See corresponding article on page 725.

Ethnic differences in the insulin resistance syndrome[1,2]

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The prevalence of diabetes mellitus is high in African American adults. African American men have a 60% higher incidence than white men and African American women have a 100% higher incidence than white women (1). Furthermore, rates of blindness, renal disease, and amputations are significantly higher in African American diabetic patients than in other diabetic patients (1). Therefore, it is crucial to identify the reasons for the elevated risk of diabetes in this population and to find effective intervention methods to prevent the onset of the disease.

It is well recognized that diet and obesity, especially visceral obesity, play significant roles in the development of diabetes mellitus (1). African Americans have a high prevalence of obesity (1). Therefore, it is commonly assumed that obesity and diet are the etiologic factors that increase the risk of diabetes in this population. It is thought that a good diet and treatment of obesity should prevent and even reverse type 2 diabetes mellitus. In this issue of the Journal, Lindquist et al (2) show that ethnic differences in early diabetes-related pathologies, such as hyperinsulinemia and insulin resistance, already exist during childhood, and unfortunately, are not the result of differences in dietary intake. In fact, when evaluated according to the food groups of the food guide pyramid, the African American children had higher vegetable and fruit intakes than did the white children, consistent with the findings of a previous report (3). These interesting and important findings force us to reconsider our traditional thinking about the pathogenesis of diabetes both in African Americans and in general.

During childhood, adolescence, and adulthood, African Americans have higher insulin and C-peptide responses to glucose, which suggest increased secretion of insulin by the pancreas (1, 4, 5). Furthermore, they have low insulin sensitivity, indicating that the metabolic action of insulin in the tissues is impaired (1, 4–7). The current article, when considered along with the 2 previous publications from the same investigative team, shows that "insulin resistance" manifests itself differently in African Americans. Classical insulin resistance, or "syndrome X," includes the findings of elevated amounts of visceral adipose tissue, elevated plasma fatty acid and triacylglycerol concentrations, and reduced HDL-cholesterol concentrations (8). In fact, the integral component of this syndrome may be the elevated amount of visceral adipose tissue, which is more susceptible to lipolysis, and therefore, raises fatty acid concentration in the circulation. According to the Randle hypothesis, excess fatty acids decrease glucose utilization in muscle on one hand and increase glucose output from the liver on the other hand (9). Furthermore, excess fatty acids in the portal circulation inhibit extraction and clearance of insulin by the liver and cause hyperinsulinemia.

An important observation is that African American children lack several components of this syndrome. First, they have low visceral fat mass (10). Although the data in this paper were reported after the differences in the visceral fat mass were accounted for, in a recent report the same investigative team showed 20–50% lower visceral and subcutaneous abdominal fat mass in African American than in white children (10). Second, African American children have lower plasma fatty acid and triacylglycerol concentrations than do white children (2, 6, 10). Third, the higher plasma cholesterol in African American children is due to higher HDL-cholesterol concentrations, and therefore, may not necessarily be a cardiac risk factor (7).

These observations raise several important questions. For example, do the children with low insulin sensitivity progress to become diabetic adults, or is the insulin resistance observed during childhood and adolescence a self-limiting and transient finding, possibly secondary to increases in growth hormone concentration (11)? What is the primary cause of insulin resistance in African Americans? Normal glucose homeostasis is achieved through a delicate balance between insulin secretion, peripheral glucose utilization, and hepatic glucose production. An alteration in any one of these metabolic pathways affects the others. For example, although insulin resistance causes hyperinsulinemia, increased insulin exposure also causes insulin resistance (12). Therefore, it is important to identify the primary site of the early pathology. Finally, if insulin resistance during childhood increases the risk of developing diabetes or cardiovascular disease later in life, is there an effective intervention to prevent its development? Although the report of Lindquist et al (2) suggests that dietary factors are not responsible for the insulin resistance in African Americans, it also shows that a high vegetable intake may have a favorable effect on insulin sensitivity. Further understanding of the mechanisms of the ethnic differences in insulin resistance will be important to reducing the morbidity and mortality related to diabetes mellitus and coronary artery disease.

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