$P < 0.01$). Higher HbA_{1c} values were found in patients with clinical or subclinical eating disorders (8.5 ± 1.9 vs. 7.2 ± 1.5, $P < 0.05$), and the difference was still significant after the elimination of patients who manipulated insulin doses. The routine assessment of eating attitudes should therefore be recommended in all IDDM women patients and in men with poor metabolic control.

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Size of the Pancreas in Type I Diabetic Children and Adolescents

Functional and pathological studies on the pancreas have been performed in diabetic subjects (1,2). Autopsy findings have revealed a significant reduction of weight and size of the gland in patients with type I diabetes (3).

The reasons why the destruction of β-cells (which constitute only 2% of the gland) induces a significant reduction of the exocrine pancreatic tissue are not clarified. It has been shown that the exocrine function of the pancreatic gland is impaired in diabetic subjects, and this deficit is closely related to the β-cell damage (4). The paracrine trophic effect of insulin seems to be responsible for the reduction of structure and size of the pancreatic gland (5,6).

In the present study, ultrasonography of the pancreas was performed in 60 children and adolescents with type I diabetes randomly selected in a large group of diabetic patients participating in the study; their age ranged from 3–15 years. The patients were subdivided into three groups of 20 (10 boys, 10 girls) aged 3–7 years (group A), 8–12 years (group B), and 13–15 years (group C), respectivey. Diabetic patients were not receiving any drug except insulin. No child was suffering from a chronic disease other than diabetes.

The control group consisted of 60 healthy subjects, sex- and age-matched, with no familiar history of type I or type II diabetes and pancreatic disease. They were selected among relatives of physicians and nurses in our hospital. Also, they were not receiving any drugs and were comparable with diabetic patients for height, weight, flanks, and waist circumferences. Informed consent was obtained by the parents and children older than 10 years. In diabetic patients, dura-

tion of disease ranged from 2 months to 11 years (mean ± SD, 4.15 ± 2.6 years); age at onset ranged from 2.8 to 13 years (6.10 ± 3.13), insulin requirement was from 0.31 to 1.6 (0.89 ± 0.23), serum C-peptide values ranged from 0.1 to 1.5 ng/ml (0.26 ± 0.32), and HbA_{1c} ranged from 5.5 to 13.2% (8.96 ± 1.67).

Both diabetic and normal children were scanned after an overnight fast. An echographic scan was performed with a convex scan (3.75 MHz) (Toshiba SSA 250). All echographic scans were performed by the same expert operator who did not know if the child was a diabetic or normal control subject.

Before the beginning of our study, the reproducibility of ultrasound measurement of the pancreas was investigated in 10 healthy volunteers (7). All patients were scanned in the supine position with longitudinal and axial scans. Evaluating the same scan of maximal visualization of the gland, the perimeter and pancreatic area (expressed in cm^2) was marked out with automatic calculation. The transverse diameter of the head from the external border near the duodenal ansa to the isthmic region of the pancreas was also measured. Sagittal scans of the head, body, and tail were performed to measure longitudinal diameters.

Finally, the sum of pancreatic diameters has been calculated to confirm the results obtained by measuring the area of the pancreas. Statistical analysis was performed using the Student's *t* test; regression analysis was determined by calculating Pearson's coefficient. Results are given as means ± SD unless otherwise stated.

In our findings, it is evident that the area of the pancreas is significantly smaller in diabetic subjects than in nondiabetic children. This difference is particularly relevant in both sexes in children 13–15 years old and in boys 8–12 years old. In girls 8–12 years old and in children of both sexes ages 3–7 years old, the reduction of pancreas size in diabetic subjects was less evident. Area of the pancreas (diabetic subjects versus control subjects) in age group 3–7 years was 8.34 ± 3.45 vs. 10.23 ± 2.20 cm^2 in boys ($P < 0.05$) and 7.84 ± 4.10 vs. 9.98 ± 3.11 cm^2 ($P < 0.05$) in girls; area in age group 8–12 was 9.38 ± 2.34 vs. 14.54 ± 4.39 cm^2 in boys ($P < 0.001$) and 9.27 ± 4.34 vs. 11 ± 69 ± 2.59 cm^2 in girls ($P < 0.05$); area in age group 13–15 was 10.89 ± 4.12 vs. 15.70 ± 3.40 cm^2 in boys ($P < 0.001$) and 9.92 ± 3.43 vs. 15.20 ± 2.74 cm^2 in girls ($P < 0.001$).

Sizes of head, body, and tail, calculated by the sum of the diameters, were all significantly smaller in diabetic children, except for body and tail in boys 3–7 years old and body in girls 3–7 years old.

The most relevant reduction of pancreatic parameters was observed in insulin-dependent adolescents (aged 13–15 years). In these patients, the reduction of pancreatic diameters was dependent on the duration of diabetes; in fact, pancreas size was already reduced after 1–2 years of the disease, but the decrease was very evident after 5–11 years. Pancreatic size was not influenced by metabolic control (as expressed by HbA_{1c}) or by insulin requirement.

