The hyperreninemia persisted despite mineralocorticoid treatment in 1987 and probably was multifactorial, due in part to congestive heart failure and diuretic therapy. In 1986, endogenous hyperreninemia provided a test of the function of the zona glomerulosa. The criteria met for diagnosis of partial corticosterone methyl oxidase type II defect were basal elevations of 18-OHB and limited aldosterone responsiveness to renin and ACTH.

The etiology of biosynthetic defects of aldosterone first detected in later life is unknown. Of relevance is the purification of a single bovine enzyme present in the zona glomerulosa and fasciculata that catalyzes 11-β-hydroxylation and both the corticosterone methyl oxidase I and II steps (7). Local factors in the zona glomerulosa probably influence the enzyme to activate its aldosterone synthetic capacity. In this case, it is reasonable to postulate acquired inhibition of biosynthesis by unknown factors perhaps related to renal disease or other complications of diabetes, causing alteration of function of proteins necessary for aldosterone biosynthesis, rather than an autoimmune or a congenital enzymatic defect.

From the Department of Medicine, Loyola University Medical Center, Maywood, Illinois.

Address correspondence and reprint requests to Susan S. Braithwaite, MD, Loyola University Medical Center, 2160 South First Avenue, Maywood, IL 60153.

Received for publication 25 September 1989 and accepted in revised form 17 January 1990.

REFERENCES

1. Ulick S: Diagnosis and nomenclature of the disorders of the terminal portion of the aldosterone biosynthetic pathway. *J Clin Endocrinol Metab* 43:92–96, 1976
2. DeLeiva A, Christlieb AR, Melbee JC, Graham CA, Day RP, Luetscher JA, Zager PG: Big renin and biosynthetic defect of aldosterone in diabetes mellitus. *N Engl J Med* 295:639–43, 1976
3. Rosler A, Ulick S: Criteria for diagnosis of aldosterone biosynthetic defects (Letter). *N Engl J Med* 295:1383, 1976
4. Tuck ML, Mayes DM: Mineralocorticoid biosynthesis in patients with hyporeninemic hypoaldosteronism. *J Clin Endocrinol Metab* 50:341–47, 1980
5. Vetter W, Vetter H, Siegenthaler W: Radioimmunoassay for aldosterone without chromatography. *Acta Endocrinol* 74:558–67, 1973
6. Martin VI, Edwards CRW, Biglieri EG, Vinson GP, Bartter FC: The development and application of a radioimmunoassay for 18-hydroxycorticosterone. *Steroids* 26:591–604, 1975
7. Yanagibashi K, Haniu M, Shively JE, Shen WH, Hall P: The synthesis of aldosterone by the adrenal cortex: two zones (fasciculata and glomerulosa) possess one enzyme for 11-β, 18-hydroxylation, and aldehyde synthesis. *J Biol Chem* 261:3556–62, 1986

# Abnormal Lipoprotein Composition in Normolipidemic Diabetic Patients

**Masahide Iwai, MD**
**Gen Yoshino, MD**
**Masayuki Matsushita, MD**
**Munetaka Morita, MD**
**Kohji Matsuba, MD**
**Tsutomu Kazumi, MD**
**Shigeaki Baba, MD**

**To see whether there are any lipoprotein abnormalities in diabetic patients without hyperlipidemia, lipoprotein composition was examined in 75 strictly normolipidemic diabetic patients. Their plasma cholesterol (chol) and triglyceride (TG) were limited to <6.0 and <1.7 mM, respectively. Body-weight– and age-adjusted normolipidemic healthy subjects served as the control group. Plasma total chol and TG and low-density lipoprotein (LDL-) and high-density lipoprotein (HDL-) chol were identical in the diabetic and control subjects. Total apolipoprotein B (apoB) in the plasma of the diabetic subjects was significantly elevated. The chol-apoB ratio in the TG-rich (very-low-density + intermediate-density) lipoprotein fraction (Sf12–400) of the diabetic subjects was significantly higher than the control value, whereas LDL-apoB levels were increased and chol-apoB ratio in the LDL fraction was significantly suppressed in the diabetic subjects. Because each LDL particle contains only one apoB molecule, apoB and chol-apoB ratio in this fraction can represent particle number and chol loading of the LDL particles, respectively. Thus, these data suggest that LDL particle number is increased, and the particles are chol depleted in diabetic subjects even if they are normolipidemic.**
***Diabetes Care* 13:792–96, 1990**

