TABLE 1
Comparison of overnight and short-term urine collection

Subjects (*n*)	Normal (12)	Diabetic (52)
Duration of overnight (min)	460 ± 40 (385–525)	429 ± 55 (300–540)
Urinary vol (ml)		
overnight	308 ± 102 (180–550)	334 ± 163 (120–1000)
short term	49.5 ± 38 (6–145)	42.1 ± 47 (9–260)
Urinary AER (μg/min)		
overnight	4.87 ± 1.7 (2.92–8.6)	7.6 ± 7.6 (0.2–38.0)
short term	4.83 ± 1.5 (1.5–6.8)	7.6 ± 7.7 (0.1–44.2)
C.V. of AER (%)		
overnight	39.4 (2.4–70)*	28.3 (1.8–41.3)†
short term	38.9 (1.6–77.3)*	40.6 (2–46.5)†

Data are expressed as means ± SD; ranges are reported in parentheses. AER, albumin excretion rate.
*Normal (n = 10) and †diabetic (n = 18) subjects who performed 3 successive overnight and 30-min urine collections.

overnight urine volumes were 6- to 8-fold higher than short-term volumes in both groups (Table 1). Mean AERs from the two collections agreed closely in both normal (overnight, 4.87 ± 1.7 μg/min vs. 30-min collection, 4.83 ± 1.5) and diabetic (overnight, 7.6 ± 7.6 μg/min vs. 30-min collection, 7.6 ± 7.7; Table 1) subjects. A significant correlation (r = .905, P < .001) was found between the two different AER measurements (Fig. 1). The mean C.V. of AER was ~30–40% for both types of collections (Table 1).

Our data indicate that a timed, standardized urine collection of only 30 min, performed in the morning, in supine patients, may allow an AER evaluation virtually identical to that provided by the overnight collection. This modality of urine collection is employed usefully for AER screening in our metabolic unit by ambulatory diabetic patients who need periodic medical examinations. Patients who have problems urinating after 30 min usually complete the collection by prolonging their recumbency for 60 min.

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REFERENCES

1. Mogensen CE: Microalbuminuria as a predictor of clinical diabetic nephropathy. *Kidney Int* 31:673–89, 1987
2. Andersen AR, Christiansen JS, Anderson JK, Kreiner S, Deckert T: Diabetic nephropathy in type 1 (insulin-dependent) diabetes: an epidemiological study. *Diabetologia* 25:496–501, 1983
3. Cowell CT, Rogers S, Silink M: First morning urinary albumin concentration is a good predictor of 24-hour urinary albumin excretion in children with type 1 (insulin-dependent) diabetes. *Diabetologia* 29:97–99, 1986
4. Jarrett RJ, Viberti GC: Risk of nephropathy in diabetes mellitus: problems of methodology and terminology (Letter). *Diabetologia* 28:181, 1985
5. Shaw AB, Risdon P, Lewis-Jackson JD: Protein creatinine index and Albustix in assessment of proteinuria. *Br Med J* 287:929–32, 1983
6. Rowe DJF, Hayward M, Bagga H, Betts P: Effect of glycaemic control and duration of disease on overnight albumin excretion in diabetic children. *Br Med J* 289:957–59, 1984
7. Nathan DM, Rosenbaum C, Protasowicki VD: Single-void urine samples can be used to estimate quantitative microalbuminuria. *Diabetes Care* 10:414–18, 1987
8. Giampietro O, Miccoli R, Clerico A, Di Palma L, Bertolotto A, Anichini R, Cristofani R, Navalesi R: Urinary albumin excretion in normal and in diabetic patients measured by a radioimmunoassay: methodological and clinical aspects. *Clin Biochem*. In press

Prediction and Immunosuppression of Type I Diabetes

Challenging current beliefs, especially with new data, is commendable. The ongoing research into prediabetes and attempts to induce remission is still in its infancy and is full of uncertainties. Thus, I was pleased to see a letter of challenge from Bell et al. (1) containing three case reports. However, as I read on, I was struck by the lack of substance of the three case reports, which presumably were included to support the assertive title.

Cases 1 and 2 are individuals who already have diabetes as well as susceptibility genes and who are positive for islet cell antibodies. Appropriate longitudinal studies in these patients would probably have shown them to be antibody positive and normoglycemic, i.e., prehyperglycemic insulin-dependent diabetic months or

years earlier. The boy in the 3rd case has susceptibility genes and autoantibodies but still has normal β-cell function. If he remains antibody positive, he may very well develop diabetes. Thus, all 3 cases support the usefulness of immunogenetic markers of prediabetes.