A significant correlation was found between the sum of pancreatic diameters and C-peptide ($r = 0.585$; $P < 0.05$); this relationship was evident in children with duration of disease shorter than 2 years, independent of age. Pancreatic area was inversely related to the duration of diabetes ($r = -0.590$; $P < 0.05$). The size of the pancreas is significantly reduced in diabetic children, and this reduction involves all portions of the gland (head, body, and tail). In our study, the reduced pancreas size, already detectable in small children and more evident in adolescents, could be related to acinar atrophy and fibrosis (5,8), probably the consequence of the lack of paracrine effect of insulin. Nevertheless, also in our patients, the decline of pancreatic structure and function was dependent on the severity of insulin deficiency; in fact, a strict correlation was found between pancreatic size and endogenous insulin secretion as estimated by serum C-peptide concentrations (particularly in the first 2 years of the disease). The relationship between pancreas dimension, insulin production, and diabetes duration is strongly supported by the evident correlation between reduction of pancreas size and duration of disease.

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The Possible Role of Insulin Release in Cardiovascular Morbidity and Mortality in NIDDM Patients

In his commentary, Lebovitz (1) underlines the roles of hyperglycemia and insulin resistance as risk factors for macrovascular disease in non-insulin-dependent diabetes mellitus (NIDDM), but he does not emphasize the roles of obesity and insulin release. NIDDM is a different disease in obese (mainly insulin resistant) and nonobese (mainly insulinopenic) patients. Body weight also seems important in the clinical picture of secondary failure (SF) of oral hypoglycemic agents, as SF is usually irreversible in nonobese patients, but reversible after weight loss in the obese (2).

In SF patients, we have evaluated risk factors for major complications and mortality. In 1989, 76 SF patients, 51 obese (body mass index [BMI] 32.8 ± 0.8 kg/m^2), and 25 nonobese (BMI 23.6 ± 0.3, $P < 0.01$), were hospitalized to ameliorate metabolic control, including body-weight reduction and adjustment of insulin treatment (patients with serum creatinine levels >1.5 mg/dl were excluded), and to evaluate C-peptide release and diabetic complications. Obese patients differed from nonobese in hypertension (systolic blood pressure [BP] 157 ± 2.9 vs. 147 ± 4.5 mmHg, $P < 0.05$; diastolic BP 91 ± 1.8 vs. 85 ± 1.9 mmHg, $P < 0.05$); use of hypotensive drugs 31/51 vs. 7/25, $P < 0.05$) and C-peptide levels (2.2 ± 0.3 vs. 1.2 ± 0.2 ng/ml, $P < 0.05$). On univariate analysis in 76 patients, ischemic heart disease (IHD) was associated with C-peptide (2.2 ± 0.3 vs. 1.0 ± 0.2 ng/ml, $P < 0.01$ at 0 min; 3.7 ± 0.5 vs. 1.7 ± 0.4 ng/ml 6 min after intravenous glucagon, $P < 0.05$), serum creatinine levels (CREA, 1.0 ± 0.0 vs. 0.9 ± 0.0 mg/dl, $P < 0.01$), and diastolic BP (92 ± 1.7 vs. 86 ± 2.1 mmHg, $P < 0.05$). CREA correlated with age ($r = 0.29$, $P < 0.05$). At stepwise regression analysis (Statview II, Macintosh), C-peptide and CREA were significant risk factors for IHD, age and sex for CREA.

Status was ascertained 48 months later in 39 patients. Six patients (five obese) had died. At baseline they differed from live patients for age (65 ± 1.4 vs. 58 ± 1.5 y, $P < 0.05$), BMI (31.6 ± 2.1 vs. 27.1 ± 0.9, $P < 0.05$), insulin dose (51 ± 12.5 vs. 29.4 ± 3.6 U/day, $P < 0.05$), C-peptide (1.1 ± 0.2 vs. 0.6 ± 0.1 ng/ml at 0 min, $P < 0.01$; 1.6 ± 0.3 vs. 1.0 ± 0.1 ng/ml at 6 min, $P < 0.05$), serum triglycerides (298 ± 75 vs. 156 ± 13 mg/dl, $P < 0.01$), CREA (1.2 ± 0.1 vs. 0.9 ± 0.0 mg/dl, $P < 0.01$), and IHD (5/6 vs. 10/33, $P < 0.05$). At stepwise regression analysis, C-peptide was the only significant risk factor for mortality.

In our view, these data underline the primary role of insulin resistance, linked inter alia to BMI, in cardiovascular morbidity and mortality and suggest that insulin or drugs stimulating insulin release should be avoided in the presence of well preserved insulin release (1–3), as is in obese NIDDM patients.

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Intrauterine Devices Are Safe and Effective Contraceptives for Type I Diabetic Women

Further evidence

Two prospective controlled trials (1,2) with state-of-the-art copper intrauterine devices (IUDs) in type I diabetic women have shown that IUDs are as safe and effective as in nondiabetic women. However, there is still a widespread belief among physicians that diabetic women have a higher risk of IUD-associated pelvic inflammatory disease (PID) (3). The skepticism is probably due to the fact that in one of the above studies, 103 women were followed for only 1 year (1) and in the other study, only 58 women were evaluated, albeit for 3 years