Diabetes mellitus is an important risk factor for coronary heart disease (1). Prolonged hyperglycemia may directly injure coronary arteries and thereby promote atherogenesis. Moreover, diabetic patients are frequently hyperlipidemic and are at higher risk even when normolipidemic (1,2). Therefore, factors associated with diabetes are presumably responsible for the higher incidence of cardiovascular complications. Several studies have described abnormalities in the composition of lipoproteins from normolipidemic diabetic patients. Our previous observation revealed an increased cholesterol (chol) concentration in the Sf20–

60 fraction of normolipidemic non-insulin-dependent diabetic (NIDDM) patients (3). Winocour et al. (4) reported an increased quantity of chol complexed with apolipoprotein B (apoB) in the low-density lipoprotein (LDL) fraction of normolipidemic insulin-dependent diabetic (IDDM) patients. Our study was conducted to examine the lipoprotein composition of normolipidemic NIDDM and IDDM patients. We also investigated the existence of any relationship between glycemic control and lipoprotein abnormalities in normolipidemic diabetic patients.

## RESEARCH DESIGN AND METHODS

Seventy-five diabetic patients (42 males, 33 females) and 30 age-matched healthy volunteers (16 males, 14 females) were studied. Patients who were obese or had thyroid, kidney, or liver disease and those taking steroids, diuretics, β-blockers, or hypolipidemic drugs were excluded. The patients' plasma chol and triglyceride (TG) levels were below 6.0 and 1.7 mM, respectively. They were divided into three groups according to treatment: insulin injection (insulin group, $n$ = 32), sulfonylurea (SU group, $n$ = 21), and diet alone (diet group, $n$ = 22). Eleven patients in the insulin group had IDDM and required insulin to prevent ketoacidosis. Thirteen patients in the SU group were treated with glyburide, and 8 were treated with gliclazide. Age-matched healthy normolipidemic and nonobese subjects served as the control group. Blood samples were taken at least 3 mo after the patients' blood glucose control was stabilized.

Blood was drawn after a 14-h overnight fast. The TG-rich (very-low-density + intermediate-density [VLDL + IDL]) lipoprotein fraction (density <1.019) was separated by ultracentrifugation. The density of 8 ml of plasma was adjusted to 1.019 by the addition of KBr solution. Samples in sealed tubes were centrifuged for 14 h at 4°C and at 39,000 rpm in a 50-Ti rotor with an L5-50B Beckman ultracentrifuge. After centrifugation, the top layer (1.5 ml), corresponding to the TG-rich lipoprotein fraction, was sliced off. The high-density lipoprotein (HDL) fraction was separated from the plasma by precipitation. LDL-chol was calculated by subtraction. The LDL-apoB value was obtained by subtracting apoB in the TG-rich lipoprotein fraction from total apoB. Chol, TG, and phospholipid concentrations were assayed enzymatically. Blood glucose was measured by the glucose oxidase method and $HbA_{1c}$ by high-performance liquid chromatography. Plasma apoAI, AII, B, CII, CIII, and E were assayed by a single radial immunodiffusion method via kits from Daiichi Kagaku (Tokyo) (5). apoB in the TG-rich lipoprotein fraction was measured by the same method. Because the KBr in this fraction did not interfere with the assay, dialysis was not performed before the measurement. The dilution curves of VLDL + IDL samples (density <1.019) from World Health Organization type IIb, III, and IV hyperlipidemic subjects were all superimposable on the one from standard apoB solution. Analysis of variance was used to determine whether there were significant differences among the groups. The two-tailed $P$ value was then calculated via Bonferroni's multiple-comparison procedure (6). Multiple regression analysis was used for the selection of variables influencing lipid-apo ratios in each lipoprotein fraction.

## RESULTS

Average age and body mass index were similar in the three treatment groups and the control group (Table 1). $HbA_{1c}$ and fasting blood glucose of the diabetic groups were significantly higher than in the control group. However, there were no significant differences in the two parameters among the diabetic groups.

