

non-significant odds ratio was found [0.31 (95% CI 0.08–1.2), $p = 0.09$]. Smoking is a strong confounding factor in relation to *NAT2* analyses and diabetic nephropathy. According to our data, in non-smoking Type 1 diabetic patients a fast acetylation capacity implies an increased risk for diabetic nephropathy.

O21

Microalbuminuria: Experience from the Danish nation-wide studies

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In 1989 a nation-wide screening for microalbuminuria was performed in 22 paediatric departments with participation of 957 Danish children and adolescents with Type 1 diabetes, age 2 to 19 years and mean diabetes duration of 6 years. Median HbA_{1c} was 9.6% and the prevalence of persistent microalbuminuria was 4.3%. Microalbuminuria was extremely rare before puberty and in our study only two girls were diagnosed.

Several previous reports have suggested a relationship between poor blood glucose control and increased urinary albumin excretion. We found that only females with microalbuminuria had significantly elevated HbA_{1c} values compared to diabetic patients with normoalbuminuria. The normal range for diastolic blood pressure in diabetic boys and girls aged 8 to 18 years with normoalbuminuria was determined. Sixty percent of adolescents with microalbuminuria had diastolic blood pressure in the upper quartile for normoalbuminuria.

A cohort of 353 children, included in the nation-wide investigation in 1989 has been followed for 6 years with assessment of metabolic control and development of diabetic nephropathy in 1995. Median HbA_{1c} was 9.7% and elevated AER ($> 20 \mu\text{g}/\text{min}$) was diagnosed in 12.8% of these patients, mean age: 20.7 ± 3.3 years and mean diabetes duration: 13.2 ± 3.2 years. Risk-factors for elevated AER (1995) were high AER ($p < 0.001$) (1989) and high HbA_{1c} (1989) ($p < 0.001$). Raised urinary albumin was not markedly dependent on diabetes duration. In the period 1989 to 1995 11.4% of the normoalbuminuric patients developed elevated albumin excretion rate ($> 20 \mu\text{g}/\text{min}$), corresponding to an annual incidence of microalbuminuria of 1.4%. Of the patients with microalbuminuria in 1989 40% were still microalbuminuric in 1995 while 60% had returned to normal albumin excretion rate and half of the macroalbuminuric patients were still macroalbuminuric in 1995 while the other half had returned to normal albumin excretion rate. None of the patients received anti-hypertensive medication.

During the past 9 years a declining incidence of microalbuminuria has been observed in children and adolescents in Denmark. In 1998 results from the Danish Registry of Childhood Diabetes (covering 211 children, approximately 35% of all aged 9–18 years) showed that median HbA_{1c} was reduced to 8.7% and only two patients had microalbuminuria (0.9%).

The prevalence of elevated AER seem to decrease in young Danish patients, presumably due to improved metabolic control in this age-group. The simultaneous remittance rate of

micro- and even macroalbuminuria seems to be high and long-term follow up studies are required to evaluate whether intervention at an early stage with ACE-inhibitors is indicated in children with elevated AER.

O22

Outcome measures while on continuous subcutaneous insulin infusion (CSII) in pediatrics

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The purpose of the present study was to determine outcome of 89 pts who have been placed on CSII; mean age 15.9 ± 3.6 yrs, mean duration of diabetes was 7.8 ± 4.3 yrs. Reasons for insulin pump initiation include diabetes control, flexibility/lifestyle change, insulin regimen mis-matching, insulin resistance, dawn phenomenon, complications, pregnancy and recurrent hypoglycemia. The computerized outcome system in our center has been designed to manage physical health/control, risk factors/complications, education/function, psychosocial/behavioral, resource utilization/cost and satisfaction parameters. Each domain is further analyzed through the use of an Outcome Research Model (descriptions \rightarrow associations \rightarrow intervention research \rightarrow risk profiling/prediction modeling) with subsequent strategies to advance practice. Physical health and diabetes control showed that mean annual HbA_{1c} prior to CSII was 8.3 ± 1.6 and 7.9 ± 1.2 after initiation ($p < 0.05$). Associations with improved HbA_{1c} included age ($p < 0.01$), knowledge ($p < 0.001$), integration ($p < 0.05$) & family behavior ($p < 0.02$). Risk factors/complications since initiation of CSII yielded 8 recurrent DKA hospitalizations (0.02 events/pt/yr), 2 ER visits (0.005 events/pt/yr) and 1 severe low blood glucose events (0.002 events/pt/yr). Education/function showed that mean competencies of pump pts was 6.9 (0–8 score) and mean knowledge score of $87\% \pm 11$. Psychosocial/behavioral measures administered included adherence (mean 78 ± 9 , NS), integration (mean 88 ± 11 , $p < 0.05$), family behavior (mean 69 ± 10 , $p < 0.02$), and quality of life (mean 4.0, NS). Significant changes in measures before and after CSII were in satisfaction ($p = 0.02$) and knowledge ($p = 0.04$). Resource utilization/cost for 1998 included mean of 3.0 ± 0.5 clinic visits/yr, $3.0 \pm .05$ nursing visits/yr and 1.0 ± 0.25 dietary visits/yr. Incidences of DKA, ER visits and severe low BG events (above) are below national and center benchmarks. 82% of pts used the phone/FAX service. Mean satisfaction score was 4.6 (0–5 scale). These data suggest that CSII can decrease HbA_{1c} in pediatric type 1 pts. Knowledge and satisfaction increase with CSII; adherence is not as critical with CSII. Behavioral programs geared to improve integration of diabetes along with advanced home management education programs should be developed and evaluated to advance diabetes outcome in pediatric pts with CSII.

P1

Carnitine and myocardial functions in diabetic children

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It is well known that carnitine may have an effect on

myocard functions. Furthermore, the question of whether patients with insulin dependent diabetes mellitus may result carnitine deficiency or not is recently being discussed. In this study, comparison of carnitine metabolism and myocardial functions in children who are followed up for insulin dependent diabetes mellitus has been aimed. The results of the 24 diabetic children (Group I: 12 diabetic children whose body surface area is between 1.1 and 1.5 m², Group II: 12 diabetic children whose body surface area is over 1.5 m²) and age matched 17 healthy children (Group III) have been compared with each other. Plasma total, free, short and long chain acyl carnitine levels have been measured by radioenzymatic method. Myocardial evaluation has been performed by doppler echocardiography. Statistical differences for blood total carnitine, short chain acyl and long chain acyl carnitine levels have not been detected between Group I, II and III ($p > 0.05$). But free carnitine levels in diabetic children (Group I and II) have been measured to be lower than the healthy control group ($p < 0.001$). Despite free carnitine deficiency, myocardial functions of the patients were normal. In addition to all these findings, levels of plasma carnitine fractions (total — free carnitine, short and long chain acyl carnitine) and dimensions of the myocardial departments (left atrium, left ventricle, right ventricle, interventricular septum) were evaluated to be not correlated to each other.

