# Diabetic Ketoacidosis in Obese African-Americans

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**Our preliminary data indicate that 15% of African-American patients presenting with diabetic ketoacidosis (DKA) are obese. To determine underlying mechanisms, we analyzed the clinical characteristics and indexes of insulin secretion and insulin sensitivity in 35 obese patients with DKA, 22 obese patients with hyperglycemia, 10 lean patients with DKA, and 10 obese nondiabetic subjects. Studies were performed 1 day after resolution of DKA and after 12 weeks of follow-up. At presentation, both obese DKA and obese hyperglycemic patients had no detectable insulin response to intravenous glucose, but they did respond to glucagon administration. The acute insulin response (AIR) to glucagon in obese DKA patients (0.9 ± 0.1 ng/ml) was lower than in obese hyperglycemic subjects (1.5 ± 0.1 ng/ml, $P < 0.01$), but significantly greater than in lean patients with DKA (0.1 ± 0.1 ng/ml, $P < 0.01$). After 12 weeks of follow-up, the AIR to glucose improved in both groups of obese diabetic patients but remained significantly lower than in nondiabetic control subjects (both $P < 0.01$). In contrast, the AIR to glucagon was not significantly different from that in obese control subjects. Insulin sensitivity was decreased in both groups of obese diabetic patients at presentation and improved after follow-up to levels similar to those in obese nondiabetic control subjects. Reactivity with islet cell antibodies was not detected in any of the patients. During follow-up, 25 of 35 obese DKA and 16 of 22 hyperglycemic patients were able to discontinue insulin therapy, with continued good metabolic control. Our results indicate that in African-Americans, obese patients with DKA represent a subset of type II diabetes. Although impaired insulin secretion and insulin action were found at presentation, decreased pancreatic insulin reserve appears to be the primary defect in the development of DKA in obese patients.** ***Diabetes*** **44:790–795, 1995**

Our preliminary data suggest that 15% of African-American patients admitted with DKA are obese (>120% of ideal body weight [IBW]) (1). In clinical practice, correct classification of these patients between type I and type II diabetes at the time of diagnosis is often difficult but clearly of importance in the choice of optimal long-term management. In the absence of precipitating causes such as infection, stress, or trauma, the presence of DKA is considered to be a cardinal feature of type I, or insulin-dependent, diabetes. In contrast, the presence of obesity and possibility of controlling diabetes in many of these patients without insulin therapy during follow-up suggest that many of these patients have type II, or non-insulin-dependent, diabetes. Because of these mixed features, the terms "diabetes type 1.5" (somewhere between types I and II) or "atypical diabetes" have been used to describe this clinical entity. Based on the absence of autoimmune markers of β-cell destruction, it has been suggested that patients with this form of diabetes have type II diabetes (2,3). While it has been presumed that these subjects have impaired insulin secretion as a cause of DKA, there have been no studies to indicate the relative contribution of impaired insulin secretion versus impaired insulin action as the cause of metabolic decompensation.

To determine if DKA in obese patients results from decreased insulin secretion and/or increased insulin resistance, we measured their pancreatic β-cell function and insulin sensitivity both at presentation and after 12 weeks of follow-up.

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AIR, acute insulin response; ANOVA, analysis of variance; DKA, diabetic ketoacidosis; GAD, glutamic acid decarboxylase; HLA, human leukocyte antigen; IBW, ideal body weight; IVGTT, intravenous glucose tolerance test.

## RESEARCH DESIGN AND METHODS

The study population of African-Americans included 35 obese patients admitted with DKA, 22 obese hyperglycemic patients, 10 lean patients with DKA, and 10 nondiabetic obese subjects (Table 1). Lean and obese patients with DKA and obese hyperglycemic patients were admitted for medical management. Obese control subjects were studied as outpatients. Obesity was defined as body weight ≥120% of IBW. The diagnosis of DKA was established by a blood pH <7.30, a plasma glucose level >13 mmol/l, a bicarbonate level <15 mEq/l, a calculated anion gap >14 mEq/l, and a positive serum ketone assay at a dilution ≥1:4. Obese hyperglycemic patients had a blood glucose level on admission of >25 mmol/l, a venous pH >7.30, a bicarbonate level >18 mEq/l, and a serum acetoacetate ≤1:2 dilutions by the nitroprusside reaction.

