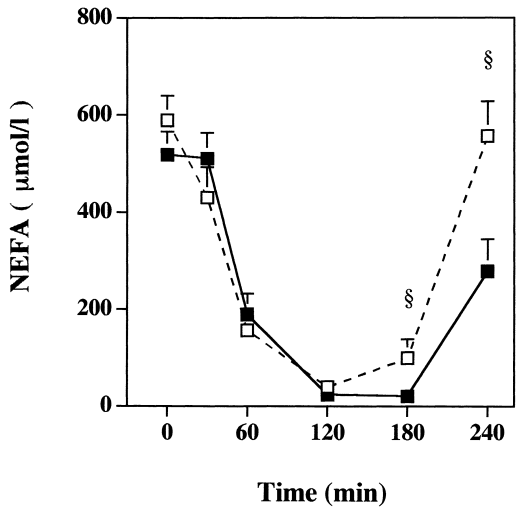

Fig. 3. Plasma levels of free fatty acids in ■ obese black and □ obese white women; $^{\S}P < 0.05$ for obese black versus obese white women.

Downloaded from www.jlr.org by guest, on June 14, 2012

TABLE 3. Fasting and postprandial lipogram results for the four groups of women

Analytes (mmol/l)	Obese White (n = 14)	Obese Black (n = 15)
Fasting		
Total cholesterol	5.76 ± 0.35	4.40 ± 0.19[a]
Triglyceride	1.70 ± 0.22	0.96 ± 0.12[a]
HDL-C	1.45 ± 0.20	1.43 ± 0.11
LDL-C	3.55 ± 0.28	2.53 ± 0.21[a]
3 hours		
Total cholesterol	5.11 ± 0.32	3.89 ± 0.26
Triglyceride	1.51 ±0.19	0.83 ± 0.13[b]
HDL-C	0.95 ± 0.08	0.91 ± 0.08
LDL-C	3.47 ± 0.28	2.61 ± 0.20
4 hours[c]		
Total cholesterol	4.79 ± 0.40	4.22 ± 0.26
Triglyceride	1.73 ± 0.27	0.89 ± 0.18[b]
HDL-C	0.84 ± 0.06	1.00 ± 0.09
LDL-C	3.14 ± 0.36	2.82 ± 0.24

[a] $P < 0.05$ OBW versus OWW;
[b] $P < 0.01$ OBW versus OWW.
[c] Blood samples collected from 9 OWW and 10 OBW.

the same time in all the subjects. Whether the circadian rhythm of cortisol secretion (30) displays ethnic variation is not known and should be investigated further. Cortisol increases the levels of serum NEFA and LPL activity (31), an enzyme crucial in the uptake of triglycerides by adipocytes. Cortisol increases lipolysis via effects on gene transcription with a recognized time lag (over 2–4 hours) between administration or secretion and response (32, 33). The high NEFA levels in OWW at 3 and 4 h after oral administration of the glucose load may, therefore, relate to the high fasting cortisol.

The high cortisol levels in OWW may also explain the high visceral fat mass in the former group (34, 35). Visceral fat is known to have a higher level of expression of glucocorticoid receptors than other fat depots (36), and this could lead to increased cortisol-associated metabolic activity. Cortisol increases adipocyte LPL levels (37) and reduces adipocyte hormone sensitive lipase (HSL) activity (38) which could potentially lead to preferential deposition and maintenance of triglyceride stores in this adipose depot. In addition, cortisol promotes adipogenesis (39), and abdominal adipose stromal cells are more responsive to this effect of cortisol than stromal cells from the femoral adipose site (40). Furthermore, visceral adipose stromal cells express higher levels of the cortisol-inducable 11β-hydroxysteroid dehydrogenase type I isoenzyme (which converts cortisone to cortisol) than subcutaneous adipocytes (41). Therefore, the higher serum levels of cortisol in OWW than in OBW may, in turn, enhance visceral fat production of this hormone in OWW. The reason for the higher serum cortisol levels in the white women is not known and obviously warrants further investigation, including measurement of hypothalamic-pituitary-adrenal axis activity.

