American Diabetes Association Annual Meeting, 1998

Type 1 diabetes; pregnancy and diabetes

ZACHARY T. BLOOMGARDEN, MD

This is the third of seven reports on the American Diabetes Association (ADA) Annual Meeting and Scientific Sessions held in Chicago in June. It deals with a number of topics related to type 1 diabetes and with pregnancy and diabetes.

CAUSES OF TYPE 1 DIABETES — In a discussion of the difficulties encountered in searching for genetic causes of diabetes, Nancy Cox, Mississippi State, MS, discussed the heterogeneity in models of gene interaction. It is difficult to identify individual genes when there are many genes involved and each has a small effect in the development of the diabetic state. Epistatic interactions among genes are easier to determine than interactions in an "additive threshold" model. It is most likely that only a minority of genes will affect treatment targets. In type 1 diabetes, the HLA genes are the major genetic contributors, although these do not explain all of the "familiality" of the illness. In type 2 diabetes, a number of monogenetic forms have been described, including mutations of insulin and the insulin receptor and mitochondrial defects. In maturity-onset diabetes of the young, an autosomal dominant inheritance has been described for mutations of the hepatocyte nuclear factors 1-α, 4-α, and 1-β and of insulin promoter factor-1 and transcriptase factors. In ~20% of cases of the syndrome, the genetic defect has not been determined. Moreover, many different alleles have been described at each of these loci (more than 80 for hepatocyte nuclear factor 1-α), making the identification of abnormal genes more difficult. Linkage studies in individual families are used to localize the genes contributing to susceptibility. Larger studies, involving several hundred families, have identified regions on chromosome 2q, at least two regions on chromosome 20, and regions on chromosomes 1, 10, and 12 that may contribute to the development of diabetes.

Approaching the causes of type 1 diabetes from an immunological perspective, Vaarala et al. compared 100 children who were exclusively breast-fed before 3 months of age with 100 children exposed to cow's milk formulas, which contain bovine insulin (abstract 126; abstract numbers refer to the Abstracts of the 58th Annual Meeting and Scientific Sessions of the ADA, *Diabetes* 47 [Suppl. 1]:1–A496). Antibodies to bovine insulin were higher in the latter group and correlated with antibodies to human insulin, although at 18 months antibody levels did not differ between the groups. Thus cow's milk, which has been linked to risk of type 1 diabetes, does result in immunization to insulin in infants. Libman et al. (abstract 568) reported a 70% prevalence of islet cell antibodies in black children at onset of type 1 diabetes versus 95% prevalence in whites, and a 40% vs. 13% prevalence of obesity, suggesting that there may be differences in the pathogenesis of diabetes between the two races. Lipton et al. (abstract 569) reported a 1.4-fold greater rate of development of diabetes among African-Americans than among Latinos aged <18 years in Chicago, particularly among those >9 years old. Among girls, 27% of African-American and 20% of Latinos were classified as having atypically evolving type 1 or early-onset type 2 diabetes based on clinical criteria, including cessation of insulin treatment >2 years after diagnosis or use of oral agents. This was also true of 16% of boys in both groups. However, Funae et al. (abstract 861) found that 110 of 599 patients initially diagnosed as having type 2 diabetes had antibodies to GAD, and 90% of such patients eventually required insulin treatment, although this appeared to be a more acutely developing process in women than in men. Similarly, Aguilar et al. (abstract 1334) showed the importance of insulin deficiency in 60 Mexican patients with early-onset type 2 diabetes. All had low or inappropriately normal C-peptide concentrations, although only 5 of 28 tested had positive titers of GAD antibodies and none of 38 tested had mutations in exon 4 of hepatocyte nuclear factor-1α, which has been reported to be associated with maturity-onset diabetes of the young. Decreased insulin sensitivity and a lipid profile with hypertriglyceridemia, low HDL-2 levels, and LDL pattern B were seen only with BMI >25 kg/m^2.

