# American Diabetes Association 60th Scientific Sessions, 2000

## Glucose tolerance, diabetes and cancer, glycemic control, monitoring, and related topics

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This is the sixth in a continuing series of articles on the American Diabetes Association (ADA) 60th Scientific Sessions held in San Antonio, TX, in June 2000. It covers topics related to use of fasting versus 2-h glucose for diagnosis of diabetes, diabetes and cancer, glycemic control, monitoring, and hypoglycemia.

### Postload Glycemia in the Diagnosis of Diabetes

At a symposium on diagnostic criteria for diabetes James Gavin, Chevy Chase, MD, discussed the dilemma that fasting and post–glucose load glucose levels are differently regulated and that diagnosis based on the two criteria therefore define somewhat different populations. The use of fasting glucose has several advantages. It is more convenient to perform and limits a missed diagnosis of diabetes. Gavin noted that microvascular complications begin to occur above a fasting glucose of 126 mg/dl. A concern, however, is that more than half of patients with diabetes diagnosed by a glucose tolerance test have a fasting glucose below 126 mg/dl. Given new data showing that the fasting glucose level is less predictive of cardiovascular disease (CVD) risk than postchallenge glucose level, Gavin concluded that "fundamentally, we are back at 'square one' in asking 'What is diabetes?'" Daniel Porte, San Diego, CA, noted that "cause and effect is not necessary when we see associations," an important caveat in the new emphasis on glucose tolerance testing and postchallenge glycemia for diabetes diagnosis.

Jaakko Tuomilehto, Helsinki, Finland, reviewed data from the Diabetes Epidemiology Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) Study of 18,048 men and 7,316 women aged 30 years or older followed for an average of 7 years after glucose tolerance testing, addressing the question of whether fasting glucose or 2-h postload glucose better predicts mortality (1) There were a total of 1,836 deaths. The World Health Organization (WHO) criteria for diabetes, based mainly on 2-h glucose >200 mg/dl, and the ADA criteria, based on fasting glucose >126 mg/dl, were shown to convey a similar (1.85-fold and 1.75-fold) increase in risk among men; but among women, the WHO criteria for diabetes conveyed a 2.43-fold increase, compared with the 1.77-fold increase with the ADA criteria. Adjusting the fasting for the 2-h glucose greatly decreased the significance of the increase in mortality risk, whereas adjusting the 2-h for the fasting glucose had little such influence. In all fasting glucose categories (normal, impaired fasting glucose [IFG], and diabetes), mortality increased with increasing 2-h glucose, but in the 2-h categories (normal, impaired glucose tolerance [IGT], and diabetes), there was little increase in risk as the fasting glucose level increased. No threshold was seen for increasing mortality with increasing 2-h glucose, whereas for fasting glucose the threshold was ~126 mg/dl. Finally, Tuomilehto pointed out that the greatest number of excess deaths occurred in the large group of individuals with normal fasting glucose and IGT determined on the basis of postload glucose.

David Nathan, Boston, MA, stressed the need to clarify the association between hyperglycemia and risk of complications, listing three questions: What is the correct glycemic threshold for diagnosis of diabetes? Do glucose levels in the subdiabetic range impart risk for diabetes? And is there therapeutic value in identifying patients in this glucose range? Most diabetes occurs in the setting of aging. $HbA_{1c}$ levels increase with age, even in patients with neither diabetes nor IGT. For diabetes-specific complications, risk increases with glucose above a threshold defined by $HbA_{1c}$ ~6.0%. The DECODE data shows, however, that subdiabetic degrees of glycemia increase the risk of CVD. Similarly, in the Framingham Offspring Study, individuals without diabetes showed an increase in CVD risk with increasing levels of $HbA_{1c}$ (2). The important question Nathan raised is whether it is glucose per se that increases the risk of CVD in this population. In the Framingham study, there is a direct and continuous relationship between blood glucose and blood pressure, triglyceride, low HDL, and a variety of other risk factors in patients without diabetes. Thus, it may be overly simplistic to conceptualize individuals as either having normal glucose tolerance or IGT. Similarly, glycemic treatment may or may not be relevant to CVD risk reduction in this population. The Diabetes Prevention Program (DPP) is studying patients in the "upper half" of IGT, allowing the potential to identify patients before the onset of disease and to prevent CVD complications. Nathan acknowledged that CVD risk factor treatment is being recommended for all patients in the DPP, including those in the control group. Thus, it may not be possible to learn from this study what are the essential characteristics of the increase in CVD risk in patients