The suppression of NEFA levels 30 min after administration of an oral glucose load was much greater in OWW than in OBW, and may be due to reduced insulin sensitivity of adipocytes from OBW. Both in vivo (10) and in vitro studies (42) have shown that adipocytes of OBW were more resistant to the antilipolytic action of insulin than those from OWW. This is mirrored by greater whole-body insulin resistance in OBW than in OWW (43), despite the higher level of visceral fat in the latter group, an observation that has also been made about Africans compared with European-Americans (44). This contradictory data may be explained by ethnic differences in adipocyte metabolism (10, 42), which is further emphasized by the finding that leptin levels are higher in OBW than in OWW (18).

It has been hypothesized that the poorer glucose tolerance observed in obese black South Africans may relate to lower pancreatic β-cell numbers (45). It has been suggested that poor fetal growth, possibly as a result of fetal malnutrition, may lead to reduced β-cell numbers and increased insulin resistance (46). A recent study has shown that there is a correlation between glucose tolerance and birth weight within an urban population of black South African children (47), and it has also been shown that the insulin sensitivity of adipocytes can be affected by nutrition during fetal and neonatal life (48). Therefore, it is possible that poor nutrition during these periods of life may cause changes in both peripheral and whole-body insulin sensitivity in this human population.

Although the number of subjects studied in this investigation was small, we believe that our conclusions are valid. The data are supported by results from other studies showing that visceral fat levels are lower in black than in white obese subjects (44, 49) and that lipid profiles are less atherogenic in the former population (8, 50, 51). Furthermore, the higher fasting cortisol and late post-glucose NEFA levels in OWW than in OBW have been confirmed in white and black obese diabetic women (C. Punyadeera et al., unpublished observations).

In summary, the present study has, for the first time in South Africa, examined lipid profiles and related factors during the early and late post-glucose phases. OWW have an adverse lipid profile compared with OBW, and this may be associated with higher visceral fat mass. The more atherogenic lipid profiles of OWW than of OBW are in keeping with data from studies in Africa (8, 17) and America (50, 51). It further appears that the high late post-glucose NEFA concentrations in the OWW could also be due to greater visceral fat mass, decreased subcutaneous adipose tissue blood flow (10), or both. Furthermore, the higher cortisol levels in the white females may promote visceral fat deposition and increase LPL levels. Therefore, multiple factors appear to offer black women from South Africa protection against IHD, despite their higher degree of muscle and adipose tissue insulin resistance.

This research was funded by the South African Institute for Medical Research (SAIMR), the South African Sugar Association, the University of the Witwatersrand Research Committee, Professor John Kalk, Servier and Roche Pharmaceuticals. We thank Sisters Nomsa Ramela and Nancy Holden for carry-

Downloaded from www.jlr.org by guest, on June 14, 2012

ing out the OGTTs. We also thank the SAIMR Chemical Pathology routine laboratories for their excellent technical assistance.

Manuscript received 24 July 2000, in revised form 15 December 2000, and in re-revised form 23 January 2001.

