Long-Term Follow-Up of Antibody-Positive Siblings of Diabetic Children
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Risk of IDDM was estimated in 234 siblings of recent-onset diabetic children, aged 2–29 years. Twelve subjects developed diabetes during a median follow-up of 11 years (range 1.7–14 years). Islet-cell antibodies (ICA) and antibodies to insulin (IAA), glutamic acid decarboxylase (GADA) and the IA-2 protein (IA-2A) were tested in sequential serum samples. ICA had the highest sensitivity (83%) and IA-2A the highest predictive value (70%). IAA and GADA had poor sensitivity and predictive value. Combinations of antibodies achieved better predictive value with lower sensitivity. The predictive values were 83% for the combination of GADA and IA-2A, 70% for any combination of two or more antibodies other than ICA. The actuarial risk progressed from around 50% after 5 years to 100% after 13 years. Taking into account HLA-DR3/4 and age ≤10 years increased the predictive value of each antibody combination, whatever the number of antibodies. Younger age was also associated with a more rapid progression to IDDM. Sequential antibody screening resulted in higher sensitivity because of seroconversion during follow-up. In conclusion, the combination of several antibodies in sequential serum samples is satisfactory for the identification of subjects at risk to develop IDDM. Age and HLA-DR3/4 as risk markers increased the predictive value of each antibody combination, whatever the number of antibodies. Younger age was also associated with a more rapid progression to IDDM. Sequential antibody screening resulted in higher sensitivity because of seroconversion during follow-up. In conclusion, the combination of several antibodies in sequential serum samples is satisfactory for the identification of subjects at risk to develop IDDM.

Concentrations of Copper and Zinc in Blood Cells in Children and Adolescents with Diabetes mellitus Type 1
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Renal losses of zinc, a special diet and an increased need in growing up could lead to a lack in zinc (Zn) and copper (Cu) in children with diabetes. Zn and Cu were analysed in plasma, whole blood, erythrocytes, platelets, and leucocytes (PL, WB, ERY, PTL, LEUCO) by electrothermal atomic absorption spectrometry. The investigated groups included 94 diabetic children (IDDM, age: 14.0 ± 4.0 years), and 41 healthy children (N, age: 12.5 ± 3.1 years). There was no difference in Zn and Cu in the compounds of whole blood between N and IDDM. Zn in IDDM with HbA1c >9% were higher in WB and ERY and lower in PL than in N (each p < 0.05). Both groups showed age-dependent changes in Zn (increases in WB and ERY, decreases in LEUCO), and Cu (decreases in WB, each p < 0.05). Further increasing age went with increasing HbA1c in IDDM. Not considering the influence of age on Zn, Cu and HbA1c, an insufficient metabolic balance led to higher Zn in WB and ERY (p < 0.05, r = 0.43 and p < 0.05, r = 0.39, respectively) and lower Zn in PL (p < 0.05, r = −0.25). The changes are thus caused on metabolic control. Hyperglycemia may lead to reduced Zn in PL by renal losses. A high activity of superoxide dismutase containing both elements explains the increase of Zn and Cu in ERY. This accumulation in ERY leads to an insufficient amount of Zn in PL, where Zn is responsible for storing and activating insulin. Decreasing Zn in LEUCO is found during the development of preschool children to adolescents. A long-term deficit of Zn is possibly associated with disturbances in wound healing and the susceptibility for infections observed in older diabetics.
Only diabetic patients over 12 years of age, with a longer disease duration, had a higher prevalence of positive cases, although not significantly so, than control subjects of the same age (27 vs. 17%).

**Conclusions:** In the first few years of disease diabetic children do not differ from the nondiabetic population. Subsequently, they show an *H. pylori* seroprevalence tendentially higher than that of controls of the same age. Therefore, *H. pylori* infection acquired in childhood and lasting several years could be one of the causes of chronic atrophic gastritis, which is more frequent in longstanding diabetes mellitus.