Also examining the etiology of diabetes from an immunological perspective, Cavallo et al. (abstract 781) reported that more than half of 32 patients recently diagnosed with type 1 diabetes showed T-cell reactivity to one or more cow's milk antigens, including α and β casein, β-lactoglobulin, and bovine albumin. Atkinson et al. (abstract 127) did not detect improvement in cellular and humoral immune responses to insulin or to islet cell autoantigens in 31 subjects undergoing prophylactic insulin therapy for the prevention of diabetes who were at risk for diabetes because they were first-degree relatives of diabetic patients and were positive for islet cell antibody. In a study by Coutant et al. (380), however, 25 patients aged >20 years who were newly diagnosed with type 1 diabetes were treated with 10 mg oral insulin, 1 mg oral insulin, or placebo in addition to subcutaneous insulin. At 6 months, basal C-peptide levels were 0.5, 0.8, and 0.3 nmol/l and stimulated levels were 0.9, 1.3, and 0.5 mmol/l, respectively, suggesting that oral insulin decreased immune-mediated islet destruction.

Zachary Bloomgarden is a practicing endocrinologist in New York, New York, and is affiliated with the Division of Endocrinology, Mount Sinai School of Medicine, New York, New York.

Abbreviations: ADA, American Diabetes Association; BOHB, β-hydroxybutyrate; CSII, continuous subcutaneous insulin infusion; MDI, multiple daily insulin; MI, *myo*-inositol.

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

GLUCOSE TESTING — Many investigators are seeking improved methods of monitoring blood glucose levels. Mastrototaro et al. (abstract 238) described a multicenter evaluation of a continuous subcutaneous glucose monitoring system with >7,000 paired sensor and meter data points from >1,100 patient-days. The median daily correlation coefficient was 0.85 with an overall bias of −8.6 mg/dl, suggesting that the device may be of clinical utility. Tamada et al. (abstract 239) reported a "painless, bloodless, glucose monitoring system based upon extraction through intact skin using a manufacturable, watch-like device" that automatically extracts glucose two to three times per hour by electro-osmosis with a low-level electric current. Sternberg et al. (abstract 240) presented results of 2-day continuous tissue glucose monitoring using an enzymatic glucose sensor in combination with microdialysis, a procedure that gave readings every 48 min. In seven patients with type 1 diabetes who were on intensified insulin therapy and whose mean HbA_{1c} was 6.9%, the mean tissue glucose was 126 mg/dl with maximal and minimal glucose concentrations of 352 and 24 mg/dl. The data showed 1.4 hypoglycemic episodes per patient per day, one-third at night, and 0.5 dawn phenomenon episodes per patient per day, suggesting that glucose control is imperfect even in this apparently optimally treated group. Burge et al. (abstract 363) studied a laser skin perforator for determination of capillary blood glucose and reported that pain and blood sample adequacy were equivalent to those with standard stainless steel lancets.

Several investigators reported studies of the accuracy of glucose meters. Horowitz et al. (abstract 731) compared glucose measurements in a 2-μl blood sample with those in a 20-μl sample and found values 17–79% lower in the small samples when using the LifeScan SureStep, Boehringer Mannheim Accu-Chek Instant, Boehringer Mannheim Accu-Chek Advantage, and Boehringer Mannheim Accu-Chek Advantage with Advantage H test strips systems. With the MediSense Precision QID glucose meter, results differed <8% between 2- and 20-μl samples. Similarly, Velazquez et al. (abstract 399) reported that a 2-μl sample volume falsely decreased the results of the Bayer Glucometer DEX by 72%, while high acetaminophen or uric acid concentrations falsely elevated DEX results by 25% and 27%. The Precision QID meter was accurate under all conditions tested in the study. (Researchers from both groups reported that they had received grant and research support from MediSense.)

Halvorson et al. (abstract 1346) compared the value of several methods of analyzing results of home glucose monitoring in predicting HbA_{1c} levels. The number of consecutive blood glucose levels >150 mg/dl had the highest association with HbA_{1c}, followed by the percentage >150 mg/dl and the average glucose level, suggesting that these are simple measures by which patients can assess overall glycemia. Kalergis et al. (abstract 409) used linear regression analysis to determine the accuracy with which various measurements predicted prelunch glucose levels in eight adults undergoing intensive management of type 1 diabetes. There was great interpatient variability in the strength and direction of the associations with breakfast carbohydrate intake, insulin dose, and activity level. Actual and predicted glucose levels showed a significant correlation, but only 36% of the variance was explained and there was a mean difference of 3.4 mmol/l between the two, showing the great difficulty with insulin-adjustment regimens. In a study by El-Kebbi et al. (abstract 410), 905 follow-up patients were randomly assigned either to a group whose HbA_{1c} test results were known to the health care provider at the clinic visit or to a group whose test results were reported later. An HbA_{1c} measurement >7% led to different results in the two groups. Oral agent treatment was initiated in 57% of patients on diet treatment in the immediate-reporting group but in only 42% of those with delayed reporting; insulin dose increases were suggested in 76% of immediate-reporting patients receiving insulin treatment vs. 66% of delayed-reporting patients.