Concentrations of TG, chol, and phospholipid and apoCII, CIII, and E in the total plasma were similar in each group (Table 2). Compared with the control group, however, apoAII was significantly decreased in the insulin group, and apoAI was significantly decreased in the diet and insulin groups, whereas apoB was significantly increased in all three diabetic groups. The increase in apoCII of the SU group was also significant. In the TG-rich (VLDL + IDL) lipoprotein fraction, chol concentration was increased in the diabetic groups (Table 3). Phospholipid concentration was also increased in the SU and diet groups. Because the apoB in this fraction was not significantly increased in the diabetic

**TABLE 1**
**Characteristics of normolipidemic diabetic and control subjects**

| Group | $n$ (M/F) | Age (yr) | Body mass index (kg/m²) | $HbA_{1c}$ (%) | Fasting blood glucose (mM) |
|---|---|---|---|---|---|
| Control | 16/14 | 54.1 ± 3.9 | 20.9 ± 0.5 | 5.70 ± 0.65 | 4.66 ± 0.36 |
| Diabetic | | | | | |
| Sulfonylurea | 13/8 | 57.7 ± 3.0 | 22.7 ± 0.8 | 7.86 ± 0.44* | 8.48 ± 0.63* |
| Diet | 12/10 | 50.0 ± 3.3 | 22.1 ± 0.6 | 8.27 ± 0.55* | 9.06 ± 0.86* |
| Insulin | 17/15 | 53.3 ± 2.1 | 20.1 ± 0.5 | 9.17 ± 0.49* | 10.61 ± 0.94* |

Values are means ± SE.
*$P$ < 0.05 vs. control value.

**TABLE 2**
**Plasma lipid and apolipoprotein levels in normolipidemic diabetic subjects**

| Group | TG (mM) | chol (mM) | PL (mM) | Apolipoprotein (mg/dl) AI | AII | B | CII | CIII | E |
|---|---|---|---|---|---|---|---|---|---|
| Control | 0.96 ± 0.06 | 4.74 ± 0.15 | 68.0 ± 1.5 | 143.5 ± 4.0 | 30.0 ± 1.0 | 81.9 ± 3.5 | 2.86 ± 0.23 | 7.14 ± 0.35 | 3.98 ± 0.19 |
| Diabetic | | | | | | | | | |
| Sulfonylurea | 1.14 ± 0.07 | 4.88 ± 0.16 | 67.6 ± 2.0 | 134.2 ± 3.8 | 31.3 ± 1.3 | 93.8 ± 4.5* | 3.68 ± 0.29* | 7.50 ± 0.40 | 4.31 ± 0.29 |
| Diet | 1.14 ± 0.07 | 4.80 ± 0.17 | 67.2 ± 2.3 | 126.0 ± 4.2* | 28.4 ± 1.0 | 92.4 ± 4.4* | 3.70 ± 0.37 | 7.62 ± 0.71 | 4.38 ± 0.30 |
| Insulin | 1.03 ± 0.07 | 4.82 ± 0.14 | 66.1 ± 2.3 | 125.5 ± 4.9* | 25.6 ± 1.1* | 90.9 ± 4.9* | 3.75 ± 0.50 | 7.32 ± 0.43 | 3.89 ± 0.26 |

Values are means ± SE. TG, triglyceride; chol, cholesterol; PL, phospholipid.
*$P < 0.05$ vs. control value.

subjects, the chol-apoB ratio was significantly elevated in the diabetic groups. In the LDL fraction, chol concentration was similar in each group (Table 4). However, because LDL-apoB was significantly increased in the diabetic subjects, their chol-apoB ratio was suppressed in the SU and diet groups. The suppression of this ratio in all diabetic subjects was also significant ($P < 0.05$). No significant differences were found in HDL-chol, HDL–chol-apoAI, and HDL–chol-apoAII among the four groups.

Thereafter, correlation analyses were performed between glycemic control (fasting blood glucose or $HbA_{1c}$) and lipid-apo ratio in each lipoprotein fraction (TG-apoB and chol-apoB in Sf12-400; chol-apoB in LDL, HDL–chol-apoAI, or HDL–chol-apoAII). There were no significant linear correlations between each parameter of the two groups.

When patient grouping was based on glycemic control, chol-apoB ratio in LDL tended to decrease as glycemic control deteriorated, and this decrease was significant ($P < 0.05$) in the poorly controlled group ($HbA_{1c}$ >10%, $n = 19$).

