

Moreover, two different female patients (cases 2 and 10) who once had palpitations when they consumed alcohol noticed the disappearance of the symptom after taking coenzyme Q<sub>10</sub>, which has a therapeutic effect on mitochondrial abnormality (3). Thus, these clinical pictures suggest that alcohol may be unpleasant toxin for DM-Mt3243 patients and that improved mitochondrial function may ameliorate the unpleasant alcohol effect.

The fact that alcohol plays a role in the phenotypic expression of the 3460 or 14484 mitochondrial DNA mutation in Leber's hereditary optic neuropathy may further support our finding (4,5). Because mitochondria is an organelle possessing aldehyde dehydrogenase, which is a key enzyme for aldehyde metabolism, and because supply of nicotinamide adenine dinucleotide, a cofactor of ethanol oxidation, is dependent on the mitochondrial membrane system, alcohol intolerance concomitant with aldehyde accumulation or with change of redox state in liver may be understandable in groups of mitochondrial diseases. In addition, because ethanol decreases cytochrome oxidase activity or protein synthesis in mitochondria, it is likely that mitochondrial function in DM-Mt3243 will easily fall into a vicious circle with ethanol toxicity.

Alcohol intolerance in a certain diabetic group has been reported by Pyke and Leslie (6). They reported families having strong incidence of non-insulin-dependent diabetes mellitus whose diabetic members are characterized by positive CPAF test. Recently, the mechanism of CPAF has been explained by the inhibition of the low- $K_m$  hepatic mitochondrial aldehyde dehydrogenase by  $N_1$ -alkyl-substituted derivative of chlorpropamide (7). Therefore, we speculate that the CPAF-positive families of Pyke and Leslie and DM-Mt3243 may each be encompassed by the pathological concept of the other. And in our DM-Mt3243 patients, the pretreatment of chlorpropamide might have altered mitochondrial environment, making the patients more

sensitive to alcohol and thus resulting in positive CPAF tests.

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## Insulin Pump Treatment for Recurrent Ketoacidosis in Adolescence

Recurrent diabetic ketoacidosis (DKA) in adolescents and young adults is generally considered to result from failure to carry out the required daily management tasks such as injecting insulin and eating regular balanced meals (1). Between admissions, excessive additional insulin dosing with irregular caloric intake may then readily exacerbate hypoglycemic episodes at peaks of insulin action, leading to a labile blood glucose pattern (2,3). Many large hospital-based diabetes programs have one or more such patients who begin to present with repetitive DKA in adolescence and make excessive demands on the diabetes team, including social service, psychologists, and pediatric housestaff (1,4). We have also been confronted with this issue and the need for comprehensive behavior-based intervention that, although successful in ameliorating family stress, failed to have an impact on the rate of hospital admissions.

We were initially reluctant to use continuous subcutaneous insulin infusion (CSII) for such patients because of the potential management risk due to unwillingness to carry out the necessary

**Table 1—Total number of admissions, total clinic visits, total annual inpatient hospital costs, and mean HbA<sub>1c</sub> levels for the four patients**

	1 year before CSII	After 6 months	After 1 year	1-year difference
Admissions/year	29	2	5	24*
Clinic visits/year	36	13	24	12*
Total costs/year (\$)	144,260	13,847	25,940	118,320*
HbA <sub>1c</sub> (%) (mean)	13.5	8.9*	11.9	1.6

The differences from the year before to the year after CSII indicate significant reduction in admissions per year and clinic visits, cost saving, and improved chronic glycemia after 6 months but not after 1 year. HbA<sub>1c</sub> was done by high performance liquid chromatography. \*  $P < 0.05$ .

tasks such as frequent glucose monitoring and physician-guided matching of basal and bolus doses to daily blood glucose analysis. However, we reasoned that insulin insufficiency, a recognized cause of recurrent DKA (1), would be less likely to occur with CSII. Also, it seemed that the potential benefits of CSII (5), even in cases with extremely brittle insulin-dependent diabetes (6), outweighed theoretical risks, provided that patients could document blood glucose monitoring with three or more tests per day for a month or more.

Four adolescent girls aged 12 to 19 years who had four or more admissions per year fulfilled these criteria and were admitted to the hospital for the transition from conventional subcutaneous injections to the insulin pump (Model 506, Minimed Technologies, Sylmar, CA). Adjustment of basal and bolus doses and comprehensive one-on-one education was achieved during a one-day admission for pump initiation. The number of admissions, diabetes clinic visits, and total hospital inpatient and outpatient costs during the year before pump therapy are compared to the same criteria estimated during the first year after pump initiation (see Table 1). HbA<sub>1c</sub> values were obtained shortly before CSII and at ~6 months and 12 months after CSII initiation, and the mean values of the four patients were compared.

No serious life-threatening events were encountered and all four patients

continued to fulfill the recommended monitoring requirements. The number of hospital admissions were significantly reduced, resulting in substantial cost savings. The number of clinic visits was reduced, and improved diabetes care was reflected by a significant reduction in the mean HbA<sub>1c</sub> level at 6 months but not after 12 months. The standard visits to the diabetes clinic were similar in quality of service, time allotted, and diabetes team involvement. However, we cannot exclude the possibility of a placebo effect due to the change in the method of insulin delivery and the fact that the patients may have been more encouraged by improved blood glucose control as reflected by their home glucose monitoring and by more positive interaction with the staff, including telephone contact.

We confirm findings in one other previous report that CSII therapy has a place in the management of patients with recurrent admissions for DKA (7). However, our experience is that selection of such patients should be cautious and based on documentation of glucose monitoring and rapport with the diabetes team. Significant reduction in hospital admissions for potentially life-threatening DKA coupled with short-term savings on inpatient hospital costs over the initial year of CSII outweigh the much lower theoretical risk of pump management failure. The prospect of lowering the HbA<sub>1c</sub> levels associated with reduction of long-term complications in some but not

all of these patients may also potentially reduce long-term costs. Furthermore, miniaturization, computerization, and built-in safety alarms have been developed to make the second generation of insulin pumps a more viable therapeutic option for such patients.

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