REFERENCES

1. Walker, A. R. P. 1995. Epidemiology and health implications of obesity in southern Africa. *In* Chronic Diseases of Lifestyle in South Africa. J. Fourie and K. Steyn, editors. South African Medical Research Association Technical Report. 73–85.
2. Seedat, Y. K. 1983. Race, environment and blood pressure: the South African experience. *J. Hypertens.* **1:** 7–12.
3. Joffe, B. I., and H. C. Seftel. 1994. Diabetes mellitus in black communities of southern Africa. *J. Int. Med.* **235:** 137–142.
4. Omar, M. A. K., M. A. Seedat, A. A. Motlala, R. B. Dyer, and P. Becker. 1993. The prevalence of diabetes mellitus and impaired glucose tolerance in a group of urban South African blacks. *S. Afr. Med. J.* **83:** 641–643.
5. Wyndham, C. H. 1979. Mortality from cardiovascular disease in the various population groups in the Republic of South Africa. *S. Afr. Med. J.* **56:** 1023–1030.
6. Isles, C. G., and F. J. Milne. 1987. Low mortality from ischemic heart disease among urban blacks in South Africa. *J. Clin. Hypertens.* **3:** 749–775.
7. Walker, A. R. P., A. Adam, and H. G. V. Kustner. 1993. Changes in total death rate and in ischaemic heart disease death rate in interethnic South African populations, 1978–1989. *S. Afr. Med. J.* **83:** 602–605.
8. Seftel, H. C., M. S. Asvat, B. I. Joffe, F. J. Raal, V. R. Panz, W. J. H. Vermaark, M. E. Lock, M. C. Rajput, M. A. K. Omar, M. S. Jeenah, K. Steyn, and P. J. Becker. 1993. Selected risk factors for coronary heart disease in male scholars from the major South African population groups. *S. Afr. Med. J.* **84:** 891–897.
9. World Health Organization Expert Committee: Physical Status: The Use and Interpretation of Anthropometry. 1995. WHO Technical Report Series Number 854. Geneva: WHO.
10. van der Merwe, M-T., N. J. Crowther, G. Schlaphoff, I. H. Boyd, I. P. Gray, B. I. Joffe, and P. N. Lönnroth. 1998. Lactate and glycerol release from the subcutaneous adipose tissue of obese urban women from South Africa; important metabolic implications. *J. Clin. Endocrinol. Metab.* **83:** 4084–4091.
11. Kvist, H., L. Sjöstrom, and U. Tylen. 1986. Adipose tissue volume determinations in women by computerized tomography. *Int. J. Obes.* **10:** 53–67.
12. Kvist, H., B. Chowbury, U. Grangard, U. Tylen, and L. Sjöstrom. 1988. Total and visceral adipose tissue volumes derived from measurements with computed tomography in adult men and women: predictive equations. *Am. J. Clin. Nutr.* **48:** 1351–1361.
13. Sachur, N., and R. H. Eckel. 1982. Insulin stimulation of adipose tissue lipoprotein lipase: use of euglycemic clamp technique. *J. Clin. Invest.* **16:** 13–20.
14. Tietz, N. W. 1995. Clinical guide to Laboratory Tests. 3rd ed. W. B. Saunders Co., Philadelphia. 268–273.
15. Sobey, W. J., S. F. Beer, C. A. Carrington, P. M. S. Clark, B. H. Frank, I. P. Gray, S. D. Luzio, D. R. Owens, A. E. Schneider, K. Siddle, R. C. Temple, and C. N. Hales. 1989. Sensitive and specific two-site immunoradiometric assays for human insulin, proinsulin, 65-66 split and 32-33 split proinsulins. *Biochem. J.* **260:** 535–541.
16. Matthews, J. N. S., D. G. Altman, M. J. Campbell, and P. Royston. 1990. Analysis of serial measurements in medical research. *Br. Med. J.* **300:** 230–235.
17. van der Merwe, M-T., J. R. Wing, L. H. Celgow, I. P. Gray, L. Lönn, B. I. Joffe, and P. N. Lönnroth. 1996. Metabolic indices in relation to body composition changes during weight loss on Dexfenfluramine in obese women from two South African ethnic groups. *Int. J. Obes.* **20:** 768–776.
18. van der Merwe, M-T., V. R. Panz, N. J. Crowther, G. P. Schlaphoff, I. P. Gray, P. Froguel, B. I. Joffe, and P. N. Lönnroth. 1999. Free fatty acids and insulin levels—relationship to leptin levels and body composition in various patient groups from South Africa. *Int. J. Obes.* **23:** 1–9.
19. Kissebah, A. H., D. S. Freedman, and A. N. Peiris. 1989. Health risk of obesity. *Med. Clin. North Am.* **73:** 111–138.
20. Björntorp, P. 1991. Adipose tissue distribution and function. *Int. J. Obes.* **15:** 67–81.
21. Hoffstedt, J., P. Arner, G. Hellers, and F. Lönnqvist. 1997. Variation in adrenergic regulation of lipolysis between omental and subcutaneous adipocytes from obese and non-obese men. *J. Lipid Res.* **38:** 795–804.
