cedure is quite extraordinary. A challenge test followed by a definitive GTT can remain a viable option if compliance approaching this figure could be achieved in all centers.

However if this is not possible, then any modification of the existing glucose tolerance testing procedure for pregnancy to one that increases the compliance and reduces the inconvenience should not be dismissed.

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Antibodies to GAD in Elderly Patients With Previously Diagnosed NIDDM

Clinical significance of seropositivity for antibodies to GAD (anti-GAD) has been extensively investigated in middle-aged patients with NIDDM (1,2). To our knowledge, however, there have been no studies on the prevalence and clinical significance of anti-GAD in elderly patients with NIDDM, despite the fact that the number of elderly diabetic patients is increasing. Thus, we examined anti-GAD by a radioimmunoprecipitation assay with recombinant human GAD65 (3) in 183 consecutive elderly patients (78 men and 105 women) ≥65 years old (mean age, 72.3 ± 6.1 years) with previously diagnosed NIDDM.

The prevalence of anti-GAD in elderly patients with NIDDM was 5.5% (10 of 183). It was 9.2% (7 of 76) in insulin-requiring NIDDM and 2.8% (3 of 107) in NIDDM well controlled by diet and/or oral hypoglycemic agents. Impaired pancreatic β-cell function was a major clinical characteristic of insulin-requiring elderly patients with NIDDM who were positive for anti-GAD (anti-GAD$^+$) compared with those negative for anti-GAD (anti-GAD$^-$) (fasting plasma C-peptide, 0.12 ± 0.10 vs. 0.56 ± 0.39 nmol/l, respectively; $P < 0.01$ by unpaired Student's t test), as is observed in middle-aged anti-GAD$^+$ NIDDM patients (4). Interestingly, seropositivity for anti-GAD alone was not predictive of the later development of insulin deficiency in elderly patients with NIDDM, but a genetic factor (HLA-DRB1) might also be a prognostic indicator in elderly anti-GAD$^+$ NIDDM patients (Table 1). In brief, anti-GAD$^+$ elderly NIDDM patients with DRB1*0405 and/or DRB1*0901, alleles that are associated with susceptibility to IDDM (5), tended to develop insulin deficiency within a short period. Even insulin-requiring anti-GAD$^+$ elderly NIDDM patients without those alleles developed insulin deficiency after a long period. In contrast, β-cell function was preserved in two patients with the DRB1*1502 allele, which protects against IDDM.

In conclusion, anti-GAD appeared to be a useful marker for predicting later development of insulin deficiency in elderly NIDDM patients and for determining their appropriate treatment when insulin is required because of secondary failure of sulfonylurea agents, which occurs in elderly as well as younger patients.

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Table 1—*Clinical profiles of elderly anti-GAD$^+$ NIDDM patients*

Patient number	Sex	Age (years)	Age at onset (years)	Disease duration (years)	BMI (kg/m^2)	sCPR (nmol/l)	uCPR (μg/day)	Current treatment	Daily insulin dose (U/kg)	Interval* (years)	HbA_{1c} (%)	HLA-DRB1 genotype
1	M	79	52	27	18	0.10	7	Insulin	0.27	26	6.6	0803/0901
2	F	65	44	21	21	0.03	ND	Insulin	0.52	16	7.2	0406/1403
3	F	71	52	19	22	0.17	15	Insulin	0.31	15	8.0	1001/1401
4	F	66	40	26	19	0.30	ND	Insulin	0.3	25	7.4	0803/1501
5	F	69	45	24	23	0.17	14	Insulin	0.46	20	8.6	0410/1302
6	F	75	66	9	23	0.03	ND	Insulin	0.19	3	7.8	0803/0901
7	F	68	64	4	25	0.03	ND	Insulin	0.94	1	11.5	0405/0901
8	M	72	57	15	19.5	0.63	41	Diet	—	—	5.5	0901/1101
9	M	71	55	16	22	0.96	ND	SU	—	—	8.3	0802/1502
10	M	67	51	16	19	0.76	ND	SU	—	—	7.0	1502/1502

*Interval between diagnosis of diabetes and initiation of insulin therapy. ND, not determined; sCPR, fasting plasma C-peptide; SU, sulfonylurea; uCPR, 24-h urinary C-peptide excretion.