All studies were performed in the Metabolic Unit at Grady Memorial Hospital, with a protocol approved by the Human Subjects Review Committee of Emory University School of Medicine; the glucagon stimulation test was performed in all study patients, while an intravenous glucose tolerance test (IVGTT) and insulin sensitivity analyses were performed in 10 patients from each obese group, selected randomly on the basis of convenience. Informed written consent was obtained from all subjects. With the exception of diabetes and obesity, none had evidence of other diseases or were taking agents known to affect carbohydrate metabolism. All patients with obvious precipitating causes for the development of ketoacidosis (i.e., stress, infection, or trauma) were excluded.

In the process of identifying patients as having type II diabetes, we used the criteria developed by the National Diabetes Data Group (4): type II diabetes is diagnosed when a patient *1*) is not ketosis-prone under basal conditions; *2*) does not require exogenous insulin for short-term survival; and *3*) has a fasting plasma glucose concentration >7.8 mmol/l or an elevated plasma glucose ≥11.1 mmol/l at 2 h and one other point during an oral glucose tolerance test.

**Assessment of pancreatic β-cell function.** Evaluation of pancreatic insulin reserve was performed 1 day after resolution of ketoacidosis and/or hyperglycemia and after 12 weeks of follow-up by measuring the

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TABLE 1
Clinical characteristics of subjects on admission

| | Obese subjects | | | Lean DKA subjects |
|---|---|---|---|---|
| | DKA | Hyperglycemia | Control | |
| $n$ | 35 | 22 | 10 | 10 |
| Age (years) | 40 ± 2 | 49 ± 2 | 42 ± 3 | 32 ± 4 |
| Sex (M/F) | 25/10 | 14/8 | 4/6 | 6/4 |
| IBW (%) | 157 ± 6 | 164 ± 9 | 171 ± 16 | 102 ± 4 |
| Newly onset diabetes | 25 (75%) | 18 (80%) | — | 1 (10%) |
| Glucose (mmol/l) | 38 ± 2 | 36 ± 2 | 5.4 ± 1 | 31 ± 2 |
| Venous pH | 7.25 ± 0.1 | 7.36 ± 0.1 | — | 7.18 ± 0.1 |
| Bicarbonate (mEq/l) | 14 ± 1 | 21 ± 1 | 24 ± 2 | 11 ± 2 |
| $HbA_{1c}$ (%) | 12.8 ± 0.4 | 12.5 ± 0.5 | 5.8 ± 0.2 | 14.9 ± 0.6 |

Data are means ± SE or $n$ (%).

changes in C-peptide levels after glucagon injection and by changes in insulin concentrations after the administration of an intravenous glucose bolus. IVGTTs were performed 1 day after the glucagon test. All studies were begun at 0800 after an overnight fast.

**Intravenous glucagon stimulation test.** Patients received 1 mg intravenous glucagon, and serum was obtained for glucose and C-peptide levels at −10, 0, 3, 6, and 10 min.

**IVGTT.** The β-cell response to a glucose load was calculated by changes in insulin levels during a frequently sampled intravenous glucose tolerance test. After a 10-h overnight fast, catheters were placed in both antecubital veins. One vein was used for injection of glucose, and the other for obtaining blood samples for glucose and insulin measurement. After the collection of four baseline samples, a glucose load of 16.7 $mmol \cdot l^{-1} \cdot kg^{-1}$ (50% dextrose) was injected within 2 min, and blood samples were collected at 1, 2, 3, 4, 5, 6, 7, 10, 12, 14, 16, and 20 min.

**Quantification of insulin sensitivity.** The minimal model of glucose kinetics developed by Bergman et al. (5) was used to calculate the insulin sensitivity index, an estimate of the ability of insulin to enhance the effect of glucose on glucose disposal, according to analysis of glucose and insulin values obtained during a frequently sampled IVGTT. After 20 min of glucose administration, regular insulin was given intravenously at a dose of 0.05 U/kg to diabetic subjects and 0.02 U/kg to nondiabetic control subjects, and blood samples were drawn at 22, 23, 24, 25, 27, 30, 40, 50, 60, 70, 80, 90, 100, 120, 140, 160, and 180 min after the initial glucose bolus (6).

Modification of the minimal model with the injection of exogenous insulin (rather than the administration of tolbutamide) has been shown to provide accurate measurement of insulin sensitivity in diabetic subjects (6,7) and to provide estimates that correlate well with results obtained by the euglycemic-hyperinsulinemic clamp method (8–10).