22. Frayn, K. N. 1996. Energy balance and body weight regulation. *In* Metabolic Regulation: A Human Perspective. Vol. 1. S. Keith, editor. Portland Press, Ltd., London. 244–245.
23. Tobey, T. A., M. Greenfield, F. Kraemer, and G. M. Reaven. 1981. Relationship between insulin resistance, insulin secretion very low-density lipoprotein kinetics and plasma triglyceride levels in normotriglyceridemic man. *Metabolism.* **30:** 165–171.
24. Grundy, S. M., H. Y. Mok, L. Zech, D. Steinberg, and M. Berman. 1979. Transport of very low-density lipoprotein triglycerides in varying degrees of obesity and hypertriglyceridemia. *J. Clin. Invest.* **63:** 1274–1283
25. Richard, E. G., S. M. Grundy, and K. Cooper. 1989. Influence of plasma triglycerides on lipoprotein patterns in normal subjects and in patients with coronary artery disease. *Am. J. Cardiol.* **63:** 1214–1220
26. Schaefer, E. J., R. I. Levy, D. W. Anderson, R. N. Dannu, and H. B. Brewer. 1978. Plasma-triglycerides in regulation of H.D.L.-cholesterol levels. *Lancet.* **2:** 391–393.
27. Cruikshank, J. K., U. Cooper, M. Burnett, J. MacDuff, and U. Drubra. 1991. Ethnic differences in fasting plasma C-peptide and insulin in relation to glucose tolerance and blood pressure. *Lancet.* **338:** 824–827.
28. Couillard, C., N. Bergeron, D. Prud'homme, J. Bergeron, A. Tremblay, C. Bouchard, P. Mauriège and J-P Després. 1998. Postprandial triglyceride response in visceral obesity in men. *Diabetes.* **47:** 953–960.
29. Roust, L. R., and M. D. Jensen. 1993. Postprandial free fatty acid kinetics are abnormal in upper body obesity. *Diabetes.* **42:** 1567–1573.
30. Weitzman, E. D., D. Fukushima, C. Nogeire, H. Roffwarg, T. F. Gallagher, and L. Hellman. 1971. Twenty-four hour pattern of the episodic secretion of cortisol in normal subjects. *J. Clin. Endocrinol. Metab.* **33:** 14–22.
31. Ottosson, M., K. Vikman-Adolfsson, S. Enerback, G. Olivecrona, and P. Björntorp. 1994. The effects of cortisol on the regulation of lipoprotein lipase activity in human adipose tissue. *J. Clin. Endocrinol. Metab.* **79:** 820–825.
32. Fain, J. N., V. P. Kovacev, and R. O. Scow. 1965. Effect of growth hormone and dexamethasone on lipolysis and metabolism in isolated fat cells of the rat. *J. Biol. Chem.* **240:** 3522–3529.
33. Morris, H. G. 1985. Mechanisms of glucocorticoid action in pulmonary disease. *Chest.* **88:** 133S–141S.
34. Rebuffé-Scrive, M., M. Krotkiewski, J. Elfverson, and P. Björntorp. 1988. Muscle and adipose tissue morphology and metabolism in Cushing's syndrome. *J. Clin. Endocrinol. Metab.* **67:** 1122–1128.
35. Mayo-Smith, W., C. W. Hayes, B. M. K. Biller, A. Klibanski, H. Rosenthal, and D. I. Rosenthal. 1989. Body fat distribution measured with CT: correlation in healthy subjects, patients with anorexia nervosa, and patients with Cushing's syndrome. *Radiology.* **170:** 515–518.
36. Rebuffé-Scrive, M., K. Lundholm, and P. Björntorp. 1985. Glucocorticoid hormone binding to human adipose tissue. *Eur. J. Clin. Invest.* **15:** 267–271.
37. Fried, S. K., C. D. Russell, N. L. Grauso, and R. E. Brolin. 1993. Lipoprotein lipase regulation by insulin and glucocorticoid in subcutaneous and omental adipose tissues of obese women and men. *J. Clin. Invest.* **92:** 2191–2198.
38. Samra, J. S., M. L. Clark, S. M. Humphreys, I. A. McDonald, P. A. Bannister, and K. N. Frayn. 1998. Effects of physiological hypercortisolaemia on the regulation of lipolysis in subcutaneous adipose tissue. *J. Clin. Endocrinol. Metab.* **83:** 626–631.
39. Hauner, H., P. Schmid, and E. F. Pfeiffer. 1987. Glucocorticoids and insulin promote the differentiation of human adipocyte precursor cells into fat cells. *J. Clin. Endocrinol. Metab.* **64:** 832–835.
40. Hauner, H., and G. Entenmann. 1991. Regional variation of adipose differentiation in cultured stromal-vascular cells from the abdominal and femoral adipose tissue of obese women. *Int. J. Obes.* **15:** 121–126.
41. Bujalska, I. J., S. Kumar, and P. M. Stewart. 1997. Does central obesity reflect "Cushing's disease of the omentum?" *Lancet.* **349:** 1210–1213.
42. Buthelezi, E. P., M-T. van der Merwe, P. N. Lönnroth, I. P. Gray, and N. J. Crowther. 2000. Ethnic differences in the responsiveness of adipocyte lipolytic activity to insulin. *Obes. Res.* **8:** 171–177.

