patients, already consecutively hospitalized in the metabolic unit of our hospital 5–13 yr before the present observation and having the diagnosis of IGT (7), were recruited.

At the first observation, body weight, height, and blood pressure were recorded; a fasting blood sample was also obtained for glucose, cholesterol, triglyceride, and uric acid determinations. At the second observation, diagnosis of diabetes was again made according to National Diabetes Data Group criteria (7). Furthermore, in all patients the 5′-flanking polymorphic region of the insulin gene was studied as described elsewhere (4), and alleles were classified according to Bell (6) as allele 1 and allele 3.

Statistical analysis was performed by one-way variance analysis, Student's t test for paired data, and χ^2-test where appropriate. Patients developing type II diabetes (13 of 26, 50%) had a mean age (38.8 ± 8.9 vs. 42.8 ± 11.2 yr, NS) and body mass index (BMI, 40.8 ± 6.3 vs. 51.0 ± 9.8 kg/m^2, $P < .05$) that was lower and a serum cholesterol level (255.0 ± 99.8 vs. 198.1 ± 41.1 mg/dl, $P < .01$) that was significantly higher than that of the group of obese subjects not developing diabetes.

Genotypes absent, heterozygote, and homozygote for 5′-flanking insertion [1/1, 1/3, 3/3 according to Bell's classification (6)] were found in 76.9, 15.4, and 7.7%, respectively, of those who developed diabetes and in 69.3, 23, and 7.7% of the other group. Therefore, the two groups did not differ in the frequency of these genotypes, and no difference was detectable versus the reference group (1/1, n = 33, 54.0%; 1/3, n = 22, 36%; 3/3, n = 6, 10%; 4).

No other anthropometric, biochemical, blood pressure, or familial parameters showed any relationship to the genotype. From our study it appears that severely obese patients with IGT are at very high risk (50%) to develop type II diabetes. We tried to evaluate predictive factors for such evolution, but except for higher values of serum cholesterol (8), lower excess body fat, and younger age, we were unable to detect any differences. In particular, the two subgroups did not differ in family history of diabetes or the occurrence of type 3 allele.

Note that the frequency of the type 3 allele was found lower in this group of severely obese patients than in the control group of our population. Type 3 allele appears to be associated with lower insulin production by β-cells (4), whereas insulin is essential for storing triglycerides in the adipose cells and excess body fat is linearly related to insulinemia. Severely obese patients might, therefore, constitute a selected group of individuals where insulin production must be high and, consequently, presence of type 3 allele uncommon. In conclusion, development of diabetes in severe obesity does not seem to be linked to the presence of type 3 allele.

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Is HbA_1 Measurement Superfluous in NIDDM?

Measurement of glycosylated hemoglobin (HbA_1), reflecting the integrated plasma glucose concentration over the preceding 6- to 8-wk period, has become a standard index of glycemic control in diabetes mellitus (1,2). Compared with measurement of plasma glucose, the cost of HbA_1 measurement is considerable in terms of assay reagents and labor. Nevertheless, many, if not most, centers use the test routinely as an accepted part of the management of both insulin-dependent (IDDM) and non-insulin-dependent (NIDDM) diabetes mellitus. At our clinic, we first measured HbA_1 in selected patients in 1977, and since November 1980 it has become an integral part of our routine outpatient service, the aim being to have an HbA_1 measurement for every patient at every review appointment. In a previous report