Urinary *myo*-inositol (MI) levels increase in type 2 diabetes because of defects in tubular reabsorption and competition of glucose with inositol for renal uptake. Oprandy et al. (abstract 1345) compared MI with HbA_{1c} in type 2 diabetes. In normal subjects, urinary MI/creatinine averaged 23 nmol/mg; in 45 diabetic patients with HbA_{1c} <7.0%, MI/creatinine was 55.23 nmol/mg; in 39 patients with HbA_{1c} 7.0–8.0%, MI/creatinine was 81.24 nmol/mg; and in 44 patients with HbA_{1c} >8.0%, MI/creatinine was 138.2 nmol/mg. Thus MI measurement may be useful for assessing glycemic control. Turk et al. (abstract 1421) described an AGE-Hb assay that might allow in vivo screening of the processes of glycation. They found levels of 6.7, 9.1, and 12.7 U AGE/mg Hb in patients with HbA_{1c} <7, 7–10, and >10%.

There are no controlled experimental data that assess the accuracy of the commonly used correction factor of a 1.6 mEq/l decrease in serum sodium for every 100 mg/dl increase in glucose. Hillier et al. (abstract 267) presented a new analysis of the correction factor for hyperglycemia's effect in lowering serum sodium levels. In six healthy subjects rendered acutely insulin-deficient with somatostatin and given 20% dextrose to raise the blood glucose over 600 mg/dl, the simple linear regression of Δsodium/Δglucose showed an average decrease of 2.43 mEq/l in serum sodium for every 100 mg/dl increase in glucose. The relationship between sodium and glucose was not linear, and the true correction factor increased with greater degrees of hyperglycemia.

INSULIN TREATMENT — There were reports on various insulin treatment methods and regimens. Bode et al. (392) reported that 97% of a group of 165 patients beginning continuous subcutaneous insulin infusion (CSII) between 1992 and 1996 continued this treatment. HbA_{1c} fell from 8.5 to 7.8%, and severe hypoglycemia decreased from 2.5 to 0.2 episodes/year, suggesting that pump therapy is becoming more acceptable with recent advances in technology. Similarly, Bell and Ovalle (735) reported that 90 CSII-treated patients had a decrease in HbA_{1c} from 8.4 to 7.7%. Oesterle et al. (abstract 1320) compared 21 adolescents who chose CSII with 44 who were treated with multiple daily insulin (MDI) injections after 6 months follow-up. HbA_{1c} levels fell from 9.1 to 7.8 with CSII and from 9.2 to 8.6 with MDI injections, and the rate of severe hypoglycemia was 2.43-fold lower in the CSII group. Of course, a randomized controlled trial is required to demonstrate that this treatment truly offers benefit over MDI injections.

Llewelyn et al. (abstract 1386) demonstrated high patient acceptance and acceptable safety in a study of 74 patients treated with a prefilled 3-ml insulin pen containing NPH, regular, or lispro insulin. Radjenovic (abstract 1260) reported that 24% of 144 children and adolescents with type 1 diabetes averaging 4 years duration had lipohypertrophy at human insulin injection sites, which was associated with lack of site rotation and with self-administration of

insulin. Chiasson et al. (abstract 1647) reported on an ultralente-regular insulin basal-bolus regimen. When meal carbohydrate varied from 21 to 188 g, regular insulin requirements were between 1.0 and 1.5 U per 10 g of carbohydrate and did not change with the glycemic index or fiber content of the meals.

