without direct visual control these techniques have been limited to small or partially liquefied necrotic lesions.[2,4] Endosonography has given access to the extraintestinal anatomy for endoscopic interventions.[5] We believe that extragastric endoscopic interventions are the logical consequence of 10 years' transmural training. Access to the retroperitoneal space through a transgastric hole of less than 20 mm is a novel atraumatic strategy. In our patients, the procedure carried no additional morbidity. Prospective studies seem warranted to compare the efficacy, safety, and cost-effectiveness of the endoscopic approach with that of open surgery.

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Association between infant growth before onset of juvenile type-1 diabetes and autoantibodies to IA-2

G J Bruining for the Netherlands Kolibrie study group of childhood diabetes

Secular growth changes have not been linked with type-1 diabetes. Longitudinal growth analysis in prediabetic type-1 children indicated increased body mass index (BMI) in the first year of life and an increased growth in length in the next 2 years. These heavier and taller children presented with autoantibodies against pancreatic islet tyrosine phosphatases at diagnosis many years later. It is possible that increased BMI during the first year of life and the development of such autoantibodies represents an additional risk marker towards earlier clinical onset of disease.

Type-1 diabetes occurs at ever younger ages in affluent countries. Affluence is associated with increased postnatal growth given abundant nutrition.[1] Early increased growth is associated with more insulin secretion. We explored infant growth of children with type-1 diabetes in relation to the rate of insulin secretion during the first years of life.

The use of longitudinal growth data to assess postnatal rates of growth in children before the onset of diabetes has not yet been reported. We assessed changes in length, height, and body mass index (BMI) in infancy and early childhood in 91 children with clinical onset of type-1 diabetes at 4–15 years of age and in their 125 healthy siblings, compared with 2151 healthy Dutch children of non-immigrant origin.[2] Children with diabetes that was newly diagnosed (n=181) were identified between 1995 and 1998 in the southwestern part of the Netherlands using the Kolibrie Diabetes Register and the Sophia Children's Hospital Register (95% ascertainment). We requested permission from parents of children with diabetes of non-immigrant origin and who also had healthy siblings. Parental heights were not substantially different from national standards.

The average age at clinical onset in the diabetic child was 8·3 years. The parents retrieved lengths and weights from the files in their local child-health clinics. We obtained full data for 91 (50%) of 181 children. On average, children were weighed and measured on 20 different occasions between 2 weeks and 5 years of life. We used the national reference values for longitudinal growth described above to compute growth in length and BMI for every child. These values were corrected for regression to the mean by use of the conditional velocity method of Cole.[3] Additionally, a repeated measurements analysis of attained length and BMI was done after transformation of the raw measurements into SD scores with the 1997 Dutch population references,[1] calculating mean and Bonferroni 95% intervals.

Prediabetic children and their healthy siblings had a normal birthweight, length, and BMI at 2–4 weeks after birth. Prediabetic children, in contrast with their siblings, had a tendency to become overweight in the first year of life. Conditional increase in rate of BMI growth in the first year was +0·31 SDs (p=0·002) in the later diabetic children and +0·10 SDs (p=0·17) in their siblings compared with the expected mean population value of zero. Both had a normal rate of length growth in the first year of life. In the second and third year of life, both groups showed rates of length growth that were significantly higher than the expected values. Mean conditional rates of length growth from 1 to 3 years of age was +0·49 SDs (p=0·001) in those who developed diabetes later and +0·47 SDs (p=0·001) in their siblings. Mean conditional BMI rates of growth over the same period were +0·09 SDs (p=0·51) and –0·09 SDs (p=0·37), respectively, indicating that there was no continued tendency for weight gain after age 1 year. In the fourth year all rates of growth were normal.

The results of the repeated measurement analysis of attained length and BMI confirmed the findings of the conditional growth velocity analysis. At 1 year, BMI-SDs became significantly higher in children with diabetes (p=0·018), but not in siblings. After 1 year, length-SDs increased significantly in both groups until the age of 4 years (p=0·0004).

In summary, in children who later developed diabetes there was increased weight (BMI) gain in the first year of life compared with their healthy siblings. Length growth was also increased in the second and third year of life in both groups. Type-1 diabetes is thought to represent a chronic autoimmune disease and increased insulin secretion is known to promote islet cell autoimmunity.[4] Interestingly, this pattern of increased early growth was associated with the presence of autoantibodies to IA-2, tyrosine phosphatase pancreatic β-cell like protein, at clinical diagnosis (p=0·038). This association was not seen with antibodies to glutamic acid decarboxylase (p=0·25) in the samples taken within 1 month of diagnosis. Insulin (auto)antibodies were not measured before treatment.