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**Abbreviations:** ADA, American Diabetes Association; CHD, coronary heart disease; CVD, cardiovascular disease; DCCT, Diabetes Control and Complications Trial; DECODE, Diabetes Epidemiology Collaborative Analysis of Diagnostic Criteria in Europe; DPP, Diabetes Prevention Program; FFA, free fatty acid; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; WHO, World Health Organization.

A table elsewhere in this issue shows conventional Système International (SI) units and conversion factors for many substances.

with postload hyperglycemia and whether efforts directed at glycemia itself are sufficient to improve their prognosis.

In the Kelley West Lecture, Eveline Eschwege, Paris, France, brought additional arguments from the Paris Prospective Study to a discussion of use of the 2-h glucose level in the diagnosis of diabetes. Many different sets of glucose tolerance test criteria have been suggested over the past three decades, with a consequent 8–41% variation in the frequency of diabetes in a group of >500 individuals in her center. Use of a 2-h glucose of 11.2 mmol/l, an increased fasting glucose requirement (from 7.2 to 7.8 mmol/l, as suggested in 1979), and a different fasting glucose criterion (7.0 mmol/l, as suggested in 1997) can be reassessed by analysis of the 2-h glucose tolerance tests in ~7,000 Paris policemen initially studied in the 1970s. Mortality follow-up showed that 8 and 23% had died at 10 and 20 years, respectively, 1.6 and 4.7% of coronary disease.

About 200 of the Paris policemen had 2-h glucose >11.1 mmol/l and fasting glucose >7.0 mmol/l, associated with 2.5-fold increases in coronary mortality. The 68 whose fasting glucose was <7.0 mmol/l with 2-h level >11.2 mmol/l, however, had lower mortality rates. Their lipid and insulin levels were similar to those in the nondiabetic group, their blood pressure was similar to that in the diabetic group, and they had higher fasting free fatty acid (FFA) levels. At 30 months, 8% of men with isolated 2-h glucose elevation vs. 2.4% of the nondiabetic group developed fasting hyperglycemia. At 10 years, 18 had died, a 2.5-fold greater mortality than in the nondiabetic group, although the coronary heart disease (CHD) mortality was 1.5%, similar to that in the nondiabetic group. At 20 years, total mortality was again 2.5-fold greater, again with similar CHD mortality to the nondiabetic group. Cancer mortality appeared to explain the increased deaths.

Patients with IGT based on postload hyperglycemia comprised 10% of the overall group, with half having normal fasting glucose and half IFG. Men with fasting glucose <6.0 mmol/l had characteristics almost identical to the nondiabetic men, whereas those with IFG were similar to the group with diabetes among the risk factors. At 30 months, 6% had fasting glucose in the diabetic range, mainly because of progression of those with IFG. At 10 and 20 years, mortality was 1.7- and 1.5-fold increased in those who had isolated postload IGT, again mainly reflecting an increase in cancer mortality, although CHD mortality was somewhat greater than in the normal glucose tolerance group at 20 years.