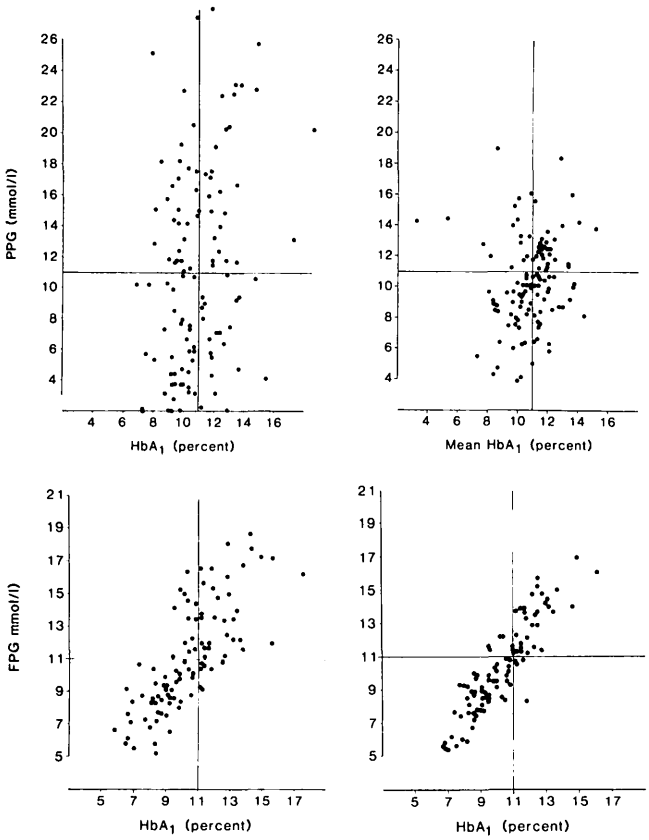

FIG. 1. *Top panels*: Postprandial plasma glucose (PPG) vs. HbA_1 in 114 IDDM patients. *Left*, values for each patient at most recent outpatient review (r = .24); *right*, mean values for each patient over study period (r = .26). *Bottom panels*: fasting plasma glucose (FPG) vs. HbA_1 in 96 NIDDM patients. *Left*, values for each patient at most recent outpatient review (r = .68); *right*, mean values for each patient over study period (r = .86). *Lines* indicate 11 mM (plasma glucose) and 11% (HbA_1) as arbitrary distinction between good and poor control.

from our clinic, we presented data supporting the view that measurement of HbA_1 provided clinical information distinct from concomitant measurement of plasma glucose in patients with IDDM (3), a conclusion also reached by other investigators (4). Because NIDDM constitutes the major portion of outpatient clinic workload, we believe it is relevant to assess whether HbA_1 measurement gives similarly unique information in NIDDM patients.

HbA_1 was measured regularly over a 5-yr period in 96 NIDDM and 114 IDDM patients selected randomly from our outpatient clinics. The results were compared with concomitant fasting plasma glucose (FPG) in NIDDM patients and 2-h postprandial plasma glucose (PPG) in IDDM patients. The 96 NIDDM patients (age range 46–75 yr, mean 61 yr; 52 women, 44 men) comprised 49 patients treated by diet alone and 47 treated by diet plus oral hypoglycemic therapy. The 114 IDDM patients (age range 15–78 yr, mean 42 yr; 62 women, 52 men) were all clearly ketosis prone and insulin dependent from the onset of their diabetes (duration 4–48 yr). A minimum of 4 paired estimations of plasma glucose and HbA_1 (mean number was 9) were required for inclusion in the NIDDM group, and 10 were required in the IDDM group (mean number was 18). This discrepancy reflected the more frequent outpatient review of IDDM patients. Plasma glucose and HbA_1 at the most recent clinic visit, together with the means of these parameters over the 5-yr study period, were calculated in each group. HbA_1 was measured by agar gel electroendosmosis (Corning, Halstead, Essex, UK) with prior incubation of erythrocytes in normal saline to remove the labile fraction. Glucose was measured by a glucose oxidase method.

In the IDDM patients, there was a poor correlation between PPG and HbA_1 at the most recent clinic visit (r = .24) and for the mean values over 5 yr (r = .26). In the NIDDM group, corresponding values (for FPG rather than PPG) were r = .68 increasing to .86 when the means of the parameters over 5 yr were calculated (Fig. 1). If poor control is arbitrarily defined as HbA_1 >11.0% (normal range 3.6–7.2%) and FPG or PPG >11 mM (198 mg/dl), then 80% of the NIDDM group compared to 58% of the IDDM group have concordant plasma glucose and HbA_1 values.

Figure 2 illustrates the similar pattern exhibited by HbA_1 and FPG when repeated observations were made over a prolonged period in two patients with NIDDM. This is true even when glycemic control is stable over

