plasma glucose was 25.4 mM and HbA_1 was 12.8%. Diabetes was controlled eventually with 16 U Novolin 30R (Novo Nordisk, Bagsvaerd, Denmark), and she was discharged 5 January 1991. Her blood pressure had been quite normal (100–120/70 mmHg) during admission. In February 1991, her postprandial blood glucose increased to >16.8 mM (302 mg/dl), and urinary glucose was >100 g/day, despite increased insulin dosage. To assess the β-cell function, glucagon test was performed 5 March 1991. After a bolus injection of 1 mg glucagon, she complained of palpitation, chest discomfort, nausea, and throbbing headache. Her blood pressure rose to 180/100 mmHg followed by the development of generalized urticaria. Initial diagnosis was glucagon anaphylaxis, and the patient was treated with prompt administration of 100 mg hydrocortisone phosphate i.v. One hour later, her blood pressure fell to 156/96 mmHg, and skin eruptions disappeared. About 12 h later, she suddenly complained of headache, chest discomfort, and nausea. Because of continuous symptoms and frequent vomiting, she sought another consultation. Her blood pressure was 220/90 mmHg, pulse rate was 84 beats/min and regular, and blood glucose was 25.8 mM (464 mg/dl). The suspicion of pheochromocytoma prompted us to administer orally 1 mg doxazosin mesilate, a long-acting α-receptor blocking agent, and her blood pressure fell to 100/70 mmHg. Urinary norepinephrine and epinephrine were elevated (142 and 61.3 μg/day, respectively). In April, left adrenal pheochromocytoma (17 g) was removed, and her diabetes was controlled with 26 U insulin.

Asymptomatic pheochromocytomas incidentally discovered by new imaging techniques have been increasingly reported (3). The incidence of pheochromocytoma in the diabetic population is not so high compared with only 11 functional pheochromocytomas in >120,000 diabetic cases at the Joslin Clinic (Boston, MA) (4). In a 50-yr autopsy series of 40,078 patients at the Mayo Clinic, however, the prevalence of pheochromocytoma was 0.13%, suggesting more undiagnosed cases in diabetes (5). In our experience, the mean ± SD body mass index of 9 patients with pheochromocytoma was 19.1 ± 2.4 kg/m^2 (range 16.0–22.6 kg/m^2), significantly lower than those in untreated non-insulin-dependent diabetes mellitus (23.9 ± 3.0 kg/m^2, n = 109) and in nondiabetic (22.7 ± 3.5 kg/m^2, n = 79) subjects. Glucagon test should be performed in diabetic patients, particularly thin patients, under the precautionary measures with phentolamine or nifedipine for hypertensive attacks, although they may be asymptomatic and not hypertensive. Furthermore, this case suggests that glucagon may cause a paroxysmal hypertension even after several hours.

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Isolated Fatty Change of Liver as Marker of Glucose Intolerance

The hepatomegaly more commonly found in diabetic subjects is due to fat (1). Creutzfeldt et al. (2) pooled the data of >1750 liver biopsies and found that fatty infiltration of the liver in diabetic patients was 25–78%, with a higher prevalence in maturity-onset (non-insulin-dependent) diabetic patients with respect to juvenile-onset (insulin-dependent) diabetic patients (63 vs. 21%, respectively). The pathophysiology of this condition is complex but seems related to an increased fatty acid afflux to the liver, as a consequence of enhanced lipolysis by adipose tissue, which in turn may lead to increased formation of triglycerides and lipoprotein and hepatic accumulation of fat.

We examined 30 consecutive patients with an ultrasonography diagnosis of fatty liver (3) made by chance during a regular check-up. Subjects ranged in age from 31 to 68 yr, and mean ± SD body mass index was 27 + 1 kg/m^2. Common laboratory tests for liver functions were in the normal range: In particular, aspartate amino transferase was 23 ± 6 U/L (normal values 0–29), alanine amino transferase was 22 ± 6 U/L (0–29), and γ-GT was 31 ± 8 U/L (8–38). Erythrocyte sedimentation rate was also normal. None of the subjects gave a history of previously known hepatic ill-

Table 1—*Clinical and metabolic characteristics of 30 subjects with ultrasound diagnosis of isolated fatty infiltration of liver and 28 matched nondiabetic control subjects*

N (M/F)	HbA_{1c} (%)	Cholesterol (mM)	Triglyceride (mM)	C-peptide (pM) Fasting	C-peptide (pM) 2-h Postglucose
21/9	5 ± 1	5.4 ± 1.3	2.35 ± 0.6	720 + 265	1250 ± 489
20/8	4.4 ± 0.8*	5.2 ± 1.3	1.82 ± 0.5*	535 ± 201*	704 ± 261*

Data are means ± SD. To convert cholesterol into mg/dl, divide by 0.0259; triglycerides into mg/dl, divide by 0.0113; C-peptide into ng/ml, divide by 331.
*Significant difference between groups.

ness or alcohol abuse nor had a jejunoileal bypass procedure. Sixteen subjects had a positive family history of diabetes. All were submitted to a standard 75-g oral glucose tolerance test (dissolved in 300 ml water flavored with lemon juice). Surprisingly, up to 90% presented alterations of carbohydrate metabolism: According to the criteria developed by the National Diabetes Data Group (4), 26 were classified as having impaired glucose tolerance, 2 as non-insulin-dependent diabetic patients, and 2 as nondiabetic subjects (Table 1). The mean HbA_{1c} was higher than that of nondiabetic control subjects (5.1 ± 1 vs. 4.3 ± 0.7%, $P < 0.05$), which suggests that the impact of glucose intolerance was strong enough to alter a reliable index of overall glucose metabolism (5).

Patients with impaired glucose tolerance frequently manifest the association between hypertriglyceridemia and hyperinsulinism, often present even in the absence of obesity (6). Although the subjects we studied were slightly overweight, the comparison with a group of nondiabetic subjects matched for age, sex, and body weight revealed triglyceride and C-peptide values (both fasting and stimulated) significantly higher for patients with fatty change of the liver (Table 1).

The use of ultrasonography in clinical medicine has been rapidly expanding, and the likelihood of ultrasound examination is more probable than an oral glucose tolerance test, especially when fasting plasma glucose is normal. A casual ultrasonography finding of isolated fat changes of the liver should lead us to investigate glucose homeostasis.

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Screening for Prediabetes at Diabetes Camp

As we attempt to provide optimal medical care for our patients with IDDM, it is important to remember our responsibility to their first-degree relatives, who are at increased risk for development of IDDM. Individuals who are at increased risk for IDDM include those who have a family history of IDDM and/or are ICA^+. If asymptomatic ICA^+ individuals have decreased ability to secrete insulin, they are considered to have prediabetes. With continued autoimmune destruction of β-cells, prediabetes becomes symptomatic diabetes. Identifying prediabetic individuals provides an opportunity to study the pathophysiology of IDDM from a very early stage and the chance to intervene with therapy before most β-cells are destroyed.

We are interested in determining the role of insulin resistance in the progression from ICA^+ to clinical diabetes. We propose that, in a subset of patients who are ICA^+, higher insulin resistance may lead to a more metabolically active pancreas that is more vulnerable to the autoimmune disease process.