Eschwege concluded that, among Paris policemen, isolated postchallenge hyperglycemia was not associated with increased CHD, but rather with increased risk of malignancy, the 10-year death rate from cancer increasing from 3 to 5 to 8% and the 20 year risk increasing from 10 to 16 to 31% in normal versus isolated postload IGT versus isolated postload diabetes, respectively. Insulin levels were not elevated in this group, arguing against the theory that these patients had insulin resistance. FFA levels appeared to be a marker of tobacco and/or alcohol consumption. FFAs were independent risk factors for cancer and were particularly a risk factor for malignancies usually felt to be related to alcohol, even excluding those with death from malignancy during the first 5 years of follow-up. The only available marker of alcohol intake was the erythrocyte mean corpuscular volume, which was higher in the isolated postchallenge hyperglycemia groups. It should be noted that other authors have suggested that increased alcohol use may be associated with isolated postchallenge hyperglycemia. Although more data are required, Eschwege suggested that the fasting glucose appears sufficient to screen for individuals at increased CHD risk and that, at least among policemen in Paris, high postload glucose indicate excess alcohol use.

**Diabetes and Malignancy**

Addressing the topic of whether diabetes is associated with an increased incidence of cancer, Julie C. Will of the Centers for Disease Control and Prevention, Atlanta, GA, discussed data pertaining to colorectal and prostate cancer. Data from the First Cancer Prevention Study, collected by the American Cancer Society, with more than 1 million participants recruited between 1959 and 1960 who had follow-up to ascertain diagnoses of cancer over the subsequent 13 years, included >15,000 patients with a history of diabetes and >850,000 without diabetes. Approximately 150 and 7,000 individuals in the two groups developed colorectal cancer, adjusting for dietary factors including consumption of fruit, cereal, etc.; BMI; pregnancy history; and cigarette use. For men, diabetes was associated with a 1.3-fold increase in colon cancer risk. There was also an 8% increase for every year of age. Family history and cigarette smoking were risk factors, whereas exercising, drinking milk, and taking aspirin were protective factors. For women, the 1.16-fold higher risk of colorectal cancer with diabetes was not statistically significant. Other studies of the association of diabetes with colorectal cancer have shown positive association for both sexes, with similar risk increases approximating 25% and peak rates at 11 years of diabetes. Potential mechanisms include slower bowel transit time increasing exposure to carcinogens, altered bacterial flora affecting bile acid metabolism, and growth-promoting effects of insulin and IGF-1.

The incidence of prostate cancer among the 6,000 men with diabetes in the same American Cancer Society database showed 65 developing prostate cancer, as opposed to 2,500 cases among the 400,000 men without diabetes. After adjustment for age, race, dietary variables, cigarettes, and exercise, there was no significant overall association of diabetes, although newly onset diabetes was associated with a 1.56-fold increase in risk. A question is whether there was detection bias for men with diabetes because of increased rectal examination and prostate-specific antigen screening or whether there were effects of altered sex hormone levels or growth-promoting effects of insulin and IGF-1 in diabetes.

Thomas A. Sellers, Rochester, MN, discussed the association of diabetes with breast cancer based on the Iowa Women's Health Study, a prospective cohort study of nearly 42,000 women that began around 1985 (3). Most participants lived in rural areas, reported little alcohol use, and had high school educations. The study was geared toward assessment of the relationship between obesity and breast cancer and included height, weight, and waist and hip girth measurements. Family history of breast cancer, age, and abdominal obesity are known to be associated with breast cancer; the waist-to-hip ratio is only associated with breast cancer in women with a positive family history, suggesting an interaction. Potential explanations include familial tendency to abdominal obesity. Sellers noted that insulin is a growth factor for

breast epithelium, that estrogen-dependent breast cancer cell lines require insulin or IGF for cell survival, and that aromatization of androgens to estrogen may play a role.

Sellers reported decreased prognosis for survival in women with breast cancer and diabetes. For patients without family history of breast cancer, diabetes did not affect risk of breast cancer, but with a family history of breast cancer, diabetes appeared to convey increased risk, most of which was accounted for by obesity. Further, among 743 individuals who developed diabetes during the follow-up period, there was a 21% increase in risk with a family history of breast cancer, again related to obesity. However, a family history of breast cancer was associated with a doubling of diabetes-related mortality, which was not explained by obesity. Having a sister with diabetes was associated with having a sister with breast cancer, independent of the obesity level of the subject, but other familial associations were not consistent. Sellers noted that measures of insulin resistance in other studies suggest an association with breast cancer as well.

