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.

Table 1—*SI and insulin secretion in prediabetic subjects*

Patient	Age (yr)	Body mass index (kg/m^2)	SI (10^{-4} min · MU^{-1} · ml^{-1})	FPIR (pM)	JDF titer
1	15	23.0	1.30	1536	80
2	26	26.0	1.41	552	320
3	18	29.3	1.45	918	80
4	16	26.1	3.66	678	320
5	12	16.9	5.49	1086	160
6	39	23.4	5.80	528	160
7	6	18.6	10.9	396	40

Diabetes camp provides an ideal setting for sampling of first-degree relatives of children with IDDM. We encourage the entire family to have serum obtained yearly for the measurement of ICA. We have identified 15 ICA^+ individuals among the 475 first-degree relatives sampled. Seven have been tested further to determine their ability to secrete insulin and their sensitivity to insulin.

Seven ICA^+ individuals were studied with the modified minimal-model FSIGT (1,2). This method involves the administration of 0.3 g/kg glucose at time zero and then 0.03 U/kg regular insulin at 20 min. With insulin and glucose concentration from FSIGT, we can calculate SI (2) and FPIR (1-min insulin plus 3-min insulin minus baseline insulin; 3). Results are shown in Table 1.

The subjects' JDF titers range from 40 to 320 and their SI values from 1.41 to 10.9 (a higher SI indicates increased sensitivity). Normal SI values in children are from 3 to 11 and in adults from 2 to 8. No correlations between FPIR and SI or JDF titer were apparent. All FPIR values except one were >402 pM, a level below which is considered predictive of clinical diabetes (3). In subject no. 7, a normal-sized 6-yr-old boy, low FPIR may be caused by increased SI (SI = 10.9), which diminished insulin need. Subject no. 2 had a low SI, high JDF titer, and normal FPIR. Both subjects will be monitored closely, and should the FPIR decline, they will be referred for immunotherapy.

The FSIGT provides a reliable, fairly easy method of determining SI and insulin secretory capacity. In individuals who are ICA^+, insulin resistance may be an additional risk factor for further β-cell damage and progression to clinical diabetes. Our ICA^+ subjects demonstrated a wide range of values for SI, and none were clearly prediabetic. Longitudinal follow-up in these subjects will be important to determine the possible role of SI in the pathogenesis of IDDM.

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IDDM, insulin-dependent diabetes mellitus; ICA, islet cell antibody; FSIGT, frequent-sampling intravenous glucose tolerance test; FPIR, first-phase insulin release; SI, insulin sensitivity; JDF, Juvinile Diabetes Foundation.

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Discussing the Role of Glucagonlike Peptide-I

We would like to comment on an article that appeared in the February issue of *Diabetes Care* by Nathan, Schreiber, Fogel, Mojsov, and Habener. The article deals with the insulinotropic action of glucagonlike peptide-I-(7–37) in diabetic and nondiabetic subjects.

However, because of a significant lack of reference to published work from European groups, some of the conclusions presented appear inaccurate and misleading:

1. In humans, glucagonlike peptide-I-(7–37) does not seem to be a naturally occurring intestinal peptide as postulated. The naturally occurring intestinal peptide is glucagonlike peptide-1 (7–36 amide) (or proglucagon 78–107 amide) as has been shown by Ørskov et al. (*J Biol Chem*, 264:12826, 1989) and Kreymann et al. (Lancet 2:1300, 1987).

2. The first to report on the insulinotropic action of glucagonlike peptide-I (7–36 amide) were Ørskov and Holst in 1986 (*Diabetologia* 29: A549). Neither this communication nor the subsequent full paper (Holst et al., FEBS Lett 211:169, 1987) (which appeared earlier than the quoted paper on "insuli-