P2

Individual indications for humalog therapy in diabetic children and adolescents cases

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General priority for modern insulin therapy in diabetes is to be close to physiology as only possible. Humalog (Lispro) gives a good chance to obtain this aim by common action with other insulin preparations. However, there are some particular indications when rapid acting analogue lets to overcome therapeutic problems better than classic short acting human insulins. The group of 78 diabetic patients (42 girls & 36 boys, 3–22 years of age range, disease duration over 1 year) was analyzed according to reasons and results of Humalog introduction into the insulin therapy:

1. Irregular daily schedule of activity and meals — 40 cases: the most frequent reason and very effective results; patients feel „free”.
2. Hypoglycemic events due to physical activity — 18 cases: lowered risk of „hypo” is important for e.g. sport active young patients.
3. Insulin resistance or elevated and less effective doses — 14 cases: resulted in diminished daily doses of insulin after 2–4 weeks of intensive and flexible therapy with Humalog (the increase activity was suggested too).
4. Insulin antibodies (measured as % of insulin binding by serum proteins which value has exceeded 25%) — 10 cases: Humalog usually leads to transitional good effects (diminished daily doses), however, recurrent relapses need specific temporal modifications of Humalog : NPH insulin ratio (omit some morning NPH doses).

5. Obesity — 6 cases : 4 cases with positive result in diminished BMI.
6. Supplementation of conventional therapy with 1–2 daily injections of Humalog — 8 cases: the aim of this model was permanent Humalog dose added before lunch and/or better glycemia control in occasional additional disease.
7. Very young children (3–6 years old) with difficult control — 4 cases: frequent postprandial insulin administration with good effects.

P3

Compliance with dietary prescriptions compared to the initial management regimen, age and glyceic control

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Children (n = 38) ages 3–15y were at the time of diabetes diagnosis randomly chosen for conventional management at a hospital ward (control group) or for treatment partly in a training apartment where the family was offered problem-based education and individualized, family therapeutic support, based on family-system thinking (study group). During the first two years the dietary compliance was compared to the initial management regimen, age of the child and the glyceic control in five years. The dietary recommendations were individualized but based on Swedish Nutrition Recommendations (SNR), which is very much the same as Recommended Daily Allowances(RDA).

Methods: The families registered at 6, 12 and 24 months after diagnosis the daily food intake of the child during 4 days. The results were computer analysed. HbA_{1c} was determined by high-pressure liquid chromatography (HPLC) , with normal value 3.5–5.3%. Glyceic control was classified as “poor” when the individual annual mean value during year 5 was > 8.3%, based on at least 4 analyses.

Results: The daily intake of protein, fat and carbohydrates was in accordance with the recommendations (SNR). No nutritional variable differed between the groups but total energy and fiber intake was lower than expected in both groups. The intake of sacharose was lowest among the youngest children of the study group. Children with poor control in five years showed higher variation of mean, daily energy intake with range 784–3337 kcal/day compared to range 1102–2973 kcal/day in children with more favourable glyceic control ($p < 0.05$).

P4

Seasonality of metabolic control in pediatric patients with type-1 diabetes: multicenter analysis including 4620 patients from 41 centers

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Background: Everyday clinical experience indicates that higher HbA_{1c} values are encountered during winter months.

More frequent infections and less physical activity are likely to explain this phenomenon. However, few studies have approached this question scientifically based on a large group of patients.

Methods: The German Pediatric Working Group on Quality Control in Diabetes has established a prospective, computer-based documentation program. Data relevant for the longterm course of diabetes can be anonymized and extracted for central analysis. 41 centers contributed their data, encompassing a total of 4620 patients beyond the remission phase (duration of diabetes > 2 year) under continuous care. Data were recorded between 1985 and 1998. A total of 50095 HbA_{1c} values was available for analysis, on average, each patient contributed 11 HbA_{1c}-values during the mean postremission observation period of 2.4 years. For each patient, all HbA_{1c} values measured during each month, as well as during the summer and winter period, were averaged.

Results: The median HbA_{1c} for all patients was 8.27% [Q1-Q3: 7.11-9.13%]. On average, HbA_{1c} was higher in girls (8.34 ± 1.71%) compared to boys (8.20 ± 1.60; p < 0.02, Wilcoxon). The average HbA_{1c} differed among calendar months, the highest mean value was recorded for January (8.39 ± 1.73%), the lowest for August (8.18 ± 1.7%). Kruskal-Wallis-test showed a significant difference among calendar months (p < 0.0001). If months May to October were defined as summer, the mean difference in HbA_{1c} between summer and winter was only 0.1%. This difference was identical for prepubertal (chronological age < 11 years) and pubertal children and also for boys and girls. In order to more objectively analyze the seasonal variability in average HbA_{1c}, a nonlinear regression model, using sine-waves with a fundamental period of one per year was fitted to the mean data. This model explained 99% of the seasonality of HbA_{1c} present in the data.

Summary: Based on a large, multicenter documentation program, small, but significant seasonal variability for metabolic control can be demonstrated in pediatric patients beyond the remission phase. The magnitude of this seasonality however is smaller than clinically expected, and most likely not relevant for the care of children and adolescents with diabetes mellitus.

P5

Cardiac dysfunction during treatment of diabetic ketoacidosis in children

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The childhood incidence of initial diabetic ketoacidosis (DKA) in Bulgaria is decreasing in the last decade although the IDDM incidence is constantly increasing. Nevertheless, there are still cases with very severe course and specific organ damage requiring intensive treatment for maintaining the homeostasis. We present two cases of severe and prolonged initial DKA with transient depression of left ventricular (LV) function. N.T.V., a 13 years old girl, was subjected to appendectomy during unrecognised initial diabetic ketoacidosis. The ketoacidosis continued for 15 days with pericardial effusion, repolarization changes on ECG and echocardiographic signs

of moderate LV hypertrophy and mild LV contractile dysfunction. The following 6 months a transient arterial hypertension was observed and the signs of LV hypertrophy persisted but resolved afterwards. T. A. U., ten years old boy, was referred to our clinic after 5 days treatment in another hospital because of initial DKA. He suffered severe bradycardic episodes and had non-specific ECG changes in repolarization for 2 weeks afterwards. Both patients experienced inadequate electrolyte infusion and prolonged electrolyte imbalance during the early stages of DKA. After proper treatment of diabetic ketoacidosis, subsequent cardiac therapy and close follow-up of the patients the cardiac function fully restored.

Possible pathogenic mechanisms of cardiac dysfunction in DKA are discussed. Relevant ways of prevention and early treatment of these complications are suggested.

P6

Continuous subcutaneous insulin infusion in the treatment of children and adolescents with type 1 diabetes

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Continuous subcutaneous insulin infusion (CSII) with a portable insulin pump has been used for several years in the treatment of adult patients with type 1 diabetes. This treatment has been utilised quite rarely in children and adolescents, however. Between 1992 and 1997 we treated 16 children and adolescents, aged 0.2-16.0 years with CSII. The median (range) duration of CSII treatment was 2.0 (0.4-4.2) years. Unacceptable glycemic control with frequent hypoglycemic episodes during conventional insulin treatment and/or the patient's desire towards more convenient treatment were the reasons for switching to CSII treatment. Diabetic ketoacidosis (DKA) developed in 6 patients during CSII treatment, twice in three of them. The development of DKA was due to technical problems related to loosening or occlusion of the infusion catheter, and the risk of DKA was further increased if the home monitoring of blood glucose was not performed according to given recommendations. Improved glycaemic control with a reduced frequency of hypoglycemic events was achieved with CSII. One of our patients suffered from severe insulin resistance. During CSII treatment her daily insulin requirement decreased 55%. The overall satisfaction with pump therapy was high both in patients and among their families. According to our experiences CSII treatment may be of benefit in infants and young children with type 1 diabetes. It can also improve the quality of life in highly motivated adolescents with unacceptable glycemic control.

P7

Premixed insulin or individual mixtures? Therapeutic considerations

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Purpose: to analyze the opportunity of using premixed insulin or individual mixtures (made from regular and interme-

diate insulin) and the consequences of these two types of treatment on the glycaemic state.