Johnston et al. (abstract 1325) studied coronary bypass patients who were treated with insulin or had fasting glucose >180 mg/dl or random glucose >200 mg/dl. Perioperative insulin was given to 37 as intermittent subcutaneous boluses, and 35 were begun preoperatively on continuous intravenous insulin infusion. Mean preoperative glucose was 201 mg/dl in both groups and intraoperative glucose was 197 and 194 mg/dl, but 24-h postoperative glucose was 290 with intermittent subcutaneous insulin and 216 mg/dl with continuous intravenous insulin, suggesting that the latter approach is clinically preferable. Umpierrez et al. (abstract 1333) compared 8 patients with alcoholic ketoacidosis with 12 having diabetic ketoacidosis. Ketoacidosis was diagnosed by serum bicarbonate <15 mEq/l, β-hydroxybutyrate (BOHB) >3 mmol/l, and pH <7.3. Both groups had severe insulinopenia and markedly elevated levels of glucagon, cortisol, catecholamine, and growth hormone. Initial BOHB levels were 6.5 vs. 7.7 mmol/l, plasma glucose levels were 578 vs. 118 mg/dl, BOHB:acetoacetate ratio was 7 vs. 3, and lactate:pyruvate ratio was 19 vs. 11. Alcoholic ketoacidosis was treated with 5% dextrose in saline, while diabetic ketoacidosis was treated with a low-dose insulin protocol.

In a fascinating study, Olson et al. (abstract 384) corrected diabetes in a rat model by administering plasmid DNA without viral vectors into the secretory ducts of the salivary glands. Allaudeen et al. (abstract 948) reported that insulin modified to improve its stability to proteolytic degradation and to increase oral absorption by means of a proprietary polymer and covalent conjugation technology is active in pancreatectomized dogs and diabetic B/B rats. Human clinical trials are in preparation.

Inhaled Insulin

In preliminary studies of this new approach, Farr et al. (abstract 235) reported an increase in plasma insulin levels of 30 μU/ml with a peak at 7 to 16 min after inhalation of regular insulin. By comparison, peak levels occurred at 55 min with subcutaneous administration. Skyler et al. (abstract 236) and Cefalu et al. (abstract 237) randomly assigned 70 patients with type 1 diabetes and 51 patients with type 2 diabetes, respectively, to receive inhaled or subcutaneous regular insulin for a 3-month period. In both studies, HbA_{1c} decreased by 0.6 to 0.8% with both subcutaneous and inhaled insulin, with similar hypoglycemia frequency and no change in pulmonary function. Gelfand et al. (abstract 388) reported similar intrasubject differences between two doses of either inhaled or subcutaneous insulin, suggesting that reproducibility of inhaled insulin delivery is good. McElduff et al. (abstract 413) showed more rapid time to peak insulin with inhaled than with subcutaneous lispro insulin, but higher maximum concentration with the subcutaneous formulation, leading to a similar overall effect.

HOE-901

HOE-901 is a biosynthetic insulin analog with more prolonged action than NPH insulin. (Disclosure: The author is an investigator in a trial of HOE-901.) Pieber et al. (abstract 242) compared two formulations of HOE-901 that differ in zinc content. HOE-901 was given at bedtime to 333 patients with type 1 diabetes, and NPH was given either once at bedtime or in the morning as well, based on patients' prestudy regimen. Fasting glucose levels and HbA_{1c} were 1.0 mmol/l and 0.14% lower and there were fewer nocturnal hypoglycemic episodes with HOE-901. Rosenstock et al. (abstract 357) presented results of a similar 4-week study of 256 patients with type 1 diabetes. Fasting glucose levels were 2.1 mmol/l lower, although with more nocturnal hypoglycemia, in the HOE-901 group than in the NPH group, with comparable overall tolerability. Matthews and Pfeiffer (abstract 394) compared two formulations of HOE-901 with NPH insulin for 4 weeks in 204 patients with type 2 diabetes. Glycemic control was similar and there were one-third as many hypoglycemic episodes with HOE-901. Raskin et al. (abstract 404) presented results of a 4-week study of 157 patients with type 2 diabetes and show no significant difference in improvement in fasting glucose levels between groups treated with two preparations of HOE-901.