## DISCUSSION

Examination of lipoprotein metabolism in diabetic subjects is important because of the relationship of abnormal lipoproteins to atherosclerosis and the high incidence of premature atherosclerotic complications and death among patients with diabetes mellitus. Previously, we revealed an increased chol concentration in the Sf20-60 fraction of NIDDM subjects (3). Because of the close relationship between this fraction and plasma TG level, we recommended a new guideline for plasma TG for diabetic patients (<1.3 mM; 7). Our finding that chol-apoB ratio in the Sf12-400 fraction was increased in diabetic subjects agrees with our previous data on NIDDM (3). Because apoB concentration indicates the number of particles, this may indicate that the particles in this fraction are chol enriched (8). Several lines of evidence implicate chol-rich VLDLs in atherogenesis and suggest that macrophages are involved in this process (9). Consequently, the abnormal lipoprotein composition we report may be one cause of the increased risk of coronary heart disease in apparently normolipidemic diabetic patients (2).

Schonfeld et al. (10) reported the presence of TG-enriched LDL (Sf0-20) in normolipidemic nonketotic diabetic patients, which may indicate an accumulation of less dense moiety of LDLs. Winocour et al. (4) also reported increased chol complexed with apoB in LDL of normolipidemic IDDM subjects, which also reduces the density of LDL. Because they estimated the LDL-chol value by calculation, this may result from a generation of IDL subclass (Sf12-20) of LDL. In contrast, our previous observation from a more precise calculation of LDL-apoB revealed no chol enrichment in the LDL fraction (Sf0-12) of Japanese normolipidemic diabetic subjects (11). Furthermore, our study demonstrated a

**TABLE 3**
**Lipoprotein lipid composition in the Sf12-400 fraction of normolipidemic diabetic subjects**

| Group | TG (mM) | chol (mM) | PL (mM) | apoB (mg/dl) | TG-apoB (mmol/g) | chol-apoB (mmol/g) |
|---|---|---|---|---|---|---|
| Control | 0.41 ± 0.05 | 0.23 ± 0.05 | 3.94 ± 0.50 | 8.31 ± 1.04 | 5.07 ± 0.33 | 3.39 ± 0.23 |
| Diabetic | | | | | | |
| Sulfonylurea | 0.49 ± 0.05 | 0.35 ± 0.04* | 5.33 ± 0.50* | 10.48 ± 2.12 | 6.97 ± 1.11 | 5.10 ± 0.70* |
| Diet | 0.53 ± 0.06 | 0.46 ± 0.08* | 6.40 ± 0.87* | 9.08 ± 1.55 | 6.09 ± 1.05 | 5.44 ± 0.91* |
| Insulin | 0.41 ± 0.05 | 0.35 ± 0.05* | 4.36 ± 0.50 | 7.80 ± 1.29 | 6.70 ± 0.85 | 5.31 ± 0.54* |

Values are means ± SE. TG, triglyceride; chol, cholesterol; PL, phospholipid; apo, apolipoprotein.
*$P < 0.05$ vs. control value.

**TABLE 4**
**Total cholesterol (chol) and apolipoprotein (apo) composition of low-density lipoprotein (LDL) and high-density lipoprotein (HDL) fractions of normolipidemic diabetic subjects**

| Group | LDL-chol (mM) | LDL-apoB (mg/dl) | LDL–chol-apoB (mmol/g) | HDL-chol (mM) | HDL–chol-apoAI (mmol/g) | HDL–chol-apoAII (mmol/g) |
|---|---|---|---|---|---|---|
| Control | 2.96 ± 0.13 | 72.3 ± 3.0 | 4.02 ± 0.13 | 1.47 ± 0.06 | 0.98 ± 0.05 | 4.79 ± 0.28 |
| Diabetic | | | | | | |
| Sulfonylurea | 2.92 ± 0.18 | 85.3 ± 4.6* | 3.47 ± 0.21* | 1.39 ± 0.08 | 1.01 ± 0.08 | 4.30 ± 0.39 |
| Diet | 2.90 ± 0.15 | 84.8 ± 4.3* | 3.50 ± 0.13* | 1.40 ± 0.09 | 1.11 ± 0.05 | 4.97 ± 0.23 |
| Insulin | 2.98 ± 0.14 | 84.6 ± 5.0* | 3.73 ± 0.21 | 1.38 ± 0.07 | 1.10 ± 0.08 | 5.03 ± 0.47 |

Values are means ± SE.
*$P < 0.05$ vs. control value.

significantly suppressed chol-apoB ratio in this fraction of normolipidemic diabetic subjects. Because the ratio represents the chol loading of LDL particles, we conclude that LDL particles are chol depleted in Japanese normolipidemic diabetic patients.

