before the development of overt diabetes (9) (presumably during a period of decreasing glucose tolerance), others have not found such an association between clinical status and deteriorating glucose tolerance (1,10). One can speculate on the number of ways in which insulinopenia, before causing overt symptoms of hyperglycemia, might be detrimental to CF patients (increased protein catabolism, intermittent glucosuria, altered immune function). Yet, to date, there is no reported evidence that treatment of asymptomatic CF patients with normal fasting glucose levels and a diabetic response to OGTT improves clinical status or delays the onset of overt diabetes.

In February 1998, a Cystic Fibrosis Foundation consensus conference recommended screening with random glucose levels, with follow-up of abnormal random glucose levels (≥126 mg/dl) by fasting glucose level. A confirmed elevated fasting glucose level (≥126 mg/dl) is diagnostic for CFRD. The OGTT is reserved for patients participating in research or for those in high-risk circumstances (unexplained polyuria or polydipsia, failure to gain or maintain weight, delayed puberty, or unexplained chronic decline in pulmonary function).

Our study revealed that screening for glucose abnormalities in CF patients is erratic and is performed using a variety of methods, but that only a handful of CF practices in the U.S. are performing OGTTs. It is hoped that this discussion, in conjunction with the new consensus conference guidelines, will raise the level of consciousness about disorders of carbohydrate metabolism in CF patients and standardize our approach to these problems. Before recommending that all adult CF patients have annual OGTTs, we must have solid evidence that a worthwhile intervention is available to those who have abnormal results.

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Glycemic Control in Type 1 Diabetes

A cross-sectional study in 1,200 Belgian patients

We read with interest the recent article by Rosilio et al. (1) reporting an HbA_{1c} value of 8.97 ± 1.98% (mean ± SD) in a French population of 2,579 patients with type 1 diabetes aged 1–19 years. Approximately 33% of their cohort had HbA_{1c} <8%, whereas 14.5% had values >11%. Rosilio et al. conclude that these overall results are unsatisfactory, since they will expose a majority of these young patients to developing microangiopathic complications.

We analyzed, in a cross-sectional survey, the clinical characteristics of a cohort of 1,200 insulin-treated Belgian patients attending our University Diabetes Center, consisting mostly (>80%) of subjects with type 1 diabetes (2,3). As in the study of Rosilio et al., the Belgian Health Service offers near total coverage of diabetes care. Patients were followed on an outpatient basis (1–4 visits/year). None had participated in interventional trials aimed at improved glucose control. Their mean age was 43 ± 19 years, with 9% of the subjects being <18 years old. Respectively 51, 22, and 23% of patients were treated with two (2ii), three (3ii), or four (4ii) daily insulin injections; continuous subcutaneous insulin infusion (CSII) was used in 4%.

In this mostly adult population, we observed a level of glycemic control, as assessed by HbA_{1c}, similar to that reported by Rosilio et al. in their pediatric cohort. Thus, HbA_{1c} was 8.63 ± 1.55% (8.54 ± 1.46% in male subjects and 8.72 ± 1.62% in female subjects). It is remarkable that this overall value of HbA_{1c} was identical to that recorded in France in the subgroup of patients followed by Rosilio et al. in university-affiliated hospitals. We found that 36 (2ii), 31 (3ii), 38 (2ii), and 21% (CSII group) had an HbA_{1c} <8%, a proportion comparable to that reported by these authors (33%). As far as home blood glucose monitoring was concerned, the mean strip consumption in our Belgian cohort was 2.2 per subject per day (vs. 2.8 in the French study). We observed no correlation between daily insulin injection number or strip consumption and HbA_{1c} levels.

In conclusion, in a mainly adult Belgian population with type 1 diabetes and free access to diabetes care, overall glycemic control, assessed by HbA_{1c} was comparable to that measured in a mostly pediatric French population.

Global HbA_{1c} levels in both studies were above the threshold suggested by the Diabetes Control and Complications Trial (DCCT) results and those of other studies (4,5), since only a third of patients in the Belgian and French cohorts could attain HbA_{1c} values <8% (i.e., below the realistic threshold beyond which there is a rapid increase in the likelihood of developing microangiopathy). Thus, both surveys

demonstrate that the degree of glycemic control in these two populations remains insufficient throughout the age span, even for those patients routinely followed in university centers. Optimizing treatment modalities, deliveries, and education to achieve levels of glycemic control comparable to those obtained during the DCCT or in similar, intervention-modified, environments, requires more medical and paramedical resources, thus producing a significant long-term demand for human and financial support.

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Response to Paris et al.

Pediatricians and diabetologists

Should it be methodologically correct to compare French and Belgian patients and doctors? We thank Dr. Paris and colleagues (1) for reassuring us collectively, as pediatricians taking care of young patients with diabetes. As a young resident in endocrinology 20 years ago, I was trained in the intangible idea that the results of adult diabetologists' efforts were indisputably more efficacious in terms of glycemic control than those of pediatricians. Was it true in those times? Remember that in many countries, including France, pediatricians were advocating free diet (freedom meaning a lot of sugar) and one insulin shot daily and discouraging the use of capillary blood in favor of the good old urinary measurements.

Those times are gone, fortunately for our patients, and we can now enjoy shameless comparisons of results with our colleagues. As an echo to Dr. Paris's letter, let us regret that besides well-known intervention studies of intensive therapy in highly selected centers and patients, there are too few reports of actual glycemic results in large cohorts (mostly adult) of patients with type 1 diabetes.

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LDL Cholesterol and Troglitazone Therapy

The recent study by Tack et al. (1) reported larger average LDL size in individuals on troglitazone therapy and appears to suggest that the increases in LDL cholesterol concentration typically observed with this agent (2,3) are not ultimately harmful to patients with type 2 diabetes because they are offset by potentially beneficial changes in lipoprotein composition and susceptibility to oxidation. This conclusion must be interpreted with caution for several reasons.

First, although several observational studies have shown an association between small, dense LDL and coronary heart disease (CHD) in patients with diabetes (4,5), the effects of changing LDL size have never been directly evaluated in any patient population. In contrast, increases in LDL cholesterol concentrations have been shown to be a strong and consistent risk factor for coronary artery disease in both cross-sectional and longitudinal analyses of individuals with or without diabetes. Furthermore, lowering LDL cholesterol concentration has been proven to decrease the incidence of cardiovascular events in several interventional studies (6,7).

Neither the American Diabetes Association nor the National Cholesterol Education Program has treatment recommendations suggesting that increases in LDL concentration are ameliorated by changes in LDL size. Thus, increases in LDL size should not be construed to negate the known risk of increases in total LDL cholesterol concentrations.

Second, the data from Tack et al. (1) showed decreased susceptibility to oxidation in the LDL after troglitazone therapy. This is consistent with the change in size because small, dense LDL are known to be more susceptible to oxidation in vitro (8). Although there are a large number of in vitro studies pointing to the importance of LDL oxidation in the atherosclerotic process, there are no clinical trials showing that changes in LDL oxidation can alter CHD risk. Manipulations that decrease oxidization ability might be of potential benefit; until clinical trial data are available, however, such manipulations associated with increasing LDL cholesterol concentrations cannot be assumed to be beneficial.

Finally, the study reported by Tack et al. (1) was not conducted in patients with diabetes. Individuals with diabetes are known to have increases in several CHD risk factors and to be at significantly increased risk for cardiovascular disease (CVD). Thus, any therapeutic regimen that results in increased LDL cholesterol concentrations in patients with diabetes must be viewed as increasing the risk of atherosclerosis in affected indi-