**Immunologic studies.** On admission, all patients underwent testing for islet cell antibodies, kindly determined at the Immunoendocrinology Laboratory at the Joslin Clinic, Boston, MA.

**Analytic methods.** Blood samples were collected in prechilled tubes and immediately centrifuged at 1200 rpm to obtain a cell-free specimen. Serum was stored at −20°C for future determination of glucose, C-peptide, and insulin levels. Serum glucose was measured by the glucose hexokinase method with a Boehringer Mannheim/Hitachi 747-200 analyzer (Boehringer Mannheim, Indianapolis, IN). Plasma C-peptide was determined by the hospital laboratory by precipitation of serum with polyethylene glycol with the use of a double-antibody radioimmunoassay kit (Incstar RIA kit, Immuno Nuclear, Stillwater, MN). Plasma insulin levels were measured by a radioimmunoassay kit (Coat-A-Count-Insulin, Diagnostic, Los Angeles, CA), with a lower limit of detection of 5 μU/ml.

**Statistical analyses.** All continuous measures are described across the four groups using means and SE. Comparisons of these measures were carried out using one-way analysis of variance (ANOVA) techniques. Repeated-measures ANOVA was used to explore the C-peptide levels across time at presentation and at follow-up. Bonferroni adjustments were implemented for pairwise comparisons of the means between groups at specified time points (baseline, 3 min, and 6 min) after glucagon injection and thereby control the overall type 1 error rate. Statistical significance was defined as a type 1 error of 0.05. Contingency table analyses and logistic regression techniques were used to find statistically significant predictors of whether or not patients were able to discontinue insulin during follow-up. Discontinuation of insulin therapy was univariately studied in relation to continuous measures using independent group $t$ tests.

## RESULTS

The clinical characteristics and metabolic parameters on admission are shown in Table 1. The obese DKA group (25 men and 10 women) included 25 patients with newly diagnosed diabetes and 10 with duration of diabetes of 1–12 years and had a mean weight 157% of IBW. The obese patients with hyperglycemia (14 men and 8 women) included 18 with newly diagnosed diabetes and weighed 164% of IBW. The lean patients with DKA (6 men and 4 women) weighed 102% of IBW and included one patient with newly diagnosed diabetes and 9 patients with a duration of diabetes of 6 ± 1 years. The obese nondiabetic control subjects (4 men and 6 women) weighed 171% of IBW. Obese patients with DKA and hyperglycemia had a strong family history of diabetes (84 and 80%), greater than the prevalence of 30% in lean DKA patients.

Obese patients with DKA had a mean plasma glucose level of 38 mmol/l, a serum bicarbonate level of 14 mEq/l, a venous pH of 7.25, an anion gap of 27 mEq/l, and a positive acetoacetate ≥1:4. Obese hyperglycemic patients had a similar plasma glucose level on admission (36.3 mmol/l) but lacked features of metabolic acidosis (serum bicarbonate 21 mEq/l, venous pH 7.36, and acetoacetate ≤ 1:2 dilutions). A similar degree of hyperglycemia was observed in lean DKA patients, but in general they were more acidotic than the obese DKA patients. Obese nondiabetic control subjects had a mean serum glucose level of 5.4 mmol/l and a mean $HbA_{1c}$ of 5.8%. Admission levels of glycosylated hemoglobin were markedly elevated in all diabetic patients, with an average $HbA_{1c}$ >12% .

On admission, all patients were treated with a low-dose insulin infusion protocol. The time required to clear the ketoacidosis in obese patients with DKA was 18 ± 2 h, similar to that in lean subjects with DKA (16 ± 2 h). After resolution of hyperglycemia and/or ketoacidosis, all diabetic patients were treated with subcutaneous insulin. Obese diabetic patients received a premixed insulin combination (Humulin 70/30) twice daily, and lean ketoacidotic patients were discharged on a split-mixed combination of intermediate-acting (Humulin N) and short-acting (Humulin R) insulin. Patients were instructed in home glucose monitoring techniques and self-adjustment of insulin dosage, and the insulin dose was adjusted to achieve fasting and premeal blood glucose levels ≤7.8 mmol/l. At discharge, patients were