## Glycemic Control

A number of studies presented at the meeting gave important additional insight into questions of the adverse effects of glycemia. The concerns from Nathan's presentation were underscored by a report on the baseline characteristics of the 3,234 participants in the Diabetes Prevention Program (abstract 303). The BMI averaged 34.0 kg/m$^2$, with 57% of the men and 73% of the women having BMI >30 kg/m$^2$. The average age was 51 years; 67.7% were women (64% postmenopausal), 55% were Caucasian, 20% African-American, 16% Hispanic-American, 5% American Indian, and 4% Asian-American. Hypercholesterolemia was present in 34% and hypertension in 28%, so if vigorous treatment of these was pursued in the control group, as is ethically required, it may be difficult to document benefit of glycemic treatment. Addressing early treatment, Komatsu et al. (abstract 299) reviewed the outcome of glyburide therapy in 111 previously untreated patients with type 2 diabetes. Those who failed to achieve $HbA_{1c}$ <6.5% had mean diabetes duration of 10.4 years, while mean duration was 4.6 years for the 69 patients whose $HbA_{1c}$ decreased to <6.5%. In the latter group, insulin resistance and decreased pancreatic β-cell function correlated with longer duration without treatment, but not with the initial $HbA_{1c}$, suggesting the benefit of early treatment.

The relationship between glycated hemoglobin and complications is complex. Manley et al. (abstract 742) derived a regression equation for the relationship between fasting plasma glucose (in millimoles per liter) and $HbA_{1c}$ (percentage) from 1,180 measurements taken in the U.K. Prospective Diabetes Study, similar to the reported relationship in the Diabetes Control and Complications Trial (DCCT). They noted the wide confidence range: an $HbA_{1c}$ of 7% corresponds to a fasting plasma glucose of 149 mg/dl, but with 95% confidence limits from 83 to 212 mg/dl. The difference between glycemia and hemoglobin glycation may be important in prognosis. McCarter et al. (abstract 195) analyzed the DCCT database, showing that patients whose $HbA_{1c}$ exceeded that expected based on their glucose profile measurements had increased development of retinopathy and nephropathy. Rates of protein glycation may vary for a given degree of glycemia and may contribute to differing rates of development of complications. Alternatively, those with higher $HbA_{1c}$ for a given mean glucose may have unrecognized glycemic variability. Bastyr et al. (abstract 389) reported stronger correlation of 2-h postprandial glucose than of fasting glucose with $HbA_{1c}$ in 131 patients with secondary sulfonylurea failure 3 months after initiating combination therapy. Leslie et al. (abstract 304) studied 44 monozygotic and 45 dizygotic pairs of twins without diabetes, showing that heritable genetic effects explained 65% of the population variance in $HbA_{1c}$. Among 33 and 45 pairs of monozygotic twins concordant and discordant for type 1 diabetes, $HbA_{1c}$ correlated with $r = 0.73$ and $r = -0.47$, suggesting that even in type 1 diabetes, factors independent of glycemia may play a role in $HbA_{1c}$ variability. In an assessment of economic implications, Menzin et al. (abstract 189) followed 2,394 patients with diabetes from 1994 on, showing a 3-year hospitalization rate of 11% and a tripling of hospitalization rate as $HbA_{1c}$ increased from 6 to 12%. Average inpatient hospitalization costs were $1,100, $1,700, and $2,500 for individuals with $HbA_{1c}$ of 8, 10, and 12%, respectively. Wiedmeyer et al. (abstract 386) reported that the intraindividual coefficient of variation in glycohemoglobin in 126 stable patients with type 2 diabetes was 4.81%, suggesting that factors other than glycemic status, such as assay variability, altered life span of red blood cells, or other biological factors, do not themselves play an important role in $HbA_{1c}$ changes for a given patient.

