was initiated by addition of diaminobenzidine tetrachloride (0.5 mg/ml) in 0.05 M Tris buffer containing 0.001% hydrogen peroxide, and after washing, the slides were mounted with AFT systems mounting medium (Behring Diagnostic, La Jolla, CA). Sera from 17 of 18 high-risk subjects, previously identified to be ICA positive by use of human pancreas and FITC-pA, were also positive by use of Wistar-Furth rat pancreas and perox-pA. Sera from 2 subjects who developed type I diabetes without ICA demonstrable with human pancreas and FITC-pA were also negative with rat pancreas and perox-pA. Sera from 34 control subjects were negative by both assays. We are now using Wistar-Furth rat pancreas and perox-pA for our screening studies to detect subjects at high risk of developing type I diabetes. Such an assay is easier and quicker to evaluate than the standard ICA assay and should be much easier to standardize.

Note added in proof. The rat perox-pA assay was used for blinded duplicate samples provided from the Immunology of Diabetes Workshop Stage III ICA standardization. Results of dilutions of three ICA-positive serum pools and normal control sera converted to Juvenile Diabetes Foundation (JDF) units are shown in Fig. 2. No control sera were positive; all three pools were detected with a minimum detection limit for the assay at 40–80 JDF U.

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Diabetic Ketoalkalosis

We report a case that presented with diabetes mellitus, metabolic alkalosis, and ketonuria. Few such cases have previously been reported (1–5). A 36-yr-old man without preexisting diabetes mellitus was admitted to the hospital in January 1985 with a 4-wk history of weight loss, polyuria, and polydipsia. Abdominal pain and vomiting had been present for 3 days. For several months he had been treated, possibly for vertigo, with a diuretic (chlorthalidone) and betahistine. On admission he was lethargic and very dehydrated, with Kussmaul respiration, and suffered from intense abdominal pain. Temperature was normal, blood pressure was 120/90 mmHg, and pulse was 92 beats/min.

Initial laboratory evaluation included blood glucose 25.8 mM, serum sodium 143 mM (normal value), potassium 3.0 mM (3.5–5.0), and creatinine 143 μM (60–125). Serum chloride was not measured. Blood gas analysis gave standard bicarbonate 21.2 mM (21.3–25.8) and pH 7.54 (7.35–7.42). P_{O_2} was 14.6 kPa (10.0–14.5) and P_{CO_2} 2.4 kPa (4.5–6.0). Urinalysis showed 3+ ketones and 3+ glucose.

Treatment with intravenous saline and potassium was started immediately, and insulin was given in hourly doses of 8 IU. After 24 h, his general condition had improved, blood glucose was normal, the ketones had disappeared, and there was no vomiting or abdominal pain. Standard bicarbonate was 27.2 mM, serum potassium 3.3 mM, and pH 7.46.

After recovery, he was taken off all medication and discharged. His blood glucose remained normal for 5 mo, but it then began to rise. He has since been maintained on a low dose of insulin (12 IU).

We have no definite explanation for the development of alkalosis in this patient. However, betahistine, like histamine, stimulates the secretion of gastric acid, and it is therefore possible that the severe vomiting caused excessive loss of acid, thus counteracting the tendency for a metabolic acidosis to develop. Although the role of thiazides in precipiting diabetes is controversial, another idiosyncrasy might have been present. Chlorthalidone and thiazides have identical side effects, and an impaired glucose tolerance might have developed during treatment, thus precipiting the diabetes. In favor of this theory is the low concentration of plasma potassium on admission, although the severe vomiting would also have contributed to this.

Patients with diabetic ketoalkalosis are severely dehydrated, and they should receive the standard treatment for ketoacidosis, i.e., intravenous saline, supplements of potassium, and hourly insulin. If not carefully investigated for ketonuria with routine blood gas analysis, the condition is easily misdiagnosed.

