Race and Ethnicity Determine Serum Insulin and C-Peptide Concentrations and Hepatic Insulin Extraction and Insulin Clearance: Comparative Studies of Three Populations of West African Ancestry and White Americans

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We examined the importance of ethnicity in terms of β-cell secretion and hepatic insulin extraction (HIE) and insulin clearance (IC) to peripheral insulin levels before and after stimulation in three populations of West African ancestry, namely African-Americans, Ghanaian immigrants, and native Ghanaians living in diverse environments, and white Americans. Following 10 to 12 hours of overnight fasting, each subject ingested a 75-g oral glucose load. Blood samples for determination of serum glucose, insulin, and C-peptide were obtained at baseline and after the oral glucose load at 30-minute intervals for 240 minutes. Basal HIE and IC were calculated as the molar ratios of C-peptide and insulin concentrations at basal steady state, and postprandial values as molar ratios of the incremental integrated C-peptide and insulin areas. Clinical characteristics of the patients were not significantly different among the four groups. During the fasting and postprandial state, serum glucose levels were not significantly different among the four groups. Surprisingly, the mean fasting insulin concentration was significantly greater in native Ghanaians (21.19 ± 0.93 μU/mL, $P < .05$) than in African-Americans (11.90 ± 1.02 μU/ML), Ghanaian immigrants (8.14 ± 0.96 μU/mL), and white Americans (7.03 ± 0.78 μU/mL). Following the oral glucose load, the mean serum peak and incremental integrated areas of insulin were significantly ($P < .05$) greater in native Ghanaians, African-Americans, and Ghanaian immigrants compared with white Americans. In contrast, there were no significant differences in postprandial serum insulin responses among the three groups of West African ancestry, irrespective of country of origin or residence. Despite the higher insulin concentrations in blacks of West African ancestry compared with whites, the corresponding basal and postprandial serum C-peptide levels were not significantly different among the four groups. Mean basal and postprandial HIE and IC were significantly ($P < .05$ to .01) reduced (25% to 52%) in the three populations of West African ancestry compared with the white Americans, but these values were not significantly different among the West African descendants. When comparing metabolic responses in obese (body mass index [BMI] > 27 kg/m^2) and non-obese (BMI < 27 kg/m^2) native Ghanaians, we found no significant differences in fasting insulin, C-peptide, and basal HIE or IC. Also, there were no significant relations between fasting and postprandial serum insulin, obesity indices, and HIE and IC in any of the groups. In summary, our study demonstrates that glucose-tolerant native Ghanaians, Ghanaian immigrants, and African-Americans of West African ancestry manifest hyperinsulinemia and a decreased HIE and IC compared with white Americans. We conclude that race and ethnicity may be the major determinants of the mechanism(s) of β-cell secretion, insulin action, and peripheral insulin levels and HIE or IC in humans. We speculate that the lower HIE and IC in blacks of West African descent appears to be a highly conserved metabolic trait irrespective of the country of residence.

PREVIOUS STUDIES have demonstrated that insulin secretion and β-cell function are under genetic control.[1-3] In addition to genetic predisposition and inheritance, environmental factors may partly account for variations in the prevalence of type II diabetes in different populations residing in diverse geographic locations.[4-12] In this regard, it is also well known that life-style changes, decreased physical activity, and adoption of a nontraditional diet associated with urban dwelling lead to greater insulin resistance and insulin concentrations and a higher prevalence of type II diabetes compared with populations residing in rural areas.[8,9,13]

African-Americans are historically and genetically linked to black people from West Africa because of the route of the transatlantic slave trade. Thus, it is theoretically possible that African-Americans inherited the genes responsible for diabetes from West Africans. In this regard, it is well established that type II diabetes is more common in African-Americans than in white Americans and native Africans.[14] Whether the disparity in the rate of diabetes in African-Americans and native Africans is due to genetic inheritance or environmental factors, eg, westernization, sedentary life-style, obesity, etc., remains unknown. Thus, it is important to compare the clinical and metabolic antecedents of type II diabetes in African-Americans and blacks from West Africa who either have migrated to the United States to live or reside in their native country. Most racial and ethnic groups living in the Western world have been extensively studied,[14-19] but glucose/insulin metabolism in native black Africans living in the Western world remains poorly investigated.[19] Thus, comparative metabolic studies among black people originating from West Africa but residing in geographically diverse countries could provide further insight into the development of type II diabetes in African-Americans. In this regard, we have recently had a unique opportunity to perform metabolic studies in recent Ghanaian immigrants living in Franklin County, Ohio, in the United States and native Ghanaians who live in Accra, Ghana, West Africa.