Lispro

Jovanovic et al. (abstract 190) presented results of administration of lispro insulin to 18 women with gestational diabetes and compared them with results from 17 women randomly assigned to receive human regular insulin treatment. Hypoglycemia occurred 24.5% less frequently with lispro, without difference in weekly glycosylated protein or in anti-insulin antibody levels. Katzeff and Gray (abstract 331) reported a case in which lispro insulin via CSII was used successfully to treat generalized insulin allergy that was unresponsive to insulin desensitization. These results suggest that antibodies might be directed at insulin in its hexameric state. Trautmann et al. (abstract 354) examined the effect of adding either preprandial lispro or bedtime NPH insulin to sulfonylureas at the time of oral agent failure in 274 patients with type 2 diabetes. Fasting glucose was 9.6 mmol/l with lispro vs. 8.1 with NPH, but postprandial glucose was 9.1 with lispro vs. 11.8 with NPH, and HbA_{1c} fell 1.6% with lispro vs. 1.2% with NPH after 2 months. The overall hypoglycemic event rates were similar and low, with more episodes from midnight to 6:00 A.M. with NPH and more from noon to midnight with lispro. Johnson et al. (abstract 355) reported characteristics of lispro versus regular insulin in patients with renal insufficiency that were similar to those seen in subjects with normal renal function. Gentile et al. (abstract 406) compared 2-month courses of lispro administered immediately preprandially versus regular insulin administered 20 min preprandially in a crossover study of 20 patients with insulin-requiring type 2 diabetes and cirrhosis. Hypoglycemia was one-third as frequent and there was lower postprandial glycemia during the lispro period.

Ahmed et al. (abstract 366) compared prelunch lispro and prelunch regular insulin, both of which may lead to late afternoon and predinner hyperglycemia, with prelunch lispro plus NPH administered to 12 patients with C-peptide–negative type 1 diabetes. The latter approach led to optimal postlunch and predinner glycemia, even when dinner was delayed until 6 to 8 h after lunch. Lalli et al. (abstract 397) used this approach to optimize glycemia. They presented results of a comparative study of 28 patients randomly assigned to receive regular insulin preprandially plus NPH at bedtime versus 28 patients randomly assigned to receive lispro plus NPH in 70:30, 60:40, and 80:20 ratios before breakfast, lunch, and dinner, as well as NPH at bedtime. Mean daily glucose was 8.9 vs. 8.2 mmol/l, HbA_{1c} was 6.7 vs. 6.4%, and the frequency of hypoglycemia was 7 vs. 4 episodes/month. Annuzzi et al. (abstract 1367) and

Colombel et al. (abstract 1396) described similar approaches with multiple NPH doses administered to 86 and 25 patients, respectively, with type 1 diabetes who were on intensive regimens.

Holcombe et al. (abstract 375) studied 61 prepubertal children treated with lispro before or 15 min after meals or with human regular insulin. Fasting and predinner glucose levels were similar with all, but 2-h postprandial glucose levels were lower with preprandial lispro, without increase in hypoglycemia. Torlone et al. (396) reported that lispro and regular insulin had similar effects when given 10–40 min preprandially, but that when these were given immediately preprandially, hypoglycemia occurred only about half as frequently and HbA_{1c} was 0.7% lower with lispro. Reviriego and Bolanos (abstract 402) randomly assigned 75 patients in a crossover study to receive two mixed injections of lispro with NPH or lispro with ultralente daily for a 2-month period on each regimen. HbA_{1c} was slightly lower with NPH, which also showed a trend to decrease hypoglycemia. Interestingly, Richards et al. (abstract 1361) described an ultralente-like formulation of lispro with protracted action similar to that of regular insulin ultralente, and Heise et al. (abstract 1378) described the use of NPL-insulin, a protamine-retarded lispro formulation that allows stable mixtures with lispro in patients with diabetes.