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Improvement of Postural Hypotension and Severe Diabetic Autonomic Neuropathy During Pregnancy

In 1976, a 10-yr-old girl presented with typical insulin-dependent diabetes. In the same year, her 31-yr-old father was found to have glycosuria when he presented with deteriorating vision due to proliferative diabetic retinopathy. By 1982, the father required dialysis for nephropathy and died 4 mo later.

The girl was treated with twice-daily insulin, but control was always poor due to severe behavior problems; over a 5-yr period, she had 18 hospital admissions with severe ketoacidosis. A common scenario was that she would be admitted in ketoacidosis and as soon as she felt better would remove the drip and discharge herself. She never attended the clinic and often ran away from home. In 1980, she had ankle edema but no proteinuria; in 1983, she had recurrent episodes of abdominal distension but absconded during each hospital admission and could not be investigated. In 1985, background retinopathy and absent knee and ankle jerks were noted, but there was no postural hypotension. In January 1986, she presented with a 6-wk history of vomiting and hypoglycemia and at gastroscopy had a normal gastric mucosa but a virtual absence of gastric contractions, suggestive of gastroparesis. The vomiting partially responded to metoclopramide. Severe proliferative retinopathy was noted and treated by light coagulation. By May 1986 (aged 20 yr), she could not walk because of severe painful neuropathy and weakness of the legs or stand because of postural hypotension (standing blood pressure was unmeasurable). She had a resting tachycardia of 120 beats/min, proteinuria (0.4 g/24 h), and a serum creatinine of 55 μM. Urea and electrolytes and a short synacthen test were normal. The vomiting persisted, and she took metoclopramide intermittently. Despite weighing only 47 kg, she continued to menstruate.

In November 1986, she complained of 19-wk amenorrhea, but ultrasound scanning suggested a 10-wk pregnancy. The leg pains and postural dizziness had resolved some weeks previously, and her blood pressure was now 120/70 mmHg, with no postural drop. She felt well, and the rest of the pregnancy was remarkably uneventful, with hemoglobin A_1 ranging from 5 to 7% (normal range 5.0–7.5%). Proteinuria persisted but fell from 0.9 g/24 h at admittance to 0.1 g/24 h at 34 wk. Creatinine clearance also declined from 96 to 66 ml/min. Blood pressure remained at ~120/80 mmHg, with a postural fall of no more than 3–4 mmHg. Her vomiting, however, did not resolve and was frequently precipitated by coughing. In May 1987, 35 wk pregnant, she was delivered by emergency cesarean section because of fever and vomiting. Within days of delivery, her postural dizziness had returned, and she had a 30–40 mmHg fall in systolic blood pressure on standing. This postural hypotension still persisted 6 mo later. Formal autonomic function tests revealed a resting heart rate of 88 beats/min, with only a 2-beat/min variation on deep breathing. The lying-to-standing ratio was 0.96 (normal >1.02), and the Valsalva ratio was 1.33 [below the 2.5 percentile for age (1)].

Comment. In patients with diabetic autonomic neuropathy the degree of postural hypotension can vary unpredictably and may correlate poorly with symptoms. However, our patient showed a striking resolution of postural hypotension within a few weeks of becoming pregnant. In theory, the two factors that might play a part are increased blood volume and improved glycemic control. It is known that renal impairment resulting in fluid retention can alleviate diabetic postural hypotension (2), and during pregnancy, total blood volume may increase by as much as 25–80% above nonpregnant levels (3). The increase in blood volume begins in the first trimester, and plasma volume has increased by around 5 ml/kg by 12 wk (4). At delivery, there is a rapid fall in blood volume by 500–600 ml, and nonpregnant levels are reached within a few weeks. Most investigators have not found an improvement in autonomic neuropathy with improved glycemic control, although Bernstein (5) recently reported resolution of severe cardiac autonomic neuropathy in a 14-yr-old girl after 15 mo of improved glycemic control. In our patient the dramatic resolution of symptoms and signs at the onset of pregnancy did coincide with near normoglycemia, but their recurrence within days of delivery suggests that the increase in plasma volume was probably responsible for the improvement.

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