Materials and methods: a group of 25 children aged between 4-18 years was selected and divided into two subgroups A and B. Subgroup A was made of 12 children using premixed insulin and subgroup B which initially used premixed insulins and at the moment of our study used individual mixtures. HbA1C and daily insulin dose were compared at both subgroups.

Results: the mean annual HbA1C in subgroup B was $7.73\% \pm 0.3$ SD when premixed insulin were used and $7.05\% \pm 0.6$ SD after therapy with individual mixtures, comparative to $10.18\% \pm 0.46$ SD in subgroup A. Subgroup A used a baseline therapy with two or three shots daily (premixed insulins at morning and evening associated with rapid acting insulin at noon). Children from subgroup A comes from poor families with low economic and social standard, two of them being analphabets, and use a therapy based on unchangeable doses. Daily insulin dose was 1.1iu/kg in subgroup A and 0.78 iu/kg in subgroup B at those using individual mixtures and 0.92 iu/kg at those using premixed insulins.

Conclusions: 1. Premixed insulins represent the optimal therapeutic solution for children with low economic and social standard, low intellectual capacities, which cannot adapt properly the insulin doses. 2. Individual mixtures are the right solutions for children with selfmonitoring which make a correct adjustment of the two types of insulin (of regular and intermediate acting insulin). 3. The opportunity of changing the proportion between regular and intermediate insulin allow to eat large meals of a high carbohydrate content.

P8

Considerations about therapy with humalog in diabetic children-preliminary results

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Purpose and objective: to evaluate the glucodynamic control in patients treated with insulin analogue (Humalog) and identify the optimal criteria to select the patients for this therapy.

Material and methods: five girls aged between 10-13,5 years carried out under medical surveillance in First Pediatric Clinic Timisoara, treated initially with regular insulin, were selected for our study by the following criteria: adherence to this treatment with Humalog the possibility of selfmonitoring daily at home (mentioning that in Romania selfmonitoring is not free of charge, busy school schedules which doesn't allow precise mealtimes personal agreement of reducing the number of meals from 6 to 3 and acceptance of a new injection with Humalog in case of an extrameal. Hemoglobin A1c, pre and postprandial blood glucose excursions were determined comparing data obtained before and after the onset of therapy with Humalog.

Results: the mean age in the group studied was 12,08 years (range 10-13,5 years), the mean duration of IDDM was 3,5 years (range 6 months -6 years and daily insulin dose was 0,84iu/kg when Humalog was used. The mean HbA1c de-

termined six months before and after the onset of the treatment with Humalog revealed a 0,33 decrease when used this therapy ($8,47\% \pm 0.21$ SD) comparative to $8,8\% \pm 1.91$ SD when patients used regular insulin. Blood glucose excursions reflected by the difference between preprandial and 2 hours postprandial glycemia were of 16,5 mg% where Humalog was used comparative to 33,5mg% when regular insulin was used. The mean of postprandial glycaemias was 135,8 mg% when regular insulin was used and 98,8% when Humalog was used.

Conclusions: the study reveals the improvement of postprandial glycaemias in patients treated with Humalog. A rigorous selection of patients is necessary for the therapy with Humalog, based on the following criteria: well trained children, with a proper medical educations about IDDM, adherence to the treatment, family which cooperate with medical team, the possibility of selfmonitoring at home. The therapy with Humalog is accepted by children with a busy school schedule, which can't or won't respect the diet with 6 meals daily.

P9

Pharmacokinetics of a rapid-acting human insulin analogue, insulin aspart, in children and adolescents with type 1 diabetes

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The pharmacokinetics of the novel, rapid-acting, human insulin analogue insulin aspart, were compared with those of soluble human insulin following subcutaneous administration in 18 children (aged 6-17 years) with stable type 1 diabetes. The trial had a randomized, double-blind, two-period crossover design. On the two study days, the children received a single, subcutaneous dose of either insulin aspart or soluble human insulin (0.15 IU/kg) in the fasted state and before breakfast.

The absorption profile of insulin aspart was significantly different from that of soluble human insulin. The maximum serum insulin concentration was 147 ± 53.5 mU/l for insulin aspart and 70.3 ± 32.1 mU/l for soluble human insulin (mean \pm SD), $P < 0.001$; the area under the serum insulin concentration-time curve from 0 to 5 h after dosing, was 339 ± 210 mU/l \times h for insulin aspart and 246 ± 153 mU/l \times h for soluble human insulin (mean \pm SD), $P < 0.001$; the median time to maximum serum insulin concentration was 40.0 min (IQ range 20-70 min) for insulin aspart and 75.0 min (IQ range 40-180 min) for soluble human insulin, $P < 0.001$. The incidence of adverse events was similar for the two insulin types.

Thus, the more rapid absorption of insulin aspart compared with soluble human insulin, as previously observed in adults, was confirmed in a paediatric population with type 1 diabetes.

P10

The introduction of continuous subcutaneous insulin infusion (CSII) in a center for diabetes in children and adolescents: A structural and methodological concept

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Objective: Since the DCCT-study displayed a reduction of diabetic late complications in the group of intensified treated patients and as one-third of these were treated by CSII, insulin pump therapy is increasingly introduced also in children and adolescents. We present the structural concept of the introduction of CSII into our Children's Hospital and the results of 8 children and adolescents on insulin pump therapy according to this concept.

Structures: Close exchange with an adult diabetes centre experienced in insulin pump therapy; curriculum on practical and theoretical aspects of CSII in children and adolescents; diabetes-team of 1 paediatric diabetologist and 2 diabetes educators experienced in pump therapy, 24 h on call service including paediatric diabetologists.

Clinical indications: Dawn phenomenon, high variation of blood glucose due to spare subcutaneous fat tissue, high insulin sensitivity, insulin resistance, flexible life style and physical activity in adolescents.

Selection criteria: Frequent and regular blood glucose (BG) testing ($\geq 4/d$), test for ketonuria if BG > 250 mg/dl, continuous documentation, practised intensified insulin therapy for ≥ 6 months, minimum age of 10 a.

Methodological concept: Well practised intensified insulin therapy for ≥ 6 months, improvement of metabolic control if HbA1c $> 8.0\%$; technical instruction and hand over of the blank pumps 2 weeks in advance to train operational skills. Start of insulin pump therapy and teaching in a 7 day training program without hospital admission, followed by a 6 week testing period on the pump.

Cases: 8 children and adolescents (age: 9.8–17.5a; duration of diabetes 2.0–16.7a; m/f: 5/3). Parameters for diabetes treatment and control 6 months before (-6), at start of (0) and 6 months practising ($+6$) CSII: No significant changes: HbA1c (mean values [MV] $-6 = 7.6\%$, $0 = 7.5\%$, $+6 = 7.3\%$), BMI (MV $-6 = 21.5$; $+6 = 21.7$). Significant changes: Meals/d (MV $-6 = 6.5$, $+6 = 3.6$), total daily insulin requirement (MV $-6 = 1.1$ IE/kg/d, $+6 = 0.82$ IE/kg/d).

Conclusion: Under the described concept CSII in children and adolescents was successful. Requirements were a critical selection of patients, a diabetes team experienced in CSII and specialised in paediatric diabetology as well as an adapted teaching program for CSII in this age group. The cooperation with an established CSII centre was critical.

During CSII therapy and ongoing diabetes education all children and adolescents became more self-reliant and independent from their parents in the management of diabetes.