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Constant Infused Glucose Regimen During the Recovery Phase of Diabetic Ketoacidosis in Children and Adolescents With IDDM

In a recent issue of *Diabetes Care*, Wiggam et al. (1) have suggested that an extended insulin regimen for diabetic ketoacidosis (DKA) can be effectively applied with the 20% glucose at a variable rate to avoid hypoglycemia and that this regimen may produce a more rapid resolution of ketosis during the recovery phase than the conventional regimen. Many physicians may agree to any regimen involving extra insulin during the recovery phase of DKA, since the reduced dose of insulin may prolong recovery, as also demonstrated by Krentz et al. (2), who used 10% glucose infusion as extra glucose with additional insulin, in comparison with the conventional 5% glucose infusion.

However, the extended insulin regimen used by Wiggam et al. (1) may cause electrolytes and fluid imbalances due to a constantly large amount of infused insulin, almost 2 U · kg^{-1} body wt · day^{-1}. The 20% glucose at a variable rate appears to be a reasonable approach to avoid hypoglycemia, but it remains empirical, since no guideline for the infusion rate was mentioned except for the hourly monitoring of the blood glucose levels. On the other hand, the 10% glucose regimen, a constant concentration of infused glucose, used by Krentz et al. (2) seems to offer a contradiction in terms of the amount of glucose to be infused per hour versus the time course of fluid replacement. As seen in an example of fluid therapy for DKA found in textbooks for pediatric (3) and adult (4) patients, the infusion rate of fluid replacement for the calculated deficit within the first 12 h, the early recovery phase, may be double that for the remaining deficit and maintenance during the next 24 h, the late recovery phase. Thus, the amount of glucose infused per hour during the late recovery phase may be halved in comparison with that during the early recovery phase. Contrarily, the patient may require a larger amount of infused glucose per hour during the late recovery phase, since the hepatic glucose output may be suppressed, and the insulin resistance, or glucolipotoxicity, may be reducing.

We have therefore suggested a constant amount of infused glucose per hour (5,6), which is based on the basal hepatic glucose output according to Bier et al. (7) (Table 1). These amounts for infancy to adulthood can also account for the amount of infused glucose calculated for the late recovery phase of DKA in the above example if using a 10% glucose infusate in any age-groups. In our experience (5), the ratio of infused glucose to insulin per hour became higher at a variable rate of infused insulin, determined on the basis of 1- to 2-hourly adjustment to keep near normoglycemic levels as DKA was improving. This ratio during the recovery phase was also useful as an index of metabolic stability or insulin sensitivity. At the endpoint, the median ratio was 7 g glucose/1 U insulin, regardless of age-group. This regimen was superior to the conventional therapy using a 5% glucose infusate in regard to the disappearance rate in serum ketone bodies. Further, such a therapy based on the constant amount of glucose, as indicated above, has also been applied safely and effectively in a prolonged fasting state of IDDM on sick days or during surgery.

Table 1—*The amount of glucose to be infused during the recovery phase after reducing blood glucose below 240 mg/dl in diabetic ketoacidosis*

Age-group	Body weight (kg)	Estimated surface area (m^2)	Glucose to be infused (mg · kg^{-1} · min^{-1})*
Infant–preschool child	10	0.46	8–6
	17	0.70	8–6
School aged–adolescent	17	0.70	6–4
	30	1.08	6–4
	40	1.30	6–4
Young adult	40	1.30	4–2
	60	1.65	4–2

*Larger values shown first because the amount of glucose infused is larger in younger than in older patients.

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