Therefore, the objectives of the present study were (1) to compare C-peptide/insulin/glucose dynamics and metabolism and hepatic insulin extraction (HIE) or insulin clearance (IC) and (2) to examine the impact of race on these metabolic parameters among nondiabetic healthy subjects of West African

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ancestry (Ghanaians and African-Americans) living in diverse environments among themselves and with white Americans before and during oral glucose stimulation. We hypothesized that before the development of type II diabetes, nondiabetic black people of West African ancestry would manifest similar metabolic characteristics when matched for age, body weight, and body fat distribution pattern, irrespective of their country and geographic location.

SUBJECTS AND METHODS

Subjects

The study population consisted of paid volunteers who belonged to the following diverse racial and ethnic groups: group 1 (n = 66), nondiabetic African-Americans; group 2, Ghanaian immigrants living in the United States (n = 31); group 3 (n = 50), native Africans (Ghanians) residing in Ghana; and group 4 (n = 36), white Americans living in the United States. The glucose tolerance status of the subjects was defined by World Health Organization criteria.[20] West African descendants and white Americans were matched for age, sex, and body mass index (BMI) as closely as possible. African-Americans were defined as individuals whose two conjugal black parents were of West African ancestry. All African-American subjects lived in Franklin County, OH, with a catchment area population of 1.2 million. Ghanaians were defined as individuals whose conjugal parents were from Ghana, West Africa. All native Ghanaian participants lived in the greater Accra metropolitan area, Ghana. The greater Accra metropolitan area has a population of 1.2 million, similar to that of Franklin County, OH. Ghanaian immigrants were defined as Ghanaians (1) whose conjugal parents were from Ghana, West Africa, (2) who were born in Ghana but migrated to the United States after the age of 18 years, and (3) who were residing in the same country as their African-American counterparts. Ghanaians who were born in the United States were not recruited for this study. The mean duration of US residency for the Ghanaian immigrants was 6 years. Similarly, white Americans were defined as individuals whose conjugal parents were of European ancestry. The subjects had no family history of diabetes and were recruited mostly from the same socioeconomic background. The socioeconomic status of various racial and ethnic groups ranged from manual laborers to professionals (eg, physicians, etc.) in both countries.

Subjects who participated in competitive and endurance athletic programs or who were receiving any medication known to influence glucose and insulin metabolism were excluded. In addition, we excluded subjects with cardiac, hepatic, renal, and thyroid disease as assessed by a thorough history and physical examination and, where necessary, appropriate laboratory testing. The subjects provided written informed consent as approved by the institutional review boards of The Ohio State University, Columbus, OH, and the University of Ghana Medical School, Accra, Ghana, after the risks involved in the study were carefully and thoroughly explained.

Study Design

Subjects were instructed to include at least 250 g carbohydrate in their diet for 3 consecutive days before the day of the study. The typical diet of the Ghanaians is 50% to 60% carbohydrate, 35% to 45% fat, and 10% to 15% protein in total caloric content. Similarly, for the typical American diet the corresponding figures are 45% to 50%, 40% to 45%, and 10% to 15%, respectively. The participants living in Franklin County, OH, were admitted to the Clinical Research Center of The Ohio State University Hospitals, Columbus, OH. The native Ghanaians living in the Accra metropolitan area were admitted to the Endocrine and Diabetes Research Unit of the University of Ghana Medical School, Accra, Ghana. All participants underwent a 10- to 12-hour overnight fast on the eve of the day of the study.