P11

Intensive insulin treatment lowers HbA1c: Is it caused by a true improvement of glycaemic control or by an increased number of hypoglycemic events?

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Background and aim: Intensive insulin treatment (IIT) has been recognized to be able to decrease HbA1c levels. Aim of the present study is to establish if this effect is related to a real improvement of metabolic control or to an increased number of hypoglycemic events associated to a wider glycaemic range.

Patients and methods: We studied 29 patients (22 boys and 7 girl) with IDDM in the first 3 years from the onset of the disease; 14 in conventional treatment (CT) (2 shots/day of a mixture of intermediate and regular insulin) and 15 in IIT (3 shots of regular insulin before the meals and long-acting insulin at bedtime). We have preliminary randomly chosen four weeks per year (the same weeks for each patient and during the three years) and we collected the blood glucose values recorded in the diary related to these periods. From these data we estimated the glycaemic mean value and the daily glycaemic range. Beside this, patients were tested every 3 months and the following parameters were taken into account: HbA1c, insulin requirement, number of hypoglycemic events, height and weight. Non-parametric Mann-Whitney test was used for statistical analysis.

Results: The HbA1c levels were significantly lower in the IIT group (6.69% vs. 7.85% in the 1st year; $p < 0.01$, 6.98% vs. 7.81%, $p < 0.05$ in the 2nd year; 7.55% vs. 8.19%, $p > 0.05$ in the 3rd year). Results concerning hypoglycemic events, BG mean and range are reported in the table; BG range values were similar in the 3 years; mean BG was statistically significantly lower and moderate hypoglycemic events more frequent in the IIT group only in the first year. **Conclusion:** We conclude that the lower level of HbA1c in patients in IIT is due to a real improvement in metabolic control and it is independent from the number of hypoglycemic events or the range of BG. The BG range is in fact similar in the 2 groups and moderate hypoglycemic events are significantly more frequent in IIT group only during the first year of disease.

	year	CT	IIT	p
Moderate hypoglycemic events (patient/year)	1rst	14.9	35.9	< 0.05
	2nd	30.5	40.7	> 0.05
	3rd	29	24.5	> 0.05
BG mean (mg/dl)	1rst	155	123	< 0.05
	2nd	151	142	< 0.05
	3rd	163	157	> 0.05
BG range (mg/dl)	1rst	124	93	> 0.05
	2nd	118	116	> 0.05
	3rd	132	129	> 0.05

P12

Postprandial insulin lispro versus human regular insulin in prepubertal children with IDDM

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Prediction of the amount of ingested carbohydrates is a major concern in parents of young IDDM children. We there-

fore studied whether postprandial insulin lispro (PL) could be used as a part of insulin therapy instead of premeal regular insulin (Humulin Regular[®]) (HR). We compared the postprandial glucose excursions, HbA1c-levels, and frequency of hypoglycemia between the use of PL and HR therapy in prepubertal children with IDDM. Study design was open, randomised cross-over, using PL or HR at breakfast and dinner (5PM). The basal insulin (Humulin NPH[®]) was given in two injections per day, a recommended ratio of 65–80% in the morning. The doses of PL and HR and timing of PL were tailored individually. Each treatment period was 3 months. Home monitoring of glucose profiles at meals (premeal, 1- and 2-hour after breakfast and dinner) were collected during 2 days at each treatment period. HbA1c (reference limit 4–6%) was measured every 1.5 months. Hypoglycemic episodes were registered by use of a diary. Of the 24 patients, 22 completed the study. One dropped out due to social crisis of the family, and the other because his parents had changed the morning PL to HR by themselves. He had experienced recurrent hypoglycemia for 2 weeks 2 hours after breakfast since starting PL. The median (range) age of the enrolled patients was 6.2 (3.9–9.9) years, diabetes duration 37 (12–72) months, and mean \pm SD HbA1c $8.1 \pm 0.9\%$. During the study four patients received PL regularly in three daily doses, and the rest in two. There were no major differences in the mean 1- or 2-hour glucose excursions between PL and HR after breakfast (1-hour PL 3.7 vs HR 2.9 mmol/l, $p = 0.3$, 2-hour -0.9 vs 0.3 mmol/l $p = 0.2$, respectively) or after dinner (1-hour -2.5 vs -0.4 mmol/l, $p = 0.07$, 2-hour -4.1 vs -0.7 mmol/l, $p = 0.05$, respectively). Mean change of HbA1c during the treatment periods was similar in both groups (PL 0.2 vs HR -0.4% , $p = 0.1$). The frequency of hypoglycemic episodes was 4.9 per patient per month during PL, and 4.4 during HR ($p = 0.3$). After the study, 18 (82%) patients and their families wanted to continue treatment with insulin lispro (pre- or postprandially) because of its convenience. We conclude that postprandial lispro as a meal insulin could be an alternative to traditional insulin treatment in young children with IDDM.

P13

Evaluation of precision plus electrodes in glucose control

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Aim of the study is to evaluate the accuracy and precision of the new Precision plus electrodes which operate with Precision Q.I.D. sensor (MediSense-Abbott). The new strips apply the 3 electrode technology and measure blood glucose by using an electrochemical detection technique. They utilize 3.5 vs 5 μ l whole blood, capillary, arterial or venous, for Hct range 20–70% vs 30–60% of the old strips. Venous blood glucose of 60 subjects, 55 (male 26) with insulin dependent diabetes mellitus and 5 healthy controls, 10–36 years old, was tested twice in the Q.I.D. system and a laboratory reference analyzer. For quality control, duplicate measurements of low (~ 50 mg/dl) and high (~ 290 mg/dl) glucose control solu-

tions were performed on the Q.I.D. each day of blood glucose testing. Similar methodology was used for quality control of the laboratory analyzer on a normal and high glucose level. For precision study, 20 replicate measurements of low and high glucose test solutions and two blood samples, one for normal and one for high glucose level, were checked once on the sensor. Precision Q.I.D. system convenience in performance was evaluated by a questionnaire given to the trained operators. Mean blood glucose value of the sensor was not different from that of the laboratory analyser (mean value \pm SD : 195.24 ± 100.1 vs 195.02 ± 107.8 , mean difference 0.22 ± 19.0 , 95% CI -5.1 to 4.7 , $p = 0.927$). There was a linear correlation between the results of the two systems ($R^2 = 0.9$, $r = 0.98$, $\beta_0 = 16.8$, $\beta_1 = 0.91$, $p = < 0.0005$) which was independent of sex, hematocrit (for range 35.5–50%) and time in between blood sampling and spinning (for range 10–40 min). No significant difference of blood glucose results was found between Q.I.D. and laboratory analyser at different glucose concentrations 20–100, 101–150, 151–200, 201–250, 251–300, 301–600 mg/dl. Precision of Q.I.D. system was very satisfactory (CV = 6.96, 3.1, 7.15 and 3.8% respectively for mean glucose values 52.7 and 284.5 for test solutions and 109 and 246.5 mg/dl for blood sampling). Quality control of low and high test solutions was very good since no significant difference was found between the duplicate measurements of each solution. The new MediSense Precision plus electrodes with Precision Q.I.D. are very accurate and precise in measuring blood glucose, easy in use, recommended for self and hospital blood glucose monitoring.