## Monitoring

Laffel et al. (abstract 369) and Fineberg et al. (abstract 426) assessed a capillary blood beta-hydroxybutyrate measurement technology for home use. Levels exceeded 0.5 and 1.0 mmol/l in 4 and 1% of 15,893 determinations in 86 children and 88 adults performing home glucose monitoring over a 4-week period. Of the elevated levels, 87% were in children, half of the episodes occurred between 5:00 and 11:00 A.M., and the risk of levels >1 mmol/l was eightfold greater in individuals with mean glucose >200 mg/dl, suggesting that such testing may be useful for selected patients. Compared with urinary ketone testing, this method showed negative or trace urine on 56 and 69%, in children and adults, respectively, of occasions when blood levels were >0.5 mmol/l, suggesting that this may prove useful for "sick day" testing. Bohannon (396) and Koschinsky et al. (abstract 461) reported on use of a home glucose monitoring device using <0.3 μl of blood, less than one-tenth of that used for fingerstick sample determination, allowing lancing of forearm and thigh for capillary glucose sampling in several hundred individuals. Accuracy was high, and patients reported decreased discomfort with the device.

Use of a device for measurement of glucose extracted through the skin by iontophoresis and measured three times per hour with an electrochemical sensor (GlucoWatch; Cygnus, Redwood City, CA) was reported on by Garg et al. (abstracts 433 and 434) and Edelman et al. (abstract 420) from a home use trial in 111 insulin-treated patients. With "pattern-management" and "sliding scale" insulin dose adjustment algorithms, the method identified five times as many dose changes as were found with twice daily capillary glucose testing, with 23–51% of patients showing postprandial hyperglycemic episodes that would not be recognized with conventional preprandial testing and for which supplemental insu-

lin could be administered. Sensitivity of the device for detection of hypoglycemia was 75%, in comparison with sensitivities of 14 and 39% for twice-daily and four-times-daily capillary glucose testing. In 15 adults using the device for 6 weeks, glucose testing performance was stable. All patients showed skin erythema from the initial use, which was mild in two-thirds and moderate in one-third at the conclusion of study. Wilson et al. (abstract 524) reported on use of the device by 103 individuals, with none developing more than moderate erythema or more than mild local edema. Tamada et al. (abstract 514) reported on 452 individuals tested with 13,676 paired capillary and device data points, showing a mean difference of <5 mg/dl, correlation of $r$ = 0.8–0.85, and >94% of tests in the "A+B" region on error grid analysis.

A number of investigators evaluated a subcutaneously placed glucose sensor that allowed measurement of interstitial glucose levels every 5 min during a 72-h period (MiniMed, Sylmar, CA). Blumauer et al. (abstract 392) used this approach in rats administered insulin, with glucose falling from 175 to 80 mg/dl over a 1-h period. Venous and interstitial glucose showed high correlation ($r^2$ = 0.74–0.80). Steil et al. (abstract 510) placed the sensor in five nondiabetic men undergoing glucose infusion to increase plasma glucose from 5.5 to 17.2 mmol/l, then stabilized at 10.2 mmol/l, with levels subsequently falling to 4.4 mmol/l. After abruptly increasing glucose levels, a lag with $t_{1/2}$ averaging 3 min was seen between interstitial and venous plasma blood glucose levels, which showed strong correlation during a 5-h period, with mean difference averaging 8%. Boyne et al. (abstract 398) assessed the time lag between interstitial and venous glucose after a meal in 11 individuals with type 1 diabetes who had two sensors inserted simultaneously, showing that interstitial glucose lags behind venous levels by a mean of 13 min. It was not possible, however, to statistically distinguish the lag in glucose fall after meals from the sensor-to-sensor variation. Bode et al. (abstract 393) used the system for two 1-week periods, changing insulin treatment on both occasions. At 5 and 10 weeks, $HbA_{1c}$ had decreased from an initial mean level of 9.9 to 8.8 and 8.6%, without significant change in total daily insulin dose, suggesting that the device allows "fine tuning," which in turn leads to improvement in glycemia. Boland et al. (abstract 397) studied the sensor in 16 children with type 1 diabetes and $HbA_{1c}$ averaging 7.6%. Interstitial and capillary glucose levels showed a mean difference of 4 mg/dl with a correlation of $r$ = 0.91. Despite only 1 patient having a clinically symptomatic episode of hypoglycemia, 10 had nocturnal glucose <55 mg/dl, with mean duration of hypoglycemia of 220 min, 5 of whom had glucose <40 mg/dl for a mean of 188 min.