Clinical Characteristics

Body weight and height were measured with the participants wearing light clothing without shoes. BMI was calculated as weight in kilograms divided by height (in meters) squared. The waist circumference was measured at the level of the umbilicus, and the hip circumference at the level of the greater trochanter. The waist to hip ratio (WHR) was used to express either lower (<0.82), intermediate (0.83 to 0.87), or upper (>0.88) body fat distribution. The body fat content and lean body mass were measured using a bioelectrical impedance analyzer.[21-23]

Oral Glucose Tolerance Tests

Following a 10- to 12-hour overnight fast, the subjects ingested a 75-g oral glucose load (Koladex; Custom Laboratories, Baltimore, MD) in a total volume of 250 mL over a 2-minute period. Blood samples were obtained at 0, 30, 60, 120, 180, 210, and 240 minutes for determination of serum glucose, insulin, and C-peptide levels. Samples were centrifuged at 4°C, and sera were stored at −20°C until assayed. The Ghanaian samples were also stored at −20°C until the day of the shipment by air to Columbus, OH. The samples were frozen under dry ice, which remained intact throughout the airlift for 12 hours. Immediately after arrival, the serum samples were stored on the same day at −70°C until assay. To avoid C-peptide degradation, the samples were separated into aliquots for each of the assays at the time of blood sampling.

Analytical Methods

Serum glucose concentrations were measured by the glucose oxidase method using a glucose autoanalyzer (Beckman Instruments, Fullerton, CA). Hemoglobin A_{1c} level was measured by a microcolumn, cationic chromatographic technique (Isolab, Akron, OH). The normal reference values in our laboratory are 4.5% to 8.5%. Serum insulin and C-peptide levels were measured by standard double-antibody radioimmunoassay techniques using commercial kits (Diagnostic Products, Los Angeles, CA). The lower limit of sensitivity for immunoreactive insulin levels was 2.5 μU/mL. Intraassay and interassay coefficients of variation (CVs) for the insulin assay were 6% and 10%, respectively. The lower limit of sensitivity for the C-peptide assay was 0.47 ng/mL, and intraassay and interassay CVs 7% and 13%, respectively. The radioimmunoassay for immunoreactive insulin cross-reacted 100% with proinsulin and its intermediate-split products in our assay. However, in a pilot study in which we used a specific radioimmunoassay for proinsulin, we found that the contribution of proinsulin to the total immunoreactive insulin concentration was less than 6%. Thus, the insulin concentration in the present study reflects all the immunoreactive insulin peptides. However, our C-peptide has no cross-reactivity with the proinsulin assay.

Calculations and Statistical Analyses

The results are presented as the mean ± SEM unless otherwise stated. The integrated area under the curve (AUC) for serum glucose, C-peptide, and insulin was determined by the trapezoidal rule. The incremental AUC was determined by subtracting the basal parameters × time from the respective total AUC. The metabolic data were adjusted for age, body weight, and WHR before analyses. Insulin levels were adjusted for body weight, age, and WHR in a covariate analysis.

Basal HIE and IC were calculated as the molar ratios of the steady-state C-peptide and insulin concentrations.[24-29] Because the liver is the major organ responsible for insulin metabolism and clearance in humans, we have equated HIE to IC in our study. During the oral

glucose tolerance test, HIE and IC were calculated as the molar ratios of the incremental integrated areas for C-peptide and insulin.[26-29] Note that the molar ratios of C-peptide and insulin at steady state reflect HIE in healthy individuals without renal dysfunction. Although Polonsky and Rubenstein[25] have described the pitfalls and limitations of the use of simple molar ratios at each time point as a reflection of HIE and IC during non–steady state, use of the molar ratios of incremental integrated areas of both peptides has been suggested as a reflection of HIE or IC.[29]

Statistical analyses were performed with an unpaired Student's *t* test and, where appropriate, ANOVA for repeated measures, with post-hoc testing using the Bonferroni method (SAS Statistical Program; SAS Institute, Cary, NC). Linear regression and correlations were assessed using the least-squares method. Statistical analyses among the four groups were performed using the Newman-Keuls multiple *t* test and Student's *t* test. Nonparametric parameters were analyzed by chi-square test and the Mann-Whitney rank test. A *P* value less than .05 was considered statistically significant.

RESULTS

Clinical Characteristics

The mean age, body weight, height, and BMI were not statistically different in the three West African–descendant groups compared with the white Americans. The mean WHR, also were not significantly different in the groups of native Africans, African immigrants, and African-Americans compared with the white Americans. When we compared the various anthropometric parameters among the three groups of African descendants, we found no significant differences. The percent body fat and BMI in the four groups indicated mild to moderate upper-body obesity (Table 1).