P14

The importance of the therapeutic scheme in the induction of the partial remission period in the children with diabetes mellitus type I

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The installation and duration of the remission in the IDDM of the child is limited in time by a series of factors. Through the present study we proposed ourselves an evaluation of the therapeutic scheme (insulintherapy, nutrition, education, self-control and monitoring) and its implications on the induction and duration of the remission period. The lot (40 children with their age at the onset ranging between $1^{8/12}$ – $16^{3/12}$ yrs) was divided, depending on the insulintherapy regimen in 3 groups: group A (2 injections daily) = 7 cases (mean age $5^{6/12}$ yrs), group B (3 injections daily) = 25 cases (mean age $7^{3/12}$ yrs), group C (4 injections daily) = 8 cases (mean age $13^{9/12}$ yrs). In the whole group the same percentual repartition of the carbohydrates on meals was recommended (breakfast = 20%, lunch = 30%, dinner = 20% and 3 snacks of 10% each, between the main meals. To verify the adhesion to the diet we elaborated a treatment notebook in which the family writes, in the first month after the onset, beside the results of the self control and the insulin doses, the food intake at each meal. The whole lot benefited by the same programme of medical education. Self-control glycosuric (3 times daily) was accomplished by 39 children; glycaemic with Reflox type

devices (15 cases) and by comparison with the colour scale (10 cases). The glycaemic values recommended (2 hours after meal and over night) were different depending on age. HbA1c was estimated each 3 months, through Abbott IMx[®] method. In order to secondary prevention, 21 children benefited of treatment with nicotinamide.

Results: In group A the remission was obtained in 2 cases (28,55%) and the mean duration of it was 7^{1/2} months; 10 cases (40%) from group B presented remission (mean duration = 8^{1/2} months), 5 cases (62,5%) from group C developed remission with a mean duration of 11 months. Depending on the type of self-control, the highest number of remission was obtained in the group with glycaemic self-control with devices (56%) and also in the group which benefited of nicotinamide treatment (47,6%) comparatively with the group without nicotinamide treatment (36,8%).

Conclusions: Intensive conventional insulintherapy (4 injections daily) and also the association of the nicotinamide to the therapy shows an increase of the incidence and duration of the remission. The intensification of the self-control, under the circumstances of a strictly respected diet represents a favourable factor for the instalation of the partial remission period. The instalation of the remission period creates the conditions needed for the adaptation of the child and his family to the new statute, that of "diabetic child".

P15

Health behaviors among older youth and young adults having diabetes

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Older youth participate in behaviors that compromise their health and challenge their quality of care based on their metabolic control and choice of behaviors. This study surveyed a broad range of health behaviors including diabetes mismanagement by questioning 107 insulin dependent adolescents and young adults (12–24 years). They were asked questions about their involvement in health-enhancing, health-compromising and diabetes mismanagement behaviors. In general, males and females reported low levels of health-compromising and high levels of health-enhancing behaviors. Older males (21–23 years) reported higher levels of health-compromising behaviors than younger males ($p < 0.0001$) as did older females ($p < 0.0006$). Females were found to report higher levels of diabetes mismanagement than males ($p < 0.02$). Health professionals working with this age group should assess all of these health behaviors, noting age and gender differences before determining an intervention.

P16

Psychological aspects and disease variables in adolescents with insulin-dependent diabetes mellitus

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The aim of this study was to observe the relations of the disease, treatment and psychosocial factors in secondary school pupils with insulin dependent diabetes mellitus (IDDM).

Subjects: 34 adolescents (13 boys, 21 girls) aged 15–19 with IDDM, without other handicaps or chronic illnesses, attending regular secondary school.

Methods: All subjects completed a questionnaire based on the Health Behaviour Questionnaire with the measures from the theoretical framework of Jessor's Problem — Behaviour Theory (e. g. Self-Esteem, Value of Achievement, perceived Parent-Friend Compability and Parent vs. Friends Influence) and some demographic and educational data. They completed also a short questionnaire concerning their treatment and dietary regimens.

Results: There were significant correlations between insulin regimen and both the perception of the parents' influence on taking decisions and the ability to keep up with expectations of the others and also taking their own decisions. Patients with the longer duration of the disease perceived their parents as less requiring reported a lower number of friends and they differed in their personal views on successful completing the secondary school. Differences between patients with better and worse metabolic control of diabetes concerned mainly the variables describing their relations with peers. Patients reporting regular physical training were less depressed.

P17

Two years analysis of insulin-dependent diabetes mellitus in children after education programme

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The aim of investigation was to compare the frequency of the acute complication of insulin-dependent diabetes mellitus (IDDM) in children after education programme in the pediatric hospital during 1995–1997 years. The education programme for children with IDDM included the following thematic sections: what is diabetes mellitus?, acute and chronic complications, self-monitoring, insulin treatment, meal planning and exercise. The results were as follows:

para- meters/ years	n	diabetic patients taken daily %	the number of 3 or more insuling injections	HBA1	
				n	%
1995	113	62 ± 4,6*	11,5 ± 3*	26	13,3 ± 0,68 +
1996	62	52 ± 6,4 +	48 ± 6,4*	30	13 ± 0,53 ^
1997	99	32 ± 4,7* +	79 ± 4,1*	37	11 ± 0,49 ^ +

(+ $p < 0,05$, ^ $p < 0,01$, * $p < 0,001$)

As the table showed the frequency of diabetic ketoacidosis in 1996 and 1997 years were decreased. In 1997 year were no cases of mortality. The number of patients giving intensified insulin therapy was increased in 1997 year.

Thus, our results suggest that education programme have beneficial effects on IDDM in children.

P18

Type 1 diabetes in children under 5: a multicentre survey of dietary habits and parental attitudes

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Background: A significant number of patients with type 1 diabetes develop the disease in the pre-school years. Eating problems in the young child are common and we wanted to observe both the diet of the very young child with diabetes and parental anxiety relating to their management in different cultural settings.

Setting: Patients recruited from 8 centres in 6 countries (Finland, Italy, Japan, Luxembourg, Poland and UK).

Subjects & Methods: Each centre identified all patients < 5 yrs age (n = 63). Data were collected on duration, presentation, family history, insulin regimen and incidence of severe hypoglycaemia. Food choice was determined using a dietary recall questionnaire, recalling foods eaten 'yesterday'. A psychological questionnaire was used to assess parental confidence (self efficacy) in their ability to manage their child's diabetes regimen, and feelings (e.g. anxiety, helplessness) experienced whilst undertaking regimen tasks.

Results: Age range 1.1–4.9 yr, duration 0.1–4.6 yr. 17% had a family history, mean insulin dose 0.63 units/kg/day (range 0.2–1.7), 44% presented in ketoacidosis. Carbohydrate exchanges were used by 64%. Food choices were compared between the centres with the largest number of children (Finland (n = 11), Poland (15) and UK (29)). The children in Finland had more healthy food choices (p = 0.005) and ate more lower fat foods (p = 0.03). The UK children choose more salty foods (p = 0.002) and more unhealthy snacks (p = 0.05). Both the UK and Polish children ate fewer low sugar products (p = 0.05). Polish children ate fewer carbohydrate foods (p < 0.001) but the analysis was qualitative rather than quantitative and may reflect cultural differences in food choice. No significant difference was found between centres in parental self confidence in their ability to manage their child's diabetes and the feelings generated by regimen tasks.

Discussion: Significant differences in foods provided and chosen for young children with diabetes can be seen between countries. The success of Finland in adopting a healthy diet is reflected in this study. This is likely to influence both glycaemic control and the long-term risk of vascular disease for these very young patients.