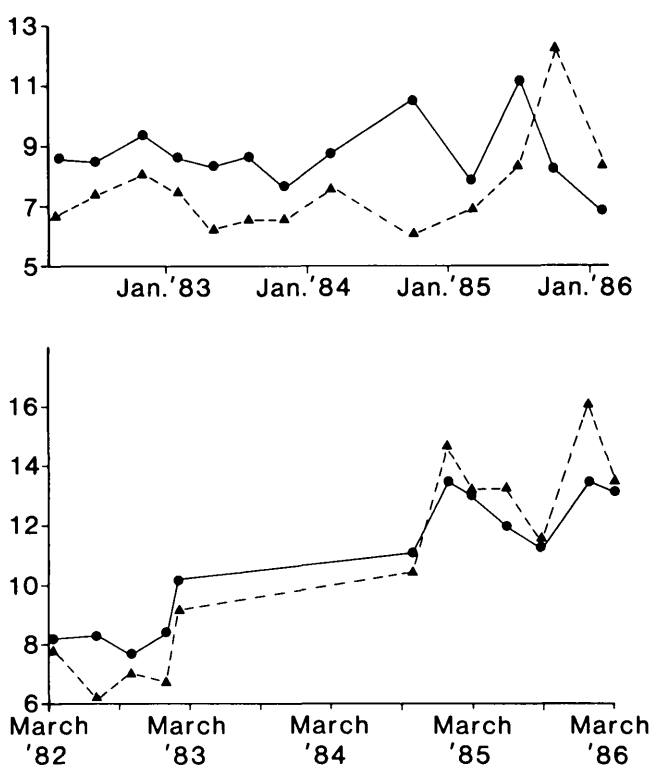

FIG. 2. Fasting plasma glucose (mM; ▲) and HbA_1 (%; ●) at outpatient clinic reviews in 2 NIDDM patients. *Top*, r = .08; *bottom*, r = .97.

a prolonged period with little variation in HbA_1 levels, so that the correlation between HbA_1 and FPG is relatively poor (Fig. 2 *top*).

The excellent agreement between FPG and HbA_1 in NIDDM patients suggests that FPG offers a reliable, simple, and adequate measure of glycemic control and leads us to question the need for routine testing of HbA_1 in such patients. Even in the unstructured setting of diabetic outpatients, the fasting blood sample has the advantage of some standardization, and fasting from the night before the test is no problem in outpatients. Theoretically, FPG measurements could indicate spuriously good control if patients dieted before a clinic visit. However, the excellent correlations we obtained over a wide range of glycemia suggest that such attempted deception is relatively rare.

At a time of increasing concern about the cost of health-care provision, it behooves physicians to exercise the greatest efficiency possible in clinical investigation and management. We do not suggest that measurement of HbA_1 should be abandoned in NIDDM patients, but we believe its use could be rationed, perhaps to no more than one measurement per year in most patients, without compromising clinical care.

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Computer-Generated Formats for SMBG Data

Advances in microcomputer software are beginning to provide physicians with a sophisticated capacity for manipulating patients' self-monitored blood glucose (SMBG) data to interpret metabolic control (1). In anticipation of greater use of this technology, it is important to determine whether the manipulation of SMBG data by computer affects physicians' therapeutic decision making. One basic question is whether specific visual formats and/or degrees of data reduction enhance or inhibit recognition of different patterns of metabolic control.

We evaluated the ability of physicians to identify and respond to glucose patterns for simulated diabetes cases in which display format and degree of SMBG data reduction were manipulated independently. Two cases were created to portray distinct patterns of control for adolescents with insulin-dependent diabetes mellitus (IDDM), i.e., a stable pattern of late-morning hypoglycemia secondary to overinsulinization and a pattern consistent with the Somogyi phenomenon. In this fashion, we compared decisions based on traditional SMBG logs (i.e., unreduced-tabular format) with those based on computer-generated portrayals of the same data.

The 44 subjects were pediatric residents (n = 15 1st-yr, 14 2nd-yr, and 11 3rd-yr postgraduates) and subspecialty fellows (n = 4) from the Indiana University Medical Center. Their training includes experience in managing patients with IDDM. SMBG data for 4 wk from actual patients were transformed into four anonymous case summaries representing the independent manipulation of two variables, i.e., whether the format was tabular or graphic and whether the data were unreduced or reduced (Fig. 1). Each physician was assigned randomly to one of the four SMBG formats. Subjects then read both case summaries and answered a series of open-ended questions concerning the diagnosis of the metabolic control pattern and therapeutic changes they would make using the available SMBG data. Responses were judged for correctness by one of the investigators (M.P.G.) who was blind to subjects' experimental conditions. Fisher's exact test was used to analyze the frequency of correct response as a function of format and degree of data reduction.

Half of the 44 subjects in all conditions identified and responded appropriately to the pattern of morning hypoglycemia. Sixty-four percent of residents using the two tabular formats responded correctly, compared to 36% of those using the line or bar graphs (14 of 22 vs. 8 of 22 correct; P = .13). The relative advantage of the tabular format was most pronounced when data were reduced. Eight of 11 residents using statistical tables responded to the problem appropriately, compared to 3 of 10 using bar graphs (P = .09).

The Somogyi phenomenon proved a much more difficult problem to identify, with only 10 (23%) of 44 subjects responding appropriately. Thirty-eight percent of residents using data-reduced SMBG formats responded correctly, compared to 10% of subjects assigned unreduced data (8 of 23 vs. 2 of 21, P = .07). This trend toward a main effect favoring data reduction is strongest when contrasting the two tabular formats. Five of 12 subjects who interpreted the statistical tables made correct responses. None of the 10 subjects given