## Hypoglycemia

A number of studies assessed aspects of hypoglycemia in patients with diabetes. Sood et al. (abstract 270) studied 14 healthy subjects and 8 subjects with type 2 diabetes to assess whether moderate ethanol use (mimicked by continuous infusion of placebo or ethanol) delays recovery from hypoglycemia in people with diabetes compared with nondiabetic individuals. Insulin was administered to reduce plasma glucose to 41 mg/dl, with rates of recovery from hypoglycemia of 33 and 34 mg · $dl^{-1}$ · $h^{-1}$ in the nondiabetic subjects during the placebo and ethanol studies, but 26 and 18 mg · $dl^{-1}$ · $h^{-1}$, respectively, in the patients with diabetes.

Stork et al. (abstract 311) studied 17 individuals with type 1 diabetes and 12 control subjects in a "state-of-the-art moving-base driving simulator" to assess driving with blood glucose levels of 5.0 and 2.7 mmol/l. At euglycemia, there was more variability in lane keeping among the individuals with diabetes, whereas this group reacted to a simulated drive through a built-up area with a reduction in speed. No adverse effect of hypoglycemia was observed.

Heptulla et al. (abstract 531) studied epinephrine, glucagon, and growth hormone responses to hypoglycemic insulin clamp studies in five healthy adult men, showing an increase in peak response of each counterregulatory hormone with ingestion of oral glucose, suggesting potentiation by gut factors or by nutrient entry into the portal circulation. Segel et al. (abstract 533) compared five insulin-requiring with five oral agent–treated patients with type 2 diabetes, showing markedly impaired response of epinephrine and, particularly, glucagon to hypoglycemia in the former group, suggesting that defective glucose counterregulation, analogous to that occurring in type 1 diabetes, develops in advanced type 2 diabetes.

Davis et al. (abstract 534) treated 16 patients with type 2 diabetes for 6 months with an intensive regimen using metformin, glipizide, and acarbose, reducing $HbA_{1c}$ from 11.0 to 6.7%, with hypoglycemia occurring at a rate of 0.6 per patient-month. After 2 weeks with complete avoidance of hypoglycemia, there was greater suppression of hepatic glucose production during a 2-h hypoglycemic clamp. Muscle sympathetic nerve activity, epinephrine and norepinephrine responses, and symptoms of hypoglycemia were less pronounced after the improvement in glycemic control, suggesting that the decrease in counterregulatory response with improved glycemia requires neither recurrent hypoglycemia nor insulin treatment. Fanelli et al. (abstract 542) compared 11 patients with type 1 diabetes whose glucose was reduced to 42 mg/dl over either 30 or 90 min. There was no difference in symptoms, norepinephrine, glucagon, or lactate levels, and epinephrine levels were greater during the slower reduction in blood glucose, but performance on psychometric tests deteriorated more with rapid glucose lowering. Spyer et al. (abstract 535) studied the counterregulatory response to hypoglycemia in 8 patients with glucokinase mutations, well-controlled type 2 diabetic subjects, and normal individuals, showing a reduction in C-peptide secretion at hyperglycemia and higher glucose thresholds for glucagon and growth hormone secretion during hypoglycemia, suggesting a role of the enzyme in glucose sensing and counterregulatory hormone release.