P19

Differences between groups of diabetic children with good and poor metabolic control

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The aim of the study was to determine the difference between groups of diabetic children with poor and good

metabolic control. 103 children with IDDM (49% girls, age 9.9 ± 3.6 years, diabetes duration 3.9 ± 2.8 years, mean \pm SD) and their parents were followed up during the five-day teaching/treatment program and reinvestigated one year after a diabetes education. Diabetes-related knowledge was evaluated a standardized questionnaire with 47 items. Mean HbA1c declined from $9.8 \pm 0.34\%$ before education to $8.6 \pm 0.22\%$ (p = 0.002) (normal range 4.0–6.5%). We formed 2 groups of patients: good (HbA1c < 8.0%, n = 33) and poor (HbA1c > 8.0%, n = 70) metabolic control. Patients of the good controlled group had measured their glycemia more than 3 times per day. Their HbA1c level was significantly lower than in patients of poor controlled group who checked glycemia less than 1 times per day ($7.5 \pm 0.35\%$ vs. $10.8 \pm 0.35\%$, p < 0.001). Sufficient diabetes-related knowledge were in 62% of patients in the group with good glycaemic control and in 18% of the patients in the group with poor control. We could not find correlation between of HbA1c level and age of children and between HbA1c and duration of diabetes. These results demonstrate that structured patients education, sufficient knowledge about IDDM and intensive metabolic control lead to improvement of compensation disease in children with IDDM.

P20

Effects of short-term summer camps on the education of IDDM children

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Education in insulin dependent diabetes mellitus (IDDM) is essential for long term self-management and for protection from the complications of diabetes. One way of education in IDDM is the summer camps. This study summarizes the effectiveness of summer camps.

One hundred and twenty eight children aged between 8–18 years participated in the summer camps for 10 days organized in 1994 (n: 35), 1995 (n: 46) and 1996 (n: 47). Every day one hour educational session was done based on interactive methods. During sports time, insulin injection time and meals, practical knowledge was re-emphasized. An exam was held at the beginning and at the end of the camp. HbA1c levels of the patients concerning the period 6 months before the camp and 6 months after the camp were recorded. The results were compared with paired-t test and the exams were scored over 100 points.

The results of the second exam at the end of the camp yielded better results than the initial one. The performance of the patients on exams who joined the camp two or three times, was better both at the beginning and the end than of the patients who came to the camp once. 6 children started doing the injections themselves. 10 children started using areas for insulin injection that they have never used before. HbA1c levels were significantly lower 6 months after the camp than of the levels before the camp.

This study shows that summer camps are effective in the continuous education which resulted in a better metabolic control as reflected by the decrease in HbA_{1c} levels.

P21

Comparison of multiple daily injections (MDI) to split-mixed insulin programs in adolescent with type 1 diabetes mellitus: satisfaction

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The Diabetes Complications and Control Trial (DCCT) was an "intention to treat" protocol showing that intensive insulin therapy decreased the risk of microvascular complications in patients (adults and adolescents) with type 1 diabetes mellitus. Because of these results, in 1994 our clinic began switching nearly all patients over the age of 11 to an MDI program of insulin administration, using 3 injections of Regular insulin before each meal and an injection of Ultralente[®] before supper or bedtime. We hypothesized that despite the increased demands required to comply with the MDI program, patient and parent satisfaction would be increased. To assess the validity of this hypothesis, we sent surveys out to 97 of our patients (along with their parents) who had undergone a switch from a mixed-split to an MDI program of insulin administration between the years 1992 and 1997. 67 (69%) of the surveys were returned. The mean age of the responding patients was 16.2 years with 37% females. The mean age of switching to the MDI program was 13.5 years. 93% of the patients and 96% of the parents felt the MDI program was superior to the mixed-split program. Reasons given included: better long-term health (patients: 75%, parents: 82%), improved control (patients: 45%, parents: 58%) and increased flexibility (patients: 49%, parents: 39%). Patients felt the most difficult aspects of the MDI program were waiting more than 20 minutes following an injection before eating (31%) followed by the need to give an insulin injection at school (18%). In contrast, parents felt that the greatest problem with the MDI program was following a meal plan (31%), followed by the need to do nighttime blood sugar tests (30%). Both patients and parents agreed that the biggest drawback to the split-mixed program of insulin administration was the need to have specific mealtimes (72% and 75%, respectively) and that the MDI program seemed to be easier to understand than the split-mixed program (57% and 54%, respectively). We conclude that intensification of the insulin program in our population of adolescents with type 1 diabetes mellitus was associated with a high degree of patient and parent satisfaction and acceptance.

P22

Diabetes in adolescents: family involvement in management tasks

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Objectives: This study was carried to evaluate the parental management tasks at its relationship with the metabolic control in diabetic adolescents type 1.

Patients and methods: A cross-sectional analysis was performed on a group of patients, older than 12 and younger than 18 years of age seen at 4 Pediatrics Endocrinology Units.

Results: 214 adolescents were included (M/ 102, F/112); 64 of those (G1) assumed alone the responsibility for the management of their diabetes; 99 adolescents (G2) shared their treatment with their mother; 44 (G3) with both parents and 7 (G4) either shared their management with other family member or didn't care about the illness at all. G1 was the oldest group (in age) at study (16.4 ± 1.6 vs 15.38 ± 1.9 vs 14.4 ± 2.1 vs 14.6 ; $p < 0.00$) and diagnosis ($p = 0.003$). There were significant differences in the prepuberty and puberty mean HbA_{1c} values between the G1 (8.4 ± 1.8 and 8.5 ± 1.5) and others groups ($p < 0.05$); the better Hb was found at the G3 (7.4 ± 1.4 and 7.6 ± 1.5). The 21,8% of G1 adolescents vs 9% of G2 and G3, and 57% G4, performed BGM only as autoanalysis but never as a self-control, not to eat, or exercise or to modify the insulin dose depending on the result ($X^2 = 21.33$; $p = 0.01$). The highest score a self-control was in G3 (6.04 ± 1.5 vs 4.9 in G1; 5.6 in G3 and 3.9 in G4 $p < 0.01$). There were not significant differences among groups in sex, puberty stage, parental marital status, insulin program, diabetes acceptance or detection of acute complications (SH or KAD). However both social problems and the absence of the father at medical follow up exerted a very important influence ($p < 0.00$). In the G1 there were a high percentage of school failure than other groups (31.2% vs 7.7% ; $X^2 = 3.2$ $p < 0.00$).

Conclusions: According to our results, parental absence in diabetes regimen task is a risk factors for poor control during puberty. The presence of firm parental guidance helps to maintain improved glycemic control as well as the active collaborations of diabetic adolescents.

P23

The effect of health education on the level of knowledge concerning the diabetes in children and adolescents with type 1 diabetes mellitus

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Clinical observation as well as literature data imply a necessity of systematic health education of patients with diabetes. Transfer of knowledge is a complex process and its efficiency depends on pedagogical factors. The aim of this study is the analysis of the effect of health education (both planned and unorganised) on the level of knowledge concerning the diabetes in children and adolescents with type 1 diabetes. The study comprised 100 patients (50 girls, 50 boys). Children and adolescents of the age of at least 12 years (average 14.9 ± 1.7) with duration of diabetes for more than a year (average 5.9 ± 3.6) were evaluated. For the evaluation of the level of knowledge concerning the diabetes, a test was created. The patient health education analysis included: 1) the participation of the patients in planned pre-education programme (at the beginning of the illness) and continued education (reduca-

tion), the frequency of participation in individual and group training and lectures, the characteristics of the last training comprising the period to pass from the training till the last examination, the length, cause, location and form of training, 2) the patient's involvement in unorganised education — the number of possessed books and subscribed magazines devoted to diabetes and the frequency of making use of them, the number of radio and TV programmes about health familiar to the patients and their making use of them. Next statistical evaluation was conducted.