The significant increase in LDL-apoB, reflecting an increased number of LDL particles, in normolipidemic diabetic patients is also an important finding (8). One explanation for this phenomenon may be a prolonged residence time of LDL particles in the circulation because of apo glycosylation (12). The appearance of chol-depleted LDL particles in diabetic patients, especially the poorly controlled group, may again suggest that apo glycosylation interferes with LDL catabolism and modifies its lipid composition.

There may be increased catabolism of HDL in diabetic patients due to glycosylation of apoAI (13). A study from Finland demonstrated decreased HDL-chol and increased total and VLDL-TG levels in NIDDM subjects (14). However, despite a lower apoAI level, the HDL-chol level of our diabetic subjects did not show a significant decrease. Neither HDL–chol-apoAI nor HDL–chol-apoAII was abnormal. Patient selection may account for an absence of abnormal HDL-chol levels in our study, because the patients in the Finnish study were hypertriglyceridemic. Further study is needed on the change in HDL metabolism in normolipidemic diabetic patients.

In conclusion, there are compositional abnormalities of lipoproteins not only in TG-rich lipoprotein (Sf12-400) but also in the LDL fraction (Sf0-12) of diabetic patients even if they appear normolipidemic. These findings may partly explain the increased risk for coronary heart disease in diabetic individuals without hyperlipidemia and justify strict management of plasma lipids in diabetic patients (7).

From the Second Department of Internal Medicine, Kobe University School of Medicine, Chuo-ku, Kobe; and the Division of Endocrinology and Metabolism, Department of Medicine, Hyogo Medical Center for Adults, Akashi, Japan.

Address correspondence and reprint requests to Dr. G. Yoshino, Second Department of Internal Medicine, Kobe University School of Medicine, Chuo-ku, Kobe 650, Japan.

Received for publication 27 June 1989 and accepted in revised form 13 December 1989.

ACKNOWLEDGMENTS

We are indebted to Dr. Frederick J. Haynes, Toronto, Ontario, Canada, for help in preparing this manuscript.

REFERENCES

1. Jarret RJ, Keen H (Eds.): Diabetes and atherosclerosis. In *Complications of Diabetes*. London, Arnold, 1975, p. 179–204
2. Nikkilä EA, Hormila P: Serum lipids and lipoproteins in insulin-treated diabetes: demonstration of increased high density lipoprotein concentrations. *Diabetes* 27:1078–86, 1978
3. Kasama T, Yoshino G, Iwatani I, Iwai M, Hatanaka H, Kazumi T, Oimomi M, Baba S: Increased cholesterol concentration in intermediate density lipoprotein fraction of normolipidemic non-insulin-dependent diabetics. *Atherosclerosis* 63:263–66, 1987
4. Winocour PH, Durrington PN, Ishola M, Anderson DC: Lipoprotein abnormalities in insulin-dependent diabetes mellitus. *Lancet* 1:1176–78, 1986
5. Sakai Y, Itakura K, Kanada T, Ebata N, Suga K, Aikawa H, Nakamura K, Sata T: Quantitation of apolipoprotein A1 in pooled human serum by single radial immunodiffusion and sodium dodecylsulfate-polyacrylamide gel electrophoresis. *Anal Biochem* 137:1–7, 1984
6. Granz SA: *Primer of Biostatistics*. New York, McGraw-Hill, 1981
7. Yoshino G, Kazumi T, Iwai M, Matsuba K, Iwatani I, Matsushita M, Kasama T, Baba S: Recommendation for strict control of plasma triglyceride in diabetic subjects. *Diabetes Care* 11:794–95, 1988
8. Knott TJ, Pease RJ, Powell LM, Wallis SC, Rall SC Jr, Inerarity TL, Blackhart B, Taylor WH, Marcel Y, Milne R, Johnson D, Fuller M, Lusis AJ, McCarthy BJ, Mahley RW, Levy-Wilson B, Scott J: Complete protein sequence and identification of structural domains of human apolipoprotein B. *Nature* (Lond) 323:734–38, 1986
9. Brown MS, Goldstein JL: Lipoprotein metabolism in the macrophage: implications for cholesterol deposition in atherosclerosis. *Annu Rev Biochem* 52:223–30, 1983
10. Schonfeld G, Birge C, Miller JP, Kessler G, Santiago J: Apolipoprotein B levels and altered lipoprotein composition in diabetes. *Diabetes* 23:827–34, 1974
11. Yoshino G, Iwai M, Kazumi T, Matsuba K, Iwatani I, Matsushita M, Baba S: Cholesterol-enrichment of low density lipoprotein fraction is absent in Japanese normolipidemic diabetics. *Horm Metab Res* 21:150–51, 1989