HYPOGLYCEMIA — Hypoglycemia decreases counterregulatory responses to subsequent episodes of hypoglycemia. Davis et al. (abstract 140) showed that two induced hypoglycemic episodes in nondiabetic healthy adults decreased subsequent epinephrine, norepinephrine, cortisol, lactate, and glucose production responses to exercise. Mevorach et al. (abstract 146) showed that at blood glucose levels above the threshold for epinephrine secretion, nondiabetic control subjects increase glucose production, while patients with type 1 diabetes do not. This suggests that either increased hepatic insulin sensitivity or defective neural mechanisms are increasing the likelihood of hypoglycemia. Strachan et al. (abstract 423) administered cognitive function tests 1.5, 8.9, and 30 days after a spontaneous episode of hypoglycemia to 20 patients with insulin-treated diabetes and at similar intervals to 20 control subjects. Despite recovery from the acute episode, the patients showed abnormality in measures of intelligence at each time point. The subjects who had experienced hypoglycemia also demonstrated persistently increased anxiety and depression. The causal relationship to previous episodes of hypoglycemia could not be ascertained. Ovalle et al. (abstract 425) reported that 2-h twice-weekly induced episodes in which glucose levels were 50 mg/dl further decreased hypoglycemic catecholamine responses and reduced cognitive dysfunction during hypoglycemia. Clinically, the number of symptomatic hypoglycemic episodes detected decreased from 49 to 30 per month, and self-monitored blood glucose levels during symptomatic hypoglycemia decreased from 51 to 46 mg/dl. Fanelli et al. (abstract 426) similarly showed that deterioration of cognitive function during hypoglycemia was diminished following a 30-min period of nocturnal hypoglycemia in 15 patients with type 1 diabetes. Hopkins et al. (abstract 431) pointed out, however, that although cognitive function may adapt to previous hypoglycemia as measured by some tests, other parameters do not reflect such adaptation and may deteriorate before hypoglycemia is recognized in patients with type 1 diabetes and hypoglycemia unawareness.

Maran et al. (abstract 424) compared hypoglycemic responses in men and women with type 1 diabetes. The epinephrine response was significantly lower in women. Sweating, warmness, anxiety, and shakiness started at a similar blood glucose in both sexes but confusion, dizziness, lack of concentration, and blurred vision were experienced by women at a blood glucose level of 2.3 mmol/l vs. 3.1 mmol/l in men, and cognitive function tests showed a similar disparity.

Meyer et al. (abstract 144) and Cersosimo et al. (abstract 158), using different methodologies, showed that the kidney accounts for about one-fifth of basal glucose production but about one-third of glucose production during insulin-induced hypoglycemia. These observations suggest that the kidney plays an important role in counterregulation.

Acute ingestion of caffeine increases the awareness of and hormonal response to hypoglycemia. Watson et al. (abstract 429) compared responses to hypoglycemia when 200 mg of caffeine was given at onset to 10 nondiabetic subjects treated for 1 week with either 200 mg caffeine twice daily or placebo. Cognitive responses were more adversely affected in the caffeine-replete state, suggesting some degree of tolerance. However, caffeine status remains relevant to hypoglycemia unawareness, as shown by Jenkins et al. (abstract 428) in a study of 25 patients with type 1 diabetes who drank coffee for 2 months followed by 2 months without caffeine. The total number of hypoglycemic episodes was unchanged, but there was a decrease in the frequency of symptomatic episodes after withdrawal, and these were associated with a reduction in adrenergic rather than neuroglycopenic symptoms.

Fanelli et al. (abstract 427) compared 18 C-peptide–negative patients with type 1 diabetes during 4 months in which they were taking regular and NPH insulin together before dinner or regular insulin before dinner and NPH at bedtime. The frequency of nocturnal hypoglycemia was 14 vs. 3 episodes/patient-month, fasting glucose was 7.7 vs. 8.9 mmol/l, HbA_{1c} was 7.05 vs. 7.61%, and epinephrine responses, symptoms, and cognitive function during induced hypoglycemia were greater with the "split dose" approach. Stather and Houlden (abstract 414) reported on 134 patients experiencing 236 episodes of hypoglycemia requiring emergency treatment over a 27-month period in Canada. There were 5.56 episodes per 100 patients per year for patients with type 1 diabetes, 0.69 for patients with type 2 diabetes, and 2.03 for patients aged ≥65 years. Muhlhauser et al. (abstract 416) reported risk factors for severe hypoglycemia in adults with type 1 diabetes. These included prior episodes, lower social status, and greater determination to reach normoglycemia. Clarke et al. (abstract 417) studied patients who used hand-held computers to record their most recent insulin dose, meal, and exercise. Although decreased food intake and increased exercise predicted lower blood glucose, treatment behaviors were similar in patients with and without severe hypoglycemia, while the frequency of prior low blood glucose episodes was a strong risk factor for hypoglycemia.