Results: The children who never participated in health training obtained the worst written test results. A positive correlation between the results of the written knowledge test and taking advantage of individual and group training, and training cycles by children was observed. Higher level of knowledge was presented by those patients who participated in training designed according to the educational plans conducted during summer health camps, than by those educated currently because of the worsening of their diabetes metabolic control. Patients educated during summer health camps than by the hospitalised patients obtained better results in the written tests. Children regularly reading books and magazines devoted to diabetes and taking advantage of radio and TV health programme were better-trained in diabetes treatment than the rest of the patients. **Conclusion:** The level of patients' education positively correlates with the frequency and intensity of the child's direct participation in health education - both planned and unorganised.

P24

Physical activity and competitive sports in children and adolescents with type 1 diabetes

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Objective: Experimental and clinical data suggest, that physical activity is beneficial and highly desirable in children and adolescents with diabetes. Therefore we evaluated the present status of physical activity of children and adolescents with type 1 diabetes in comparison with healthy siblings.

Research design and methods: 142 Children and adolescents with diabetes of school age (6–17 years) and 97 healthy siblings of similar age and body mass index were interviewed in respect to their time spent for physical activity and sports in school, in competitive sports and in general using a structured questionnaire. In addition we asked for the favourite sports in general and in competitive sports. In the diabetes group, mean HbA1c over the preceding year, number of insulin injections and insulin dose as well as clinical data were documented. In the control group weight, height and body mass index (BMI) were recorded.

Results: The groups did not differ in terms of time spent for sports in school or in competitive sports. In spare time, the diabetes group reported significantly more physical activity than the controls. Interestingly, the favourite sports in general did not differ between diabetic versus control boys (ranking: 1st biking, 2nd soccer, 3rd inline skating) or girls (ranking: 1st

biking, 2nd inline skating, 3rd swimming). Within the diabetes group (total n = 142), those who regularly took part in competitive sports (n = 42) in addition were significantly more active in the rest of their spare time (p = 0.006), while mean BMI, daily insulin dose and HbA1c were only slightly lower in the group who reported no competitive sports activity.

Conclusions: Overall, children and adolescents with diabetes did not differ in habits of sporting and physical activity from their healthy siblings. They did not appear to be restricted by diabetes in physical activity in general or in competitive sports. Within the diabetes group, attending competitive sports was associated with higher overall sporting activity.

P25

Can we improve specificity of GAD antibody screening for the prediction of type I diabetes in the general population?

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Population based prediction of type I diabetes has become available with the development of radiobinding assays (RBA) for GAD and IA2 antibodies. Highly specific screening is of particular importance for ethical reasons and to achieve high power in diabetes intervention trials. Therefore we studied whether the specificity of the RBA for GAD antibodies (GADA) in the general population may be improved by threshold adjustment to age and sex and if brain damage, which may occur due to epileptic insults, may lead to the formation of GADAs. The frequency of GADAs was established in a general population (GP) of 1287 individuals by RBA. The correlation between GADA levels (GAD-index) and age and sex was studied. In addition, the frequency in a population of 394 epilepsy patients divided in a group of sera taken at onset of epilepsy (A) and at longer duration of epilepsy (B) was studied. The results are shown in the table.

Population:	GP	Epilepsy (all)	Epilepsy (A)	Epilepsy (B)
N	1287	522	218	294
Age range (mean)	6 – 86	6 – 19	0 – 14	1 – 19
Disease duration range	n.a.	0–50 Mo	0–1.5 Mo	2–50 Mo
median GAD index	0.04	0.01	0.03	0.02
% positive (n)	1% (13)	0.8% (4)	0.9% (2)	0.6% (2)

There was a slight, but significant, correlation between GAD index and age in the general population (Spearman R: 0.161, p < 0.001) and the GAD index was higher in female than male (p = 0.009, median GAD-idx 0.0037 and 0.0043 respectively). However, we did not observe a clinically significant effect of threshold adjustment to age or sex. The GAD index in the general population was significantly higher in the GP than in epilepsy patients (p < 0.01). This is consistent with our earlier observation that the GAD index in this GP was higher than in

a population of 1403 schoolchildren. We excluded that this difference was due to age effects and hypothesize that the storage conditions of the GP sera have resulted in increasing levels of antibodies, possibly by freeze drying effects.

We conclude that, although GAD antibody levels are increasing with age, adjustment of thresholds to age or sex does not significantly improve sensitivity and specificity of screening. In addition, epilepsy does not result in false positivity in GAD antibody screening. However, care should be taken in storage of sera for antibody screening, since poor storage conditions may result in a significant increase in GAD antibody levels.

P26

GADA persistence in young patients with type 1 diabetes mellitus: A ten year - follow-up study

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Several autoantibodies have been observed at diagnosis of type 1 diabetes, but little is known about their persistence thereafter. We evaluated glutamic acid decarboxylase antibodies (GADA) and their relationship to genetic risk markers and degree of metabolic control in 30 children and adolescents with Type 1 diabetes [13 males (M) and 17 females (F)], at diagnosis (mean age 8.6 yrs, range 1.7-14.6 yrs) and yearly during a 10-year follow-up. GADA were detected by radioimmunoassay and the upper limit of normal range was 0.9 U/ml (3 SD above normal mean). All samples from each patient were assayed simultaneously. Metabolic control was expressed as HbA1c annual mean levels. All patients (pts) underwent HLA-DR typing and DQ region molecular analysis. At diagnosis 21 pts (70%), 6 M and 15 F, were positive for GADA while at the end of 10 year follow-up, GADA were present in 11 pts (36.6%), 3 M and 8 F. No significant difference was for sex. When pts were divided into 2 groups (G) by presence of pubertal development at diagnosis [G1 (n = 15) prepubertal and G2 (n = 15) postpubertal], we observed that at diagnosis GADA were present in 60% G1 pts and in 80% G2 pts ($p = 0.06$ Fisher's test). During follow-up GADA persisted positive in 20% G1 pts and in 53.3% G2 pts ($p = 0.12$), became negative in 40% G1 pts and in 26.6% G2 pts ($p = 0.6$), persisted negative in 40% G1 pts and in 20% G2 pts ($p = 0.4$). GADA fluctuated in 5 pts (3 G1 and 2 G2 pts). No significant association was found between GADA and either HLA DR phenotype or number of DQ heterodimers. During follow-up, a significant increase in HbA1c annual mean levels was found in persistently positive GADA pts ($p = 0.014$), not observed in those who became GADA negative ($p = 0.69$). During follow-up, mean GADA levels showed significant decrease in G1 pts ($p < 0.001$), and not in G2 pts.