Oral Glucose Tolerance Test

Mean fasting serum glucose levels were not different among African-Americans (78.4 ± 1.7 mg/dL), Ghanaian immigrants (76.7 ± 1.9 mg/dL), native Africans (75.0 ± 1.5 mg/dL), and white Americans (70.6 ± 1.14 mg/dL). Following the oral glucose load, the mean glucose increased to a peak level at 30 minutes in the four groups (Fig 1a). Mean peak glucose levels were not significantly different in the African-Americans (115 ± 5 mg/dL), Ghanaian immigrants (130 ± 7 mg/dL), or native Ghanaians (118 ± 4 mg/dL) compared with the white Americans (113 ± 2.3 mg/dL). Between 60 and 240 minutes, mean serum glucose responses were not different in the three groups of African descendants and white Americans. The mean AUC for glucose also was not significantly different among the four groups. Similarly, mean serum glucose responses were not different among the three groups of African ancestry.

Table 1. Clinical Characteristics of the Subjects

Characteristic	NG	GI	AA	WA
No. of subjects	50	31	66	36
Age (yr)	34.1 ± 1.0	37.2 ± 1.6	33.3 ± 0.9	28.7 ± 1.0
Sex (F/M)	28/22	11/20	50/16	25/14
Weight (kg)	77.1 ± 2.2	79.7 ± 2.7	75.7 ± 2.6	72.9 ± 3.6
Height (m)	1.62 ± 0.02	1.67 ± 0.02	1.63 ± 0.01	1.65 ± 0.04
BMI (kg/m^2)	29.45 ± 2.18	29.25 ± 0.68	28.26 ± 0.89	28.32 ± 1.28
LBM (kg)	63.23 ± 1.54	69.92 ± 1.24	67.44 ± 1.96	68.40 ± 3.55
BFM (%)	26.77 ± 1.53	30.07 ± 1.24	32.38 ± 1.94	30.69 ± 3.57
WHR	0.82 ± 0.02	0.84 ± 0.02	0.84 ± 0.06	0.87 ± 0.01
Biceps skinfold (mm)	9.27 ± 1.26	10.70 ± 1.01	10.42 ± 1.03	7.20 ± 1.51
FSG (mg/dL)	75.0 ± 1.5	76.7 ± 1.9	78.4 ± 1.7	70.6 ± 1.14
FSI (μU/mL)	21.19 ± 0.93*	8.14 ± 0.96	11.9 ± 1.00	7.03 ± 0.78
FCP (ng/mL)	1.59 ± 0.22	2.15 ± 0.22	1.78 ± 0.13	1.56 ± 0.18

NOTE. Values are the mean ± SEM.

Abbreviations: LBM, lean body mass; BFM, body fat mass; FSI, fasting serum insulin; FSG, fasting serum glucose; FCP, fasting C-peptide; NG, native Ghanaians; GI, Ghanaian immigrants; AA, African-Americans; WA, white Americans.

*$P < .001$ *v* Ghanaian immigrants, African-Americans, and white Americans.

Fasting serum insulin levels were significantly greater in the native Ghanians (21.19 ± 0.93 μU/mL) than in the African-Americans (11.9 ± 1 μU/mL, $P < .05$), Ghanaian immigrants (8.14 ± 0.96 μU/mL, $P < .05$), and white Americans (7.03 ± 0.78 μU/mL, $P < .01$). After the oral glucose load, mean incremental insulin responses were greatest in the native Ghanaians, intermediate in Ghanaian immigrants and African-Americans, and lowest in white Americans at 30, 60, 120, 180, 210, and 240 minutes (Fig 1b). Mean peak insulin levels were 81 ± 7 μU/mL in African-Americans, 84 ± 8 μU/mL in Ghanaian immigrants, and 90 ± 7 μU/mL in native Ghanaians (white Americans, 53 ± 7 μU/mL, $P < .001$ *v* African descendants). Similarly, the mean AUCs for serum insulin were significantly greater in the three groups of African descent than in the white Americans. However, there were no differences in the mean integrated incremental AUC for serum insulin among the three groups of African descent.