12. Steinbrecher UP, Witztum JL: Glucosylation of low-density lipoproteins to an extent comparable to that seen in diabetes slows their catabolism. *Diabetes* 33:130–34, 1984
13. Witztum JL, Fisher M, Pietro T, Steinbrecher UP, Elam R: Nonenzymatic glucosylation of high-density lipoprotein accelerates its catabolism in guinea pigs. *Diabetes* 31:1029–32, 1982
14. Lassko M, Voutilairen E, Sarlund H, Aro A, Pyorala K, Penttila I: Serum lipids and lipoproteins in middle-aged non-insulin-dependent diabetics. *Atherosclerosis* 56: 271–81, 1985

# Accuracy of Reported Family History of Diabetes Mellitus

## Results From San Luis Valley Diabetes Study

**Louise B. Kahn, BSN**
**Julie A. Marshall, PhD**
**Judith Baxter, MA**
**Susan M. Shetterly, MS**
**Richard F. Hamman, MD, DrPH**

**There are two possible sources of bias in the assessment of family history of diabetes: *1*) a person with diabetes may be more likely to report a diabetic relative than a nondiabetic person would be, and *2*) relatives of individuals with diabetes may be more likely to be tested for diabetes than relatives of nondiabetic individuals. We conducted a study on a subsample of families of subjects in the San Luis Valley Diabetes Study to examine these issues. A sample of 5 White and 5 Hispanic subjects (probands) with diabetic glucose tolerance tests and the same number with normal glucose tolerance were selected. The 20 probands all provided contact information on their 227 primary family members. Ninety-two percent of the family members had interviews completed by themselves or, if deceased, by surrogates other than the proband. Family members were asked by telephone if they had ever been tested for diabetes, when they had been most recently tested, why they had been tested, and if they had ever been told they had diabetes. The results showed that study subjects accurately reported family history of diabetes, because there were no discrepancies between proband and family reports. A positive family history of diabetes was associated with increased reported screening in Hispanics, but a similar effect in White families was not seen. Women were also more likely to report being screened than men regardless of whether there was a positive family history of diabetes. These data indicate that, although diabetic and control subjects accurately report their family history of known diabetes, indications of differential screening exist that may alter the amount of known and subsequently reported diabetes in families. *Diabetes Care* 13:796–98, 1990**

Family history reports are often the only source of information available regarding mortality and morbidity of family members of study subjects in epidemiological research. There are two possible sources of bias in the historical assessment of a family history of diabetes: *1*) a person with diabetes may be more likely to have knowledge of and/or report a diabetic relative than a nondiabetic person, and *2*) relatives of diabetic individuals may be more likely to be tested for diabetes than relatives of nondiabetic individuals (1,2). The Tecumseh Community Health Study reported that only 35% of direct family history reports by participants were confirmed with interviews of family members (3). We conducted a study on a sample of families of subjects in the San Luis Valley Diabetes Study to examine these issues (4).

## RESEARCH DESIGN AND METHODS

A sample of 20 study subjects was selected who had a baseline clinic visit in the month of April of any year between 1984 and 1987. Subjects were selected sequentially until 5 non-Hispanic White and 5 Hispanic subjects with diabetic glucose tolerance tests according to World Health Organization criteria and 5 White and 5 Hispanic subjects with normal glucose tolerance tests at the baseline clinic visit had been identified (5). These subjects are referred to as probands. We selected at least 2 of each group of 5 to have reported a positive family history of diabetes mellitus at the baseline clinic visit. A positive family history was defined as at least one member of the primary family other than the proband with diabetes, including parents, siblings, and children of the proband. When examining the differences in reported screening by family history, any history of diabetes, including the proband's status, was used to classify families as positive or negative. The family members were telephoned and asked if they had ever been tested for diabetes, and details were requested.

Because data on family members do not represent independent observations, we used the family as the unit of analysis. To test for differences between family subgroups of interest, the average proportion within families was used as a summary measure, and analysis of variance was used to test for significance of differences.

There were 227 primary family members; 145 family members (64%) were alive and could be located. Only