In a large Finnish survey, IA-2 antibodies and not those to glutamic acid decarboxylase were associated with reduced C-peptide concentrations and higher insulin dosages at 18 and 24 months of treatment.[5] This finding suggests that increased growth in infancy could occur with a

more rapid decay of pancreatic islet cell functioning once IA-2 autoantibodies are present, and that this combination could represent an additional risk towards earlier development of clinical disease.

The Kolibrie study group consists of 27 regional paediatricians in South-West Netherlands and of Manda de Ridder, Jan Van den Broeck, Manou Batstra, Henk Jan Aanstod, Stef van Buuren, Remy Hirasing, Bart Roep, and Jan Bruining.

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Hyponatraemia associated with lamotrigine in cranial diabetes insipidus

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We report the cases of two children with cranial diabetes insipidus who were treated with lamotrigine for seizures and who had accompanying changes in desmopressin requirements. Lamotrigine is a new anticonvulsant chemically unrelated to other existing antiepileptic drugs. Studies suggest it acts at voltage-sensitive sodium channels and also decreases calcium conductance. Both of these mechanisms of action are shared by carbamazepine, which can cause hyponatraemia secondary to inappropriate secretion of antidiuretic hormone. It is possible that the effect of lamotrigine on fluid balance in the cases described is also centrally mediated.

Lamotrigine is a new anticonvulsant chemically unrelated to other antiepileptic drugs. Studies suggest that it acts at voltage-sensitive sodium channels to stabilise neuronal membranes[1]—an action similar to that of carbamazepine.[2] Both drugs also decrease calcium conductance.[3] Carbamazepine causes hyponatraemia by inducing inappropriate secretion of vasopressin, probably via altered sensitivity of hypothalamic osmoreceptors to serum osmolarity.[4] Desmopressin is a synthetic preparation with greater antidiuretic activity than its natural analogue. It binds to specific receptors in the kidney, stimulating cyclic AMP production, which leads to increased water permeability. We describe two children with cranial diabetes insipidus who, when treated with lamotrigine for seizures, had accompanying changes in desmopressin requirements.

Case 1 was a 12-year-old girl with cranial diabetes insipidus and primary panhypopituitarism. She was treated with carbamazepine for focal seizures, and was receiving hormone replacement therapy including desmopressin. At 9 years of age, lamotrigine was introduced because of continuing seizure activity. A few weeks later, after a gradual lamotrigine dose increase from 50 mg to 150 mg, her parents noted a decrease in desmopressin requirements, which had been stable for the previous 6 months. This trend continued with further increases in lamotrigine and no other concurrent drug changes. A year later, carbamazepine was withdrawn, leading to a predicted increase in desmopressin requirements. Currently the lamotrigine dose is being reduced in 50 mg decrements, and has led to 25–50 μg increases in desmopressin requirements.

Case 2 was a 15-year-old girl who started hormone replacement therapy after removal of a craniopharyngioma at the age of 10 years, which left her with panhypopituitarism. She had a stroke 2 weeks after surgery. Her seizures started 2 years later and she was treated with lamotrigine. Her parents noted an initial increase in desmopressin requirements which was confounded by concomitant changes in her hydrocortisone replacement therapy. The total daily dose of desmopressin decreased further with subsequent increases of lamotrigine of up to 7 mg/kg per day.

Some anticonvulsants—eg, carbamazepine and oxcarbazepine—are known to cause fluid disturbances such as hyponatraemia.[4] So far there have been three reported cases of hyponatraemia associated with lamotrigine (from the Adverse Drug Reactions On-line Information Tracking database), two of whom developed Stevens-Johnson syndrome and disseminated intravascular coagulation. The third case had associated thrombocytopenia and was also on four other anticonvulsants. Hyponatraemia resolved in each case, but lamotrigine had to be withdrawn in one. In the two cases we describe, the parents, who were highly experienced in managing their child's fluid status, were prompt in noticing a change in desmopressin requirements, usually within a few days of a change in lamotrigine dose. This change in desmopressin was not noted with any other drugs, except carbamazepine in case 1 and hydrocortisone in case 2.

The mechanism of a possible effect of lamotrigine on fluid balance is unknown, but since it shares some similar mechanisms of action with carbamazepine, the effect may be centrally mediated.

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