Wysocki et al. (abstract 1331) showed no difference in intelligence quotient among 67 children with type 1 diabetes with or without a history of severe hypoglycemia. Intensively treated patients showed a 62% greater likelihood of experiencing episodes. Ferguson et al. (abstract 536) showed no effect of the frequency of hypoglycemia on brain structure, based on magnetic resonance imaging, or in cognitive function in 74 individuals with type 1 diabetes. There was, however, an association of both duration of diabetes and microvascular disease with cortical atrophy and brain leukoaraiosis, suggesting that while recurrent hypoglycemia has no demonstrable effect, there may be adverse consequences of cumulative glycemia. Jacobson et al.

(abstract 537), however, reported that among 16 patients with type 1 diabetes of longer duration, those with five or more episodes of unconsciousness from hypoglycemia had more abnormal magnetic resonance imaging results, were more likely to have had psychiatric illness, particularly depression, and had lower intelligence quotients.

### Health Care Issues

Reviriego et al. (abstract 922) assessed direct and indirect costs of hypoglycemia in 100 patients with type 1 diabetes in Spain, showing annual direct costs of $US 227, of which $174 was accounted for by the cost of hospitalization, while indirect costs from lost work amounted to $120. Patients receiving three or more insulin doses per day showed annual cost of $281, while those with one or two insulin doses had annual cost of $583, suggesting actual benefit of intensive treatment in this population. Zheng et al. (abstract 780) used statewide emergency room visit data to assess determinants of repeated visits for hypoglycemia. Of 3,150 individuals with at least one visit, 480 had repeat visits for hypoglycemia; men were 57% more likely than women, and African-Americans 51% were more likely than Caucasians to have visits. Patients with Medicare and Medicaid had 76% more visits than those with private insurance or self-insurance.

Addressing issues of health care cost, Ettaro et al. (abstract 185) analyzed data on insurance and the use of health services for 658 individuals with type 1 diabetes enrolled in the Pittsburgh Epidemiology of Diabetes Complications Study seen biennially for 10 years between 1986 and 1988 and 1996 and 1998. Those patients with health insurance were 77% more likely to inject insulin at least three times daily, had lower $HbA_{1c}$ and albuminuria, and had a lower frequency of neuropathy. Bagust et al. (abstract 892) reported that the lifetime health care cost per patient in the U.K. is 2.5 times greater for men with diabetes and 1.9 times greater for women with diabetes than for their nondiabetic counterparts, being 5.9- and 3.8-fold greater for men and women 35–49 years of age and 1.8-fold more expensive for both sexes for individuals over 85 years of age. Benjamin et al. (abstract 893) reported that the 1996–1998 Behavioral Risk Factor Surveillance System population-based telephone interview showed that 20% of individuals with diabetes were aware of having had an $HbA_{1c}$ measurement in the past year, 51% a dilated eye exam, and 47% a foot examination and that 37% performed self-monitoring of blood glucose at least daily.

### Specialist Versus Generalist Diabetes Care

A number of studies examined features of specialist versus generalist care of patients with diabetes. Champagne et al. (abstract 1357) compared responses to a questionnaire about health care in 413 individuals with diabetes who had attended an 8-h educational conference; 49% were treated by a diabetes specialist vs. 51% by a general practitioner. The groups reported an average of 4.2 and 4.4 visits per year. Of the specialists, 41% discussed the patient's diabetes for 15 min versus 17% of the general physicians, 83 vs. 54% encouraged self-care, 95 vs. 82% had ordered an $HbA_{1c}$ determination, 93 vs. 79% explained the $HbA_{1c}$ results, 93 vs. 63% reviewed home glucose monitoring records, and 95 vs. 74% were felt by the patients to give "adequate care."