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**IDDM in a Boy with 10p Trisomy: Is GAD2 Gene Involved?**

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In the last 20 years trisomy 10 was reported, isolated or associated with other chromosomal rearrangements, in about 40 patients with mental retardation, craniofacial anomalies including dolichocephaly and hypertelorism, congenital heart disease, renal anomalies and flexion deformity of the limbs. This is a report of a 13-year-old boy with severe mental retardation due to a de novo total 10p trisomy. The karyotype was 46,XY,–22,+der(22)t(10;22)(p11.1;p11.1). We used high-resolution QFQ and GTG banding for cytogenetic definition of the rearranged chromosome. For FISH analysis, we used Cytocell multiprobe multipainting, cosmId pretelomeric 10p probe, and the following YAC probes: 940-F-9; 754-D-10; 837-B-5 and 895-C. The patient was hospitalised in our medical center. The method of study consisted of cytogenetic, clinic and laboratory study. We performed a cross-sectional study of 245 patients, whose average age was 15.74 ± 5.37 years, hospitalised in our medical center. The method of study consisted of orthophotomicroscopy and a semiquantitative determination of the microalbuminuria by the Micral test. The results were correlated with the patients’ age and sex, the average duration of the disease, the HbA1 concentration, and the performing of self-control. We thus found DR in 14.28% of patients aged 18.87 ± 5.32, with 10.86 ± 5.30 years of IDDM evolution; 68.57% among them had a background DR, and 31.42% a proliferative DR, 4 of them being treated

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**Seasonal Variation of the Duration of Exclusive Breastfeeding Corresponds to the Seasonal Variation of IDDM**

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There is a seasonal variation of diagnosis of IDDM in children. Recent studies have shown that there is also an association between month of birth and the risk of developing type 1 diabetes. As breastfeeding has been considered to protect against diabetes in children, we decided to investigate if the seasonal variation of type 1 diabetes can be explained by seasonal variation of exclusive breastfeeding. Retrospectively, we studied a population-based group of 297 children with diabetes and 792 individually matched referent children. Reliable data were collected from well-baby clinics. Children (both with diabetes and controls) born during summer were breastfed exclusively for a period of 2.2 months (mean). Corresponding figures for children born during winter were 2.8 months (p < 0.2), spring 2.5 months (n.s.) and autumn 2.7 months (p < 0.04). Children born in June had the shortest period of exclusive breastfeeding (2.0 months) while children born in February had the longest (3.2 months). Children who got diabetes before 10 years of age had no significant seasonal variation while children diagnosed between 10 and 15 years of age showed a seasonality with a very short duration of breastfeeding if they were born during summer. The same age group had also the most pronounced seasonal variation of onset of diabetes with nadir during summer.

We conclude that there is a seasonal variation in duration of exclusive breastfeeding, which corresponds to the risk of getting type 1 diabetes during childhood.
Elevated Serum Insulin Levels in a Case of Congenital Hypertrichosis, Gum Hyperplasia and Macromastia

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A 13-year-old girl presented with congenital hypertrichosis, gum hyperplasia and macromastia. She had normal glucose tolerance with elevated serum insulin levels. The patient was born at full term by normal vaginal delivery. At birth, she was reported to have short dark hair all over her body and her gums were enlarged. Developmental milestones were normal. Her scholastic performance had been average. She had onset of breast enlargement at the age of 12 years, which rapidly progressed to large pendulous breasts reaching the inguinal region. There was no galactorrhea. Menarche occurred at the age of 13 years. Her father and brother were reported to have hypertrichosis. The patient was 150 centimeters tall (75th percentile by Indian standards for her age). Body mass index was 22.2 kg/m². There was no acanthosis nigricans. There was dark terminal hair all over her body. Axillary and pubic hair were normal. Both her breasts were large and pendulous, reaching the inguinal region, and the overlying skin was ulcerated. External genitalia were normal. No visceromegaly was present. After 75 g oral glucose tolerance test, fasting blood glucose value was 150 mg/dl, after 1 h 150 mg/dl and after 2 h 110 mg/dl. The corresponding serum insulin levels were 2,450, 6,000 and 710 pmol/l, respectively. Intravenous glucose tolerance test revealed normal K value for glucose utilisation (K = 2). Serum estradiol, luteinizing hormone, follicle-stimulating hormone and prolactin were normal. Basal and post-ACTH-stimulated serum cortisol, testosterone, dihydrotestosterone, androstenedione and 17-hydroxyprogesterone were also normal. Reduction mammoplasty was performed. In summary, we describe an association of insulin resistance and hyperinsulinemia in this rare syndrome.
was highest in girls with IDDM (14 of 17). As a direct result of screening, new thyroid disease was diagnosed in 14 (8.1%) of the children screened. The commonest diagnoses were subclinical hypothyroidism (2.3%) and hypothyroidism (2.3%), followed by hyperthyroidism (1.4%) and subclinical hyperthyroidism (0.5%).