Downloaded from www.jlr.org by guest, on June 14, 2012

43. van der Merwe, M-T., N. J. Crowther, G. Schlaphoff, I. P. Gray, B. I. Joffe, and P. N. Lönnroth. 2000. Evidence for insulin resistance in black women from South Africa. *Int. J. Obes.* **24:** 1340–1346.
44. Lovejoy, J. C., M. Klemperer, J. A. de la Bretonne, and R. Tully. 1996. Abdominal fat distribution and metabolic risk factors: effects of race. *Metabolism.* **45:** 1119–1124.
45. Joffe, B. I., V. R. Panz, J. R. Wing, F. J. Raal, and H. C. Seftel. 1992. Pathogenesis of non-insulin-dependent diabetes mellitus in the black population of southern Africa. *Lancet.* **340:** 460–462.
46. Hales, C. N., and D. J. P. Barker. 1992. Type 2 (non-insulin dependent) diabetes mellitus: the thrifty phenotype hypothesis. *Diabetologia.* **40:** 398–404.
47. Crowther, N. J., N. Cameron, J. Trusler, and I. P. Gray. 1998. Association between poor glucose tolerance and rapid postnatal weight gain in seven-year-old children. *Diabetologia.* **41:** 1163–1167.
48. Ozanne, S. E., B. T. Nave, C. L. Wang, M. W. Dorling, and C. J. Petry. 1999. Early growth retardation leads to adipocyte insulin resistance. *Diabetologia.* **42 (Suppl.):** A15.
49. Conway, J. M., S. Z. Yanovski, N. A. Avila, and V. S. Hubbard. 1995. Visceral adipose tissue differences in black and white women. *Am. J. Clin. Nutr.* **61:** 765–771.
50. Linn, S., R. Fulwood, M. Carroll, J. G. Brook, C. Johnson, W. D. Kalsbeek, and B. M. Rifkind. 1991. Serum total cholesterol: HDL cholesterol ratios in US white and black adults by selected demographic and socioeconomic variables (HANES II). *Am. J. Public Health.* **81:** 1038–1043.
51. Metcalf, P. A., A. R. Sharrett, A. R. Folsom, B. B. Duncan, W. Patsch, R. G. Hutchinson, M. Szklo, C. E. Davis, and H. A. Tyroler. 1998. African American-white differences in lipids, lipoproteins and apolipoproteins by educational attainment among middle-aged adults: the atherosclerosis risk in communities study. *Am. J. Epidemiol.* **148:** 750–760.

ASBMB JOURNAL OF LIPID RESEARCH JLR

Downloaded from www.jlr.org by guest, on June 14, 2012