Zgibor et al. (abstract 186) studied the 429 participants in the 10-year follow-up exam of the Pittsburgh Epidemiology of Diabetes Complications Study, reporting that there were significant decreases in neuropathy, nephropathy, and coronary artery disease in those individuals cared for by a board-certified endocrinologist, diabetologist, or diabetes clinic, controlling for duration, sex, income, health care practices, and known physiologic risk factors. Philis-Tsimikas et al. (abstract 190) compared 64 patients with diabetes in a managed care insurance program treated in a nurse-managed group with 59 patients treated by primary care providers. All the patients in the nurse-managed group received instruction on self-monitoring of blood glucose and foot exams. $HbA_{1c}$ and cholesterol decreased from 8.2 to 7.7% and from 194 to 173 mg/dl, respectively, in the nurse-managed group while increasing from 8.3 to 8.6% and from 210 to 224 mg/dl with primary care providers. Emergency room and hospitalization costs were 72 and 45% lower, but laboratory, medication, and nursing costs were 52, 3, and 300% greater, for a 31% higher total cost in the primary care group. Ziemer et al. (abstract 191) compared 1,925 patients treated in a diabetes clinic staffed by nurse providers and endocrinologists with 353 patients in a medical clinic staffed by general medicine residents and faculty. Despite similar demographics, use of insulin was more frequent, treatment was more likely to be intensified when glycemic control was poor, and mean $HbA_{1c}$ was 7.6 vs. 8.5%. Aubert et al. (abstract 192) compared 79 patients assigned to a nurse care manager with 76 receiving usual care in a managed care organization, showing decreases in $HbA_{1c}$ from 9.5 to 8.0% vs. 9.3 to 8.7%, with similarly greater fall in fasting glucose, without evidence of adverse events.

One approach to improving access to nurse or physician specialists involves the novel use of telephone-delivered care. Edelman et al. (abstract 421) compared 14 patients instructed to perform home glucose monitoring without further intervention with 11 patients who performed home glucose monitoring and measured fructosamine at home using a fingerstick method, with weekly medication adjustment by telephone for fructosamine $>350$ μmol/l. $HbA_{1c}$ decreased from 9.4 to 9.1% at 3 months without additional advice, but from 8.2 to 8.0% with weekly telephone adjustment. Allen et al. (abstract 889) traced costs and outcomes for telephone care as an adjunct to office visits by three pediatric endocrine nurses and three pediatric endocrinologists in 1998. Nurses spent 12.1 h weekly on telephone calls and 9.7 h documenting the calls, and physicians spent 6.4 and 6.1 h. The total weekly personnel cost for telephone care was $1,002 for the 355 patients with diabetes, or $202 per patient per year, with evidence of a decrease in hospitalizations and emergency room visits. Halvorson et al. (abstract 906) reported on 9,892 telephone calls to the nursing team using a 24-h new-patient pager, a diabetes hotline, and voicemail/pagers, lasting 7 min each, at a total cost of $59,352 in 1999. Hospitalizations and emergency room visits decreased because of this service, providing further rationale that telephone consultation be reimbursed. Sone et al. (abstract 381) reported results of the Japan Diabetes Complications Study of 2,547 patients in 40 institutions randomized to telephone instruction and other information regarding diet and exercise given mainly by public health nurses or a conventional therapy group. $HbA_{1c}$ levels were 7.8 and 7.9% in the intervention and control groups at baseline, 7.7 and 7.8% at 1 year,

7.6 and 7.8% at 2 years, and 7.5 and 7.7% at 3 years, with the latter two differences being statistically significant.

**References**

1. DECODE Study Group: Glucose tolerance and mortality: comparison of WHO and American Diabetes Association diagnostic criteria. *Lancet* 354:617–621, 1999
2. Singer DE, Nathan DM, Anderson KM, Wilson PWF, Evans JC: Association of $HbA_{1c}$ with prevalent cardiovascular disease in the original cohort of the Framingham Heart Study. *Diabetes* 41:202–208, 1992
3. Folsom AR, Kushi LH, Anderson KE, Mink PJ, Olson JE, Hong CP, Sellers TA, Lazovich D, Prineas RJ: Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. *Arch Int Med* 160:2117–2128, 2000