the differences occurring in the literature may be the different prevalences of HT in the tested groups of diabetic patients with or without CHD. A larger-scale study to confirm these results is needed.

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Unpleasant Alcohol Effect in Diabetes Associated With 3243 bp Mitochondrial tRNA$^{Leu(UUR)}$ Mutation

Diabetes due to 3243 base pair (bp) mitochondrial tRNA$^{Leu(UUR)}$ mutation (DM-Mt3243) is a new disease entity, and its characteristic was known to be maternal transmission and an associated sensorineural hearing loss (1).

Recently, we found the clinical trait of alcohol intolerance in this subtype. Of 16 unrelated patients, 14 patients easily flush after ingestion of a tiny quantity of wine or Japanese sake (Table 1). Most of them had noticed weakness since their first experience of alcohol intake. Of 15 patients who gave consent to receive a chlorpropamide alcohol flushing (CPAF) test, all showed positive rise of facial temperature after sherry (2).

Interestingly, cases without intolerance had strange histories. One male (case 13) noticed abrupt onset of paresthesia of his left arm and chest pain. The symptoms worsened when he abused alcohol. Soon after, he developed tinnitus, hearing loss, and extreme hyperglycemia (fasting plasma glucose level 9.8 mmol/l). After he stopped abusing alcohol, all symptoms disappeared. In another case (case 11), a woman's paresthesia of legs worsened when she drank a large amount of alcohol, so she stopped drinking. Thus, all our DM-Mt3243 patients are now abstaining from alcohol consumption by their own will, irrespective of their initial alcohol tolerance.

Table 1—*Clinical characteristics, alcohol intolerance, and positivity of CPAF test of the diabetic subjects with mitochondrial tRNA$^{Leu(UUR)}$ mutation at position 3243*

Case no.	Sex	Type of diabetes	Age	Hearing impairment on audiometry	Alcohol intolerance	CPAF test	Alcohol habit at present
1	M	NIDDM	60	−	+	+	none
2	F	NIDDM	61	+	+	+	rare
3	M	NIDDM	43	+	+	+	none
4	M	NIDDM	72	+	+	+	none
5	M	NIDDM	51	+	+	+	none
6	M	NIDDM	51	+	+	+	none
7	F	NIDDM	54	−	+	+	none
8	F	NIDDM	68	+	+	+	none
9	F	IDDM	34	+	+	+	none
10	F	NIDDM	48	+	+	+	rare
11	F	NIDDM	60	+	−	+	abstinent
12	F	NIDDM	82	+	+	ND	none
13	M	NIDDM	40	+	−	+	abstinent
14	M	IDDM	37	+	+	+	none
15	M	NIDDM	68	−	+	+	none
16	M	NIDDM	60	+	+	+	none

For the CPAF test, the subjects were on 250 mg chlorpropamide daily for 3 days. After subjects drank sherry of 20–40 ml, facial warmth, facial flushing, burning of the face, and peak increment in facial skin temperature over 1°C were regarded as criteria for a positive reaction. NIDDM, non-insulin-dependent diabetes mellitus; IDDM, insulin-dependent diabetes mellitus. ND, not done; the patient did not give informed consent to receive the test. She was afraid to receive the test because she was so intolerant to alcohol.

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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_{10}, 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 organella 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 membraneous 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

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