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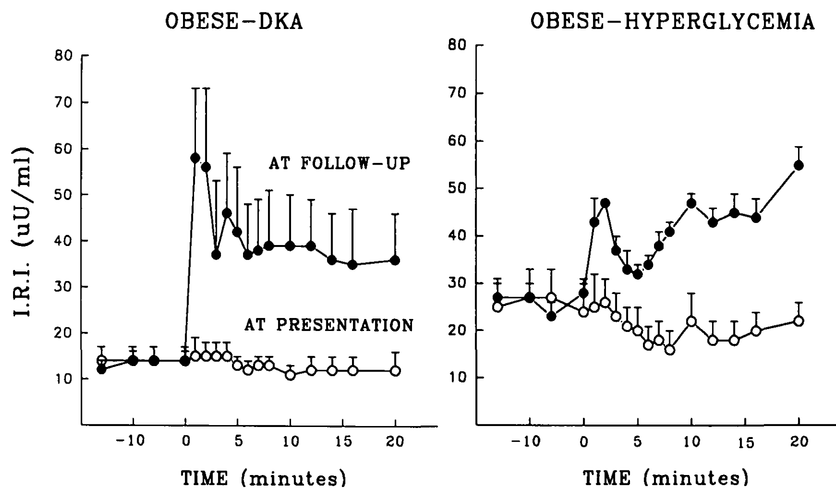


FIG. 1. Insulin secretion in obese patients with DKA and hyperglycemia after an intravenous glucose bolus (16.7 mmol · $l^{-1}$ · $kg^{-1}$). Studies were performed 1 day after resolution of DKA and/or hyperglycemia (at presentation) and 12 weeks later (at follow-up). Values are means ± SE.

followed in the Diabetes Clinic at Grady Memorial Hospital every 2 weeks for the first 2 months, and then every month with a mean duration of follow-up of 12 ± 2 months. At approximately 12 weeks after discharge, patients underwent repeat studies.

Islet cell antibodies determined on initial admission were negative in all obese patients with decompensated diabetes but were negative in lean DKA patients as well.

**Pancreatic β-cell function.** Figure 1 shows the mean glucose and insulin levels during the first 20 min of the IVGTT in 10 obese DKA patients and 10 obese hyperglycemic patients, both at presentation and during follow-up. IVGTTs were performed only once in the 10 control subjects. At the initial IVGTT, the mean ± SE basal glucose levels were 11.5 ± 1 mmol/l in obese DKA patients, 10.5 ± 1 mmol/l in obese hyperglycemic subjects, and 5.3 ± 0.1 mmol/l in obese control subjects. The mean insulin level after glucose infusion in obese nondiabetic subjects was 215 ± 15 μU/ml, compared with 13 ± 0.4 μU/ml in obese patients with DKA and 21 ± 1 μU/ml in hyperglycemic patients ($P < 0.01$ vs. both; obese hyperglycemic also greater than obese DKA, $P < 0.01$). Thus, intravenous glucose challenge shortly after resolution of ketoacidosis and/or hyperglycemia did not evoke any insulin response in diabetic patients. Improvement of metabolic control during follow-up resulted in a threefold increase in insulin levels compared with those obtained during the initial test ($P < 0.01$). Despite the enhanced insulin concentration in both obese diabetic groups, the mean insulin response during the final IVGTT was only 20% of that observed in the control nondiabetic group.

With glucose levels averaging close to 38 mmol/l, the mean C-peptide level on admission before insulin therapy was higher in obese patients with DKA (2.8 ± 0.1 ng/ml) compared with lean DKA patients (0.6 ± 0.1 ng/ml, $P < 0.01$) but lower than in obese hyperglycemic patients (3.3 ± 0.1 ng/ml). Pancreatic insulin reserve determined by changes in C-peptide levels after glucagon administration, both one day after resolution of DKA and after 8-12 weeks of follow-up, is shown in Fig. 2. One day after resolution of DKA, with glucose averaging ~11 mmol/dl, basal and stimulated C-peptide levels in the obese DKA patients (1.5 ± 0.1 and 2.5 ± 0.2 ng/ml) were significantly greater than levels in lean DKA patients (0.7 ± 0.1 and 0.8 ± 0.1 ng/ml, both $P < 0.01$) but were lower than in obese patients with hyperglycemia (2.0 ± 0.1 and 3.2 ± 0.2 ng/ml). The acute insulin response to glucagon (acute insulin response [AIR], incremental change in C-peptide over baseline levels) was 0.9 ± 0.1 ng/ml in obese patients with DKA, lower than the AIR of 1.5 ± 0.1 ng/ml in obese hyperglycemic subjects ($P < 0.01$). In both groups, responses were significantly lower than in obese nondiabetic control subjects, in whom basal and stimulated