Daniels et al. (abstract 1401) reported that more intensive treatment, lack of hypoglycemic symptoms, living alone, previous ambulance visits, long diabetes duration, and lack of glucagon availability increased the risk of severe hypoglycemia and ambulance calls in patients with type 1 diabetes. Concerns about inability to cope with hypoglycemia have been used as rationales for not administering insulin to the elderly. For a 12-month period, Miles et al. (abstract 329) prospectively assessed 82 patients aged

70–90 years who required insulin treatment for hyperglycemia. Of these patients, 23% lived alone and 21% had poor vision. HbA_{1c} decreased from 12.4 to 8.7%. Mild self-treated hypoglycemic symptoms were experienced by 41 patients, and 8 had a total of 15 episodes requiring help from another person, with 1 episode requiring hospitalization. Allen et al. (abstract 602) studied 418 children, adolescents, and young adults with type 1 diabetes. Of these subjects, 32% had hypoglycemia 2–4 times/week and 8% had lost consciousness from hypoglycemia in the previous 6 months. Glycemic control was a strong risk factor for hypoglycemia in 5-year-old patients, a weaker risk factor at age 15, and not a significant risk at age 25. Barkai and Vamosi (abstract 433) reported that 48 type 1 diabetic children and adolescents with impaired awareness had 63 episodes of severe hypoglycemia per 100 patient-years, while 82 reporting normal awareness had 24 episodes per 100 patient-years. In the two groups, 50 vs. 10% of hypoglycemic episodes occurred without warning. Predictors of severe hypoglycemia included impaired awareness, previous severe episodes, and >5% of home blood glucose readings ≤3.3 mmol/l in the preceding month.

KIDNEY-PANCREAS TRANSPLANTATION — Benedini et al. (abstract 293) studied 55 patients after successful kidney-pancreas transplantation. Of these, 11% had mild hypoglycemia with glucose ≤3.35 mmol/l during 1-day metabolic profiles, and 20% reported having had major hypoglycemia with glucose ≤2.78 mmol/l. These symptoms were not seen in nondiabetic subjects following kidney or liver transplantation, suggesting it to be a specific defect of type 1 diabetes after kidney-pancreas transplant. Luzi and Bretzel (abstract 1311) discussed the results of islet allografts performed in 45 patients. Partial function was seen in 53 and 22% of patients at 1 and 2 years, but full function was seen in only 27 and 20% of patients. Fasting glucose was 8 and 6 mmol/l in patients with partial and full function, in contrast to 14 mmol/l without islet function. Protein and lipid metabolism were also considerably improved, suggesting that there are additional metabolic benefits of this treatment.

PREGNANCY AND DIABETES — Lachin et al. and the DCCT research group (abstract 191) reported that in the Diabetes Control and Complications Trial, 94 of 345 women in the intensive treatment group had 135 pregnancies and 86 of 335 women in the conventional treatment group had 135 pregnancies. The latter were advised to change to intensive therapy before or soon after conception. Independently of the change in HbA_{1c}, in the intensive treatment group, retinopathy and albuminuria worsened in 38 and 67% during pregnancy, while in the conventional treatment group, these conditions worsened in 47 and 59%, emphasizing the increased risk of complications of type 1 diabetes during pregnancy. Siulc et al. (abstract 579) reported that menarche occurred later among 143 women with type 1 diabetes than among 186 nondiabetic sisters (13.5 vs. 12.5 years) and menopause occurred earlier (41.6 vs. 49.9 years). Irregular menses, longer cycles, and longer menstruation were also more common, and women with type 1 diabetes had 1.8 vs. 2.5 pregnancies, suggesting that decreased reproductive potential is a complication of the disease.

Williams and Herman (abstract 1245) analyzed 230 women with gestational diabetes identified over the period from 1987 to 1997. If the 1997 ADA recommendation that screening not be performed for women at low risk based on age <25 years, BMI <27, negative family history, and white race, had been followed, >97% of women would still have been identified. Sigal and Meltzer (abstract 194) compared 256 postpartum women who had had gestational diabetes with 64 control subjects. HDL cholesterol was 1.29 vs. 1.61 mmol/l and triglyceride was 1.41 vs. 1.06. In a comparison of the 143 patients with normal glucose tolerance, 85 with impaired glucose tolerance, and 26 with diabetes, it was found that HDL cholesterol decreased and triglyceride increased with worsening glucose tolerance.