This study suggests that thyroid function should be screened annually in children with IDDM to detect asymptomatic thyroid dysfunction which is increased in frequency even in the youngest age groups of patients with diabetes mellitus.

Abstracts

**Variable and Ethnic Differences in Carbohydrate Intake Predisposing to Nocturnal Hypoglycaemia**

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Modern dietetic recommendations emphasise healthy eating (high carbohydrate (CHO) and low fat) without measurement of grams/exchanges. To study the hypothesis that children from Indo-Asian (IA) culture have fewer nocturnal hypoglycaemic (NH) episodes because of later evening meals of different nutritional quality, we chose two age- and sex-matched groups, each of 11 children (age range 10–17) from white Caucasian (WC) and IA families. They completed 3-day diet intake diaries with timed recordings of BG (including 3 a.m.) and insulin doses.

**Results** showed a weak correlation between mean bedtime and 3 a.m. BG but on individual nights there was wide variability. 21% of 63 BG at 3 a.m. were less than 4 mmol/l, occurring in 7/11 WC and 3/11 IA. BG less than 7 at bedtime preceded BG less than 4 at 3 a.m. in 24% (5/21) measurements.

**Diet** analysis revealed extreme variability in evening CHO intake: mean variation 97% in WC and 85% in IA. CHO eaten during the evening by children having 3 a.m. BG less than 4 was significantly less on hypo (96 g) than non-hypo nights (119 g) and in several cases clearly explained the low night-time BG. IA children ate more CHO, had later meals, had fewer low BG recordings and had higher fat intake (WC 35%, IA 42%).

**Conclusions:** Modern dietary recommendations for diabetes are associated with wide variations in CHO intake, continuing high fat intake and, despite regular advice, occasions occur when insufficient evening CHO is consumed predisposing children and adolescents to nocturnal hypoglycaemia.

**Intensive Insulin Therapy for Treatment of Diabetes mellitus Type 1 in Preschool and Early-School Children**

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The method of multiple insulin injection regimen is rarely used in the therapy of diabetes mellitus type 1 in young children. The aim of this study was to estimate effectiveness and safety of intensive insulin therapy (IIT) in preschool and early-school children. 14 diabetic children (8 male, 6 female) aged 1.5–9 years (6.4 ± 2) with duration of diabetes mellitus 0.5–7.5 years (2.7 ± 2) were recruited. The patients’ current diabetic regimen consisted of mixtures of soluble and isophane insulin. We estimated the metabolic control (HbA1c), total insulin dose and frequency of severe hypoglycaemia. As a result of IIT, we achieved an improvement of metabolic control. There were significant decreases in HbA1c values: 9.17% before, 8.53% after 6 months, 7.5% after 12 months, 6.97% after 18 months, 7.66% after 24 months and 7.42% after 36 months (p < 0.01; Wilcoxon test). There were no significant differences in insulin dose. The yearly incidence rate of severe hypoglycaemia was 0/patient/year in the first year, 0.14 in the second, and 0.14 in the third year. This method of IIT was accepted by the patients and their parents. During these 3 years nobody resigned from this method of treatment. In conclusion, this study showed that insulin intensive therapy can be effectively and safely used in young children.