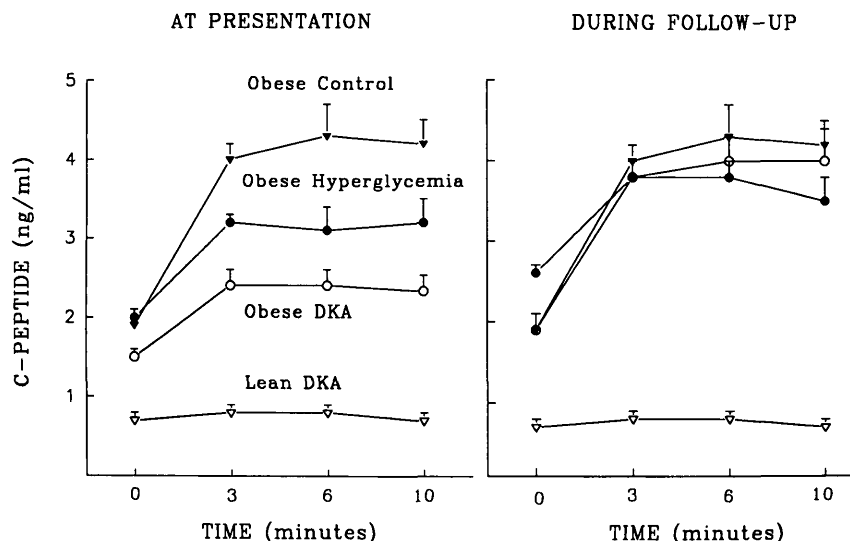


FIG. 2. Plasma C-peptide levels before and after stimulation with intravenous glucagon (1 mg) in 35 obese patients with DKA (Obese DKA), 22 obese patients with hyperglycemia (Obese Hyperglycemia), 10 lean patients with DKA (Lean DKA), and 10 obese nondiabetic subjects (Obese Control). Studies were performed 1 day after resolution of DKA and/or hyperglycemia (at presentation) and 12 weeks later (at follow-up). Values are means ± SE.

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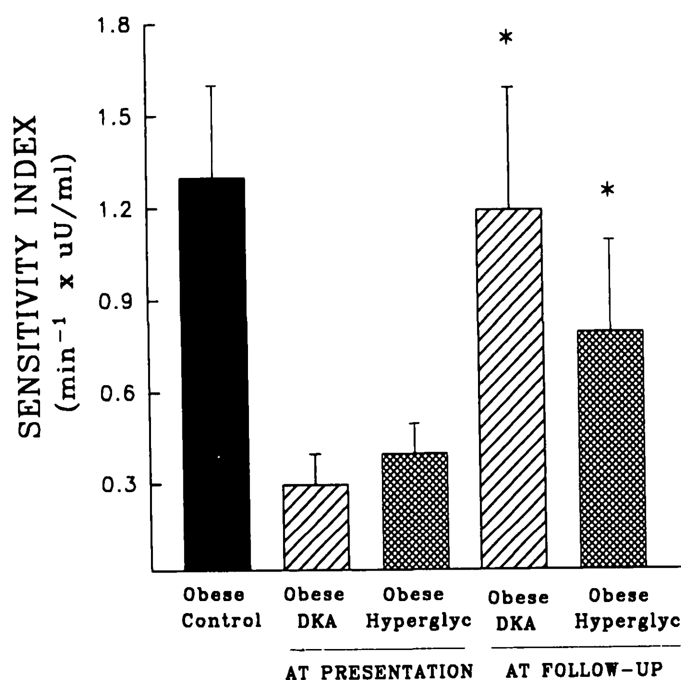


**FIG. 3. Comparison of insulin sensitivity ($S_i$) determined by minimal model analysis of a frequently sampled IVGTT in obese nondiabetic control subjects, obese patients with DKA, and obese patients with hyperglycemia. In diabetic subjects, $S_i$ was determined both 1 day after resolution of DKA or hyperglycemia and 12 weeks later. $P < 0.01$ vs. $S_i$ at presentation.**

C-peptide levels were 1.9 and 4.2 ng/ml (AIR 2.4 ± 0.3 ng/ml, both $P < 0.01$). During follow-up, the obese DKA and obese hyperglycemic patients exhibited a significant improvement in basal and stimulated C-peptide levels, but the AIR to glucagon in both diabetic groups remained lower than in obese control subjects ($P < 0.01$).