Mean fasting serum C-peptide levels were not different in the African-Americans (1.78 ± 0.13 ng/mL), Ghanaian immigrants (1.25 ± 0.22 ng/mL), or native Ghanaians (1.55 ± 0.10 ng/mL) compared with the white Americans (1.56 ± 0.18 ng/mL). Following oral glucose ingestion, serum C-peptide increased to a peak at 30 minutes in all four groups (Fig 1). Although peak values were variable among the groups, there were no significant differences among the four groups (Fig 1). Serum peak C-peptide levels were 8.14 ± 0.60 ng/mL in African-Americans, 8.18 ± 0.54 ng/mL in Ghanaian immigrants, 6.09 ± 0.67 ng/mL in native Ghanaians, and 6.51 ± 0.19 ng/mL in white Americans. Similarly, the mean integrated incremental postprandial C-peptide AUCs were not significantly different in the three groups of African descent compared with the white Americans. Among the three groups of African ancestry, the mean AUCs for C-peptide also were not significantly different.

Basal and Postprandial HIE and IC

The mean basal HIE or IC was significantly lower in African-Americans (6.43 ± 0.69, $P < .05$), Ghanaian immigrants (6.60 ± 1.20, $P < .05$), and native Ghanaians (4.50 ± 0.23, $P < .01$) compared with white Americans (9.54 ± 1.71). These values were 32%, 30%, and 52% lower in the three groups of African descent, respectively, compared with white Americans. Following oral glucose ingestion, HIE or IC remarkably decreased in all four groups from the basal values, as expected. The postprandial reduction in HIE or IC was 36%, 21%, and 52% lower in African-Americans, African

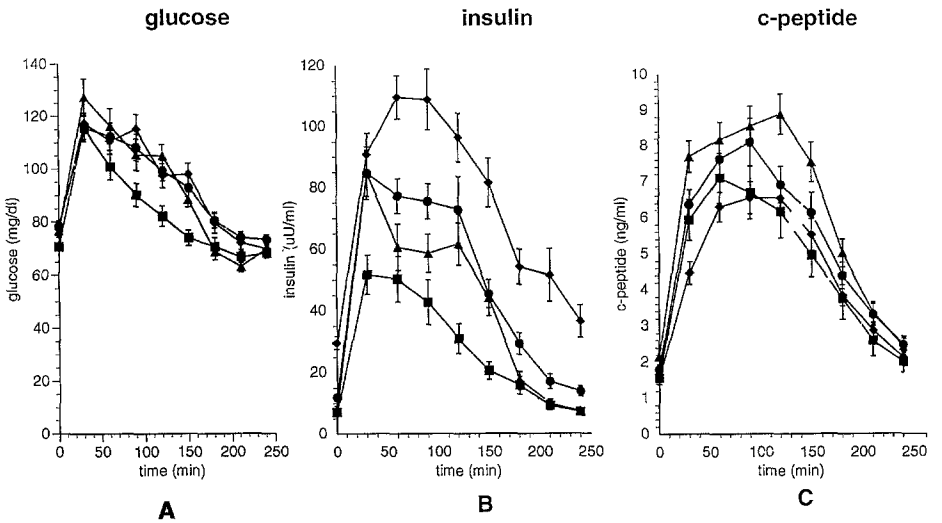

Fig 1. Mean ± SEM serum glucose, insulin, and C-peptide before and after oral glucose ingestion in (●) healthy African-Americans, (▲) Ghanaian immigrants, (◆) native Ghanaians, and (■) white Americans.

immigrants, and native Ghanaians, respectively, compared with white Americans. The differences in postprandial HIE and IC were statistically significant in the three groups of African descent compared with the white Americans ($P < .05$ to .001). Among the three groups of African ancestry, basal and postprandial HIE were not statistically different, although the mean values tended to be lower in native Ghanaians residing in Ghana.