The fact that the third patient developed psychiatric difficulties is probably a coincidence. In my experience (~2000 children tested and >12 found positive) and in the even greater experience of other investigators (2–6), to my knowledge, no such case has been found. In fact, a positive attitude of the tested families has been reported (7). Conclusions drawn from one case vis-a-vis such a large number of cases are misleading.

Bell et al. also express their concern about cyclosporin treatment in diabetic children. This concern is shared by many, including myself. Cyclosporin should only be used in carefully planned and conducted randomized trials. In fact, I question why patient 1 was treated with cyclosporin in what seems a rather casual context. However, cyclosporin is not the only type of treatment being studied for diabetes. There are other intervention protocols (e.g., nicotinimide) that seem to be generally free of toxicity and offer some promise of inducing remissions. These drugs are already being tested in prediabetic individuals.

Even if no intervention means were available, study of the autoimmune dysfunction in the prehyperglycemic stage of type I diabetes would still be of great interest to further characterize the autoimmune pathogenesis of this disorder. If Bell et al. meant that none of these activities are ready to be adopted by general practitioners, then I would wholeheartedly agree. However, the message I perceived was one of condemnation of these studies, which I think is inappropriate.

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REFERENCES

1. Bell DSH, Acton RT, Barger BO, Vanichanan C, Clements RS Jr: Futility of predicting onset of type I diabetes mellitus (Letter). *Diabetes Care* 10:788–89, 1987
2. Srikanta S, Ganda OP, Eisenbarth GS, Soeldner JS: Islet cell antibodies and beta-cell function in monozygotic triplets and twins initially discordant for type I diabetes. *N Engl J Med* 308:322–25, 1983
3. Bottazzo GF, Florin-Christensen A, Doniach D: Islet cell antibodies in diabetes mellitus with autoimmune polyendocrine deficiencies. *Lancet* 2:1279–83, 1974
4. Keller U, Beglinger CH, Berger W: Identification of subjects with a high risk of developing type I (insulin dependent) diabetes. *Diabetologia* 28:57–58, 1985
5. Gingsberg-Fellner F, Witt M, Franklin B, Yagihashi S, Toguchi Y, Dobersen M, Rubinstein P, Notkins A: Triad of markers for identifying children at high risk of developing insulin-dependent diabetes mellitus. *JAMA* 254:1469–72, 1985
6. Riley W, Krischer J, Clarke D, Malone J, Rotter J, Shah S, Vadheim C: Islet cell antibodies (ICA): relative risk (RR) of developing insulin dependent diabetes (IDD) is 166 (Abstract)! *Diabetes* 36:70A, 1987
7. Johnson SB, Hansen CA, Nurick M: Will I get diabetes? The psychological impact of ICA screening (Abstract)? *Diabetes* 36:72A, 1987

REPLY

The intent of our letter to *Diabetes Care* was to emphasize the point to which Dr. Barbosa refers, namely that immunogenetic diagnosis of prediabetes has not yet advanced to the point that it is of use to the practitioner. In fact, unless such practices are a part of ongoing studies of the immunologic basis of type I (insulin-dependent) diabetes, they may cause undue confusion on the part of the practitioner and his or her patient. We strongly support the ongoing studies that are attempting to unravel the autoimmune basis of type I diabetes mellitus and to capitalize on this information to develop rational preventive and therapeutic strategies.

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DNA Polymorphism of the Insulin Gene, Diabetes, and Severe Obesity

Some reports have suggested that alleles with larger insertion in the 5'-flanking region of the insulin gene (type 3 allele) may be genetic markers of non-insulin-dependent (type II) diabetes (1–5). Aoyama et al. (5) have recently reported in this journal that frequency of larger 5'-flanking insertion is particularly high in non-overweight and <40 yr-of-age type II diabetic patients. In their study, type 3 allele has been found not related to the excess body fat. In our study, complementary to that by Aoyama, we aimed to evaluate the predictive value of type 3 allele on the worsening to type II diabetes of severely obese patients with previous impaired glucose tolerance (IGT).

Twenty-six (17 females and 9 males) severely obese