**Insulin sensitivity.** Results of the insulin sensitivity analysis are shown in Fig. 3. One day after resolution of hyperglycemia and/or ketoacidosis, insulin sensitivity was decreased equally in obese patients with DKA or hyperglycemia (0.3 ± 0.1 and 0.4 ± 0.1 $min^{-1} \cdot \mu U \cdot ml^{-1}$, respectively), compared with nondiabetic obese subjects (1.3 ± 0.3 $min^{-1} \cdot \mu U \cdot ml^{-1}$, both $P < 0.01$). Lean nondiabetic subjects usually have an insulin sensitivity of 2–5 $min^{-1} \cdot \mu U \cdot ml^{-1}$ (6). During follow-up, improvement of metabolic control resulted in a marked improvement in insulin action in both diabetic groups. The insulin sensitivity rose to 1.2 ± 0.4 $min^{-1} \cdot \mu U \cdot ml^{-1}$ in obese patients with DKA and to 0.8 ± 0.3 $min^{-1} \cdot \mu U \cdot ml^{-1}$ in obese hyperglycemic subjects. While the rise in insulin sensitivity was greater in the obese patients with DKA, the change was not significantly greater than those in obese patients with hyperglycemia, and both levels were not significantly different from values in obese control subjects.

**Clinical course.** In obese diabetic patients, insulin therapy was tapered after blood glucose was at targeted levels for 2–4 weeks or sooner if a patient experienced hypoglycemic reactions. During follow-up, discontinuation of insulin therapy was possible in 25 of 35 obese patients with ketoacidosis and in 16 of 22 obese hyperglycemic subjects, with continued good metabolic control with diet therapy and/or oral antidiabetic agents. Levels of $HbA_{1c}$ decreased from 12.8 ± 0.4 to 6.8 ± 0.2% in obese patients with DKA and from 12.5 ± 0.5 to 7.0 ± 0.2% in obese patients with hyperglycemia (both, $P < 0.01$). Despite a similar improvement in metabolic control, all 10 lean patients with DKA continued to require insulin therapy.

Interestingly, weight loss was not an absolute requirement for discontinuation of insulin therapy. Despite continuous dietary counseling for both obese diabetic groups, approximately one-third of the patients lost weight, one-third of the patients remained at the same level of body weight, and the other third gained weight during follow-up. There was no difference in weight changes among patients who could not discontinue insulin therapy and those whose diabetes was controlled with diet alone.

## DISCUSSION

In contrast with the chronic insulin dependence of type I diabetes patients with ketoacidosis, most obese patients with a history of DKA show a different clinical course. After presenting with clinical features of type I diabetes (ketoacidosis), subsequently they exhibit a phenotype more typical of type II diabetes. This unusual form of diabetes in African-Americans has been recognized previously (2,3). Winter et al. in 1987 (2) reported that some young patients may have symptoms of insulin deficiency, with or without ketoacidosis, but display clinical and metabolic features of type II diabetes. Obesity was present in 46% of their patients, and insulin secretion was intermediate between secretion in nondiabetic control subjects and that in patients with type I diabetes. Recently, Banerji et al. (3) reported 21 black patients with DKA who had similar clinical features except for older age at onset and lower prevalence of obesity. These patients had an increased frequency of human leukocyte antigen (HLA)-DR3 and HLA-DR4 markers but an absence of autoimmune indicators of β-cell destruction (glutamic acid decarboxylase [GAD] and islet cell antibodies). Our study patients appear to have similar clinical, metabolic, and immunological characteristics and confirm these previous observations of the wide spectrum of clinical presentation of type II diabetes in African-Americans.

Our study demonstrates that obese African-American patients with DKA differ from lean DKA patients (classic type I diabetes) in several respects. The pancreatic insulin reserve in obese patients with DKA was significantly greater than in lean patients with DKA. Moreover, during follow-up, two-thirds of the obese patients with DKA were able to discontinue insulin therapy and remain in continued good metabolic control; in contrast, none of the lean patients with DKA could discontinue insulin therapy. Thus, in obese African-American patients, the development of ketoacidosis, a cardinal feature of insulin dependence or type I diabetes, is not a reliable guide to classify patients as having type I or type II diabetes. In agreement with previous reports (11–14), our results suggest that measurement of C-peptide after glucagon administration is a simple procedure that may be used to differentiate patients with classic type I diabetes from those with type II diabetes and this unusual clinical presentation.