Comparison of Basal Metabolic Parameters in Obese and Non-obese Native Ghanaians

To determine whether overall serum insulin levels were adversely impacted by obesity in native Ghanaians living in Accra, Ghana, we compared non-obese (BMI < 27 kg/m^2; mean ± SEM, 21.56 ± 0.632 kg/m^2) and obese (BMI > 27 kg/m^2; mean ± SEM, 33.15 ± 0.53 kg/m^2) subjects. Apart from age and the degree of obesity, fasting serum glucose, insulin, and C-peptide and HIE or IC were not significantly different between the two groups (Table 2). Similarly, postprandial responses were not different (data not shown).

Table 2. Clinical Characteristics of Obese and Non-obese Native Ghanaians

Parameter	Non-obese (BMI <27 kg/m^2)	Obese (BMI >27 kg/m^2)
No. of subjects	33	17
Age (yr)	28 ± 1	33 ± 3*
Sex (F/M)	13/20	15/2
Height (m)	1.65 ± 0.02	1.61 ± 0.02
Body weight (kg)	59 ± 2	85 ± 3†
BMI (kg/m^2)	21.56 ± 0.24	33.15 ± 1.2†
Fasting serum insulin (μU/mL)	19.41 ± 0.62	24.56 ± 0.52
Fasting serum C-peptide (ng/mL)	1.53 ± 0.13	1.67 ± 0.15
Fasting serum glucose (mg/dL)	72.0 ± 3.6	79.6 ± 1.8
HIE and IC	3.62 ± 0.20	3.14 ± 0.96

NOTE. Values are the mean ± SEM.
*P 0 .05, obese v non-obese.
†$P < .001$, obese v non-obese.

Correlation Coefficients

There were no significant relations between fasting insulin and C-peptide, obesity indices, HIE, and age when considered by group or within each group.

DISCUSSION

The prevalence of type II diabetes varies among racial and ethnic groups residing in diverse geographic areas.[14] Previous studies have extensively investigated the metabolic risk factors for diabetes, especially insulin resistance with concomitant hyperinsulinemia, in recent and remote immigrants of the Western world.[4,5,8,9,13-16] In most populations, hyperinsulinemia has been attributed predominantly to β-cell hypersecretion. Because we are not aware of any comparative metabolic studies on β-cell function and HIE or IC in West African descendants who reside in diverse populations, we sought to characterize some aspects of glucose regulation and/or β-cell insulin secretion in native West Africans living in Africa and in a Western industrialized country (ie, recent and remote immigrants). The premise of our study was that the metabolic antecedents of type II diabetes in nondiabetic blacks originating from the west coast of Africa are similar, although the actual incidence and prevalence of clinical type II diabetes and impaired glucose tolerance vary depending on other confounding risk factors such as obesity and sedentary life-style.

In the present study, we found that both fasting and poststimulation serum glucose concentrations generally were not statistically different in African-Americans, Ghanaian immigrants, and native Ghanaians compared with white Americans. Similarly, the AUCs for glucose were not significantly different in people of West African descent compared with white Americans. When the three groups of West African descent were compared among themselves, ie, African-Americans versus Ghanaian immigrants versus native Ghanaians, there were no significant differences in the glucose responses. However, mean fasting serum insulin levels were surprisingly twofold to threefold greater in native Ghanaians residing in Accra, Ghana, than in the Ghanaian immigrants, African-Americans, and white Americans. Simi-

larly, we found significantly higher serum insulin concentrations following the oral glucose load in African-Americans, Ghanaian immigrants, and native Africans (Ghanaians) compared with white Americans. Based on our previous report and others in native Africans such as Nigerians[30] and black South Africans,[31] we expected serum insulin concentrations in the native Ghanaians living in Accra, Ghana, to be markedly lower than those found in Ghanaian immigrants and African-Americans living in the United States. However, this was not the case. We do not believe that the higher insulin levels in Ghanaians living in Ghana were due to assay artifacts, since the serum samples were assayed in the same batches with those from other healthy subjects such as the African-Americans, Ghanaian immigrants, and white Americans in our study.