To examine mechanisms that may explain DKA in obese subjects, we determined their insulin secretion and insulin sensitivity at presentation and during follow-up. While insulin sensitivity was comparably depressed in both groups of obese diabetic patients at presentation, insulin secretion in obese ketoacidotic patients was significantly lower than in obese hyperglycemic patients. During follow-up, improve-

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ment of metabolic control resulted in a marked increase in AIR to both glucagon and glucose and in improvement of insulin action to levels similar to those in obese nondiabetic subjects. Thus, our results indicate that although obese subjects with ketoacidosis have defects in both insulin secretion and insulin action, impaired insulin secretion appears to be the dominant defect in the development of DKA.

The evaluation of β-cell function in patients with type II diabetes has proved difficult and is complicated by the potential effects of hyperglycemia per se on insulin secretion (15–17). Characteristically, first-phase insulin secretory responses to an oral or intravenous glucose tolerance test are lost in patients with established type II diabetes and plasma glucose levels >7.8 mmol/l (19,20). Further increases in fasting glucose levels are associated with loss of second-phase responses as well (19,21). In contrast, the β-cell continues to respond to nonglucose secretagogues (i.e., glucagon, arginine, and β-adrenergic agonists) in the presence of hyperglycemia (18,20–22). Improvement of metabolic control in patients with type II diabetes has been shown to increase β-cell responses both to glucose and to glucagon stimulus (23–27). In multiple studies, the average increment in insulin secretion was 70% (range 30–150%) after intensified insulin therapy in patients with type II diabetes. In agreement with these reports, we found that obese DKA and obese hyperglycemic patients had a blunted response to the administration of intravenous glucose, but a continued response to glucagon, and that correction of hyperglycemia resulted in a marked improvement in insulin responses to both glucose and nonglucose challenges. This improvement in insulin secretion indicates that the initial poor insulin response cannot be attributed to irreversible damage to β-cells but was functional in nature and was probably a consequence of hyperglycemia, which is known to impair insulin secretion (18,23,27,28).

In addition to the effect on β-cell secretion, hyperglycemia has also been shown to impair glucose disposal (25,29,30). This concept, "glucose toxicity," is well accepted and has been discussed recently (17,19,31). Although the pathogenesis of glucotoxicity is not completely understood, it appears that chronic hyperglycemia induces a generalized downregulation of the glucose transport system; at the level of the pancreas, this may lead to impaired β-cell function (insulinopenia), and in peripheral tissues this may result in impaired insulin action (insulin resistance). In addition, long-term exposure of the β-cell to high concentrations of glucose may decrease insulin gene transcription and/or expression (32). The putative role of glucotoxicity in diabetic patients has important implications in the management of patients with decompensated diabetes and implies that hyperglycemia should be viewed not only as the consequence of altered β-cell function and insulin resistance but also as an important factor in the pathogenesis of diabetic decompensation.

Islet cell antibodies were not found in any of the obese patients with DKA. Winter et al. (2) and Banerji et al. (3) also found that in contrast with Caucasian patients with classic type I diabetes, African-American patients with the atypical form of diabetes have negative titers for islet cell antibodies or GAD antibodies. While such findings might suggest that their diabetes may not result from autoimmune β-cell destruction, we are unable to draw such a conclusion since our lean DKA patients also had negative antibody tests. The absence of islet cell antibodies in the lean DKA subjects might be explained in part by longer duration of diabetes, as islet cell cytoplasmic antibodies tend to disappear in most patients within 2 years after the onset of type I diabetes (33).

In summary, DKA is common in obese African-American patients whose disease subsequently follows a clinical course typical not of type I diabetes but of type II diabetes. At presentation, obese hyperglycemic subjects with or without DKA have similar impairment of insulin sensitivity. However, obese hyperglycemic patients without ketoacidosis have a higher insulin secretory reserve, indicating that pancreatic β-cell dysfunction appears to be the primary defect in the development of DKA. In addition, our study indicates that aggressive management of decompensated diabetes in obese patients may result in improvement in β-cell function and insulin sensitivity sufficient to allow discontinuation of insulin therapy.

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