Fasting serum insulin is regarded as a biological and metabolic correlate of insulin resistance in humans and experimental animals. Since previous studies have suggested that native Africans living in diverse areas of the African continent tend to be more insulin-sensitive than African-Americans, we were therefore surprised to find the twofold higher fasting serum insulin concentrations in Ghanaians who reside in Ghana compared with Ghanaian immigrants and African-Americans (Table 1). When Ghanaians were divided into obese (BMI > 27 kg/m^2) and non-obese groups (BMI < 27 kg/m^2), we found no significant differences in the two native-Ghanaian subgroups (Table 2). Furthermore, there were no significant relations between serum insulin levels and body indices in any of the groups. Thus, we are unable to explain the disparity in the serum concentrations in the native Ghanaians of the present study and those of previous reports on other African populations. Shire et al[31] have reported that obese South African blacks have lower plasma insulin and C-peptide concentrations compared with their obese white counterparts. Taken together, these studies tend to underscore the tremendous heterogeneity in glucose and insulin metabolism in African populations residing in different parts of the continent. Because previous studies on migrant people of several ethnic populations and racial groups in the Western world found higher insulin concentrations and a greater incidence of type II diabetes than those in the indigenous populations residing in their native countries, our present findings in the two Ghanaian populations living in a modern and a semi-traditional environment, respectively, are at variance with those obtained in other migrant populations.[4-6,8,9,11,13] The major differences in the prevalence or incidence of type II diabetes in these populations have been differences in the rate of obesity in the respective ethnic and racial populations. In the present study, body weight, BMI, and WHR were similar among the four groups.

To determine the mechanism(s) of the peripheral hyperinsulinemia in the people of West African descent and the white Americans in our study, we measured serum C-peptide levels (a better marker of β-cell secretion) and HIE or IC (C-peptide to insulin molar ratios) before and during an oral glucose challenge. In this regard, we have previously demonstrated that HIE and IC are lower in African-Americans compared with white Americans.[17] Similarly, Cruickshank et al[18] found a lower HIE in African-Caribbeans than in whites living in the United Kingdom. None of these investigators compared their data with data obtained in black individuals who reside in their native African country or the West Indies, respectively. In the present study, we found that although peripheral insulin responses were markedly increased in the three groups of West African descent compared with the white Americans, corresponding C-peptide levels were not statistically different. Therefore, β-cell hypersecretion, as assessed by C-peptide, is unlikely to be responsible for the greater peripheral insulin concentrations. Since we have no reason to believe that within the range of physiologic C-peptide concentrations the clearance of C-peptide is different in blacks of West African descent, we have inferred that the peripheral hyperinsulinemia in the three groups of West African descent can be attributed predominantly to the alterations in HIE and IC. Because recent studies have indicated that upper-body obesity may be associated with decreased HIE,[32-34] we examined body fat distribution patterns using the WHR. Mean WHR were similar in the four groups. Thus, we cannot ascribe the disparities in HIE or IC and peripheral insulin levels among the West African descendants and white Americans to differences in body fat distribution patterns per se. The etiology of the lower HIE and IC in the three groups of West African descent remains unknown. However, because of the limitations in the use of molar ratios of C-peptide and insulin as a reflection of HIE or IC during non–steady state, we believe that estimating prehepatic insulin secretory and posthepatic insulin delivery rates using the deconvolutional two-compartment model of C-peptide kinetics will be necessary to validate the alterations in HIE and IC found in the African-Americans and Ghanaians of West African ancestry.[25,26]

In summary, to the best of our knowledge, this is the first comparative metabolic and anthropometric study to characterize glucose and insulin metabolism and β-cell function in black populations of West African descent living in diverse environments. We have shown that young glucose-tolerant blacks of West African descent have (1) higher fasting and/or stimulated serum insulin concentrations, (2) similar C-peptide concentrations, and (3) decreased HIE and IC compared with white Americans. These alterations in peripheral insulin and IC in people of West African ancestry appear to be independent of obesity indices and body fat distribution patterns.

We conclude that race and ethnicity determine the regulation of glucose homeostasis and insulin secretion and metabolism in people of West African ancestry (irrespective of country of residence and origin and obesity) and white Americans with comparable anthropometric characteristics. We speculate that the lower HIE and IC with the resultant hyperinsulinemia in the West African descendants is a common genetically inherited trait that seems to be highly conserved in people of West African ancestry living in diverse geographic locations. Although the mechanisms underlying these alterations are uncertain, understanding these multiple metabolic aberrations could provide insight into the pathogenesis of type II diabetes in blacks of West African descent living in diverse environments.

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