P27

Early onset of type 1 diabetes in a child with congenital cytomegalovirus (CMV) infection. A one year follow-up

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Genetic, immunological and environmental factors are the possible causes of type 1 diabetes mellitus, whose early onset could be due to the precocious influence of environmental factors, like viral infections. In particular, CMV shows a selective tropism for pancreatic β -cells and could trigger the autoimmune response. Our patient, delivered at the 34th week of pregnancy, was suffering from congenital CMV infection, characterized by severe growth retardation [weight 1870 g (< 10th percentile), length 43 cm (10th percentile), petechial rash, jaundice, hepatosplenomegaly. Central nervous system involvement included microcephaly (head circumference 28 cm, \ll 10th percentile), ventriculomegaly by CT and severe neurological impairment. The child was formula-fed, received the recommended vaccinations and, at 6 month age, underwent surgical intervention of ventriculoperitoneal shunt. Thereafter anticonvulsant therapy was started. At the age of 20 months, the child showed dry mouth and weight loss followed by fever, hyporexia, gradual loss of consciousness evolving to coma. He was admitted for suspected obstruction of ventriculoperitoneal shunt and pre-surgical exams showed glycemia 1878 mg/dl, high white blood cells, blood urea nitrogen and creatininemia due to dehydration. After neuro-surgical intervention, intravenous fluid, electrolyte and insulin therapy were started, followed by recovery from dehydration, and by gradual normalization of haematological parameters. Then subcutaneous insulin therapy, in multiple daily administrations, was started. Autoantibody screening revealed presence of GADA (5.15 U/ml, n.v. < 0.9 U/ml) and IA2Ab (5.03 U/ml, n.v. < 0.75 U/ml) and absence of other organ-specific and non organ-specific autoantibodies. HLA type was A2,30(19); CW5; B18(W6), 41(W6); DRB1*0304; DQB1*02 and molecular analysis of DQ region revealed 4 heterodimers of susceptibility. CMV antigenemia was negative, while virus was isolated from the urine. Insulin requirement was high (1.8-2 U/Kg/day) particularly during the upper and lower respiratory tract infection episodes. Severe hypoglycemia as well as ketoacidosis were not observed. Other autoimmune diseases were not diagnosed. One year after, GADA and IA2 disappeared, while CMV persisted in the urine. In our patient, carrying a genetic susceptibility to type 1 diabetes, prenatal CMV infection could have triggered the autoimmune reaction against β -cells, with their precocious destruction and subsequent early onset of type 1 diabetes.

P28

Frequency and trend of children's becoming ill of diabetes

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Diabetes is a chronic metabolic disease with special characteristics at the children's age. The aim of the paper: the characteristics of the disease, the frequency and trend of registration of new cases.

Materials and method: The research involved four communities of the Rasina region in the period of 1986–1998. The population living on this territory is 247530 inhabitants and it has a total number of 36467 children to the age of 15. The disease was diagnosed by means of the existing criteria and the diagnosis was confirmed in the referent Republic institution. Since 1998 each new case has been sent to the rehabilitation centre of a special purpose with the staff specially educated which introduce, patient and parents with the nature of the disease, the method of its treating, the way of nourishment and activities of the children with diabetes. The child and parents are educated how to control the disease and recognise its complications. The diseases children discovered before 1989 were sent to the same centre, but in the later stage.

Results of research: In the course of research 24 diseased children were discovered, the youngest was 11 months and the oldest 14 years old. From 1 to 5 patients a year were registered with average rate of appearing of 0,14‰. The rate of prevalence in the researched area is 0,658‰. The total number of diseased children 14 (58%) were girls and 10 (42%) boys. The disease mostly appeared in children of the age of 4–6 and 10–12. Positive parents' anamneses had 33% of the diseased. Complications in the form of night hypoglycemia, glucosurias, acetonurias, lipodystrophies, neuropathies, retinopathies and hepatomegalias appear with different frequency but they are more frequent in correlation with the length of disease. The complications in some children appeared almost after the first year of disease. Linear trend of children's becoming ill of diabetes is rising. Interpolished values on Y axis of 0,86 in the first year of research rise to 2,84 in the last one. By extrapolation of values we predict the rise of the number of new diabetes cases in 1999 by 3,2 and in 2000 by 3,38.

Conclusion: Diabetes appears with considerable frequency in children and shows the tendency of rising trend of new diabetes cases. Education of patients and parents is very useful for avoiding and postponing the complications of disease. It is also very important to follow the children in families with bigger risk of becoming ill of diabetes.

P29

Age- and gender-specific differences in incidence rates of type 1 diabetes in Antwerp, Belgium (1989–1997)

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A rise in incidence rate of type 1 diabetes in young children and a postpubertal male-to-female excess have been reported in several countries. We have studied the incidence of type 1 diabetes in the Antwerp district according to age at diagnosis and gender from January 1, 1989 until December 31, 1997 in the age-group 0–39 years with the capture-recapture method. During this 9-year period 442 new cases were reported with a

completeness of ascertainment of $\geq 85\%$. The incidence rate (95(b/ CI), expressed as $n/10^5/\text{year}$, was 11.0 (9.3–12.8) under age 15 years and 9.4 (8.4–10.6) above that age ($p < 0.05$ by Chi-square test).

During 3 consecutive 3-year-periods (1989–1991, 1992–1994 and 1995–1997) the incidence rates were respectively 9.8 (7.2–13.0), 13.1 (10.1–16.7) and 9.9 (7.4–13.1) in the age group 0–14 years and 9.4 (7.6–11.5), 9.1 (7.3–11.2) and 9.9 (7.9–12.0) in the age group 15–39 years ($p < 0.05$). Neither was there a gradual rise in incidence rate in the age group 0–9 years. During the 9-year observation period the incidence rate in males did not differ between patients under age 15 years and patients after age 15 years: 10.4 (8.2–13.0) vs 11.5 (9.9–13.4). However, in females a strong decline in incidence rate was noted after age 15 years: 7.3 (6.0–8.8) vs 11.6 (9.2–14.3) under age 15 years ($p = 0.004$). This postpubertal protection from type 1 diabetes in females cannot be explained by a beneficial effect of pregnancies as nondiabetic sisters of type 1 patients ($n = 151$) had not been pregnant more often than diabetic women ($n = 199$), matched for diabetes-free fertile years, had been during their preclinical phase.

In conclusion, no consistent increase in incidence of type 1 diabetes was noted in Belgian children. Pregnancies do not seem to contribute to the postpubertal protection against diabetes observed in women.

P30

An epidemiological study of autoimmunity in Danish children with insulin dependent diabetes mellitus

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Insulin dependent diabetes mellitus (IDDM) is often accompanied by other autoimmune disorders. The aim of the study was to investigate the prevalence of different autoantibodies in children with IDDM and to evaluate thyroid ultrasonography as a marker of autoimmune thyroid disease.

Patients and methods: The study included 106 Danish diabetic children, comprising 91.4% of the total population of children with diabetes in the county of Funen. The children had a median age of 12.8 years (range 2–18) and a median duration of diabetes of 4.8 years (range 0–13). As controls 106 age- and sex-matched healthy children were included. Sera were analyzed for glutamic acid decarboxylase- (GAD), tyrosine phosphatase- (IA2), islet cell- (ICA), thyroid peroxidase- (TPO), thyroglobulin- (TGA), adrenal- (AA), parietal cell- (PCA), IgA gliadin- (GA) and endomysium (EMA) antibodies. All children were investigated by ultrasonography of the thyroid gland.

Results: The prevalence of β -cell related autoantibodies were clearly increased in the IDDM population: GAD: 62%, IA-2: 42% and ICA: 11%. Two of the diabetics were previously known with autoimmune thyroid disease. Furthermore, 3 diabetics were found with subclinical hypothyroidism. Seventeen diabetics (16%) had thyroid autoantibodies compared to

2 (2%) of the controls. Thyroid ultrasonography showed morphological abnormalities in 45 (42%) of the diabetics compared to 11 (10%) of the controls. Among the 17 diabetics having thyroid antibodies 10 also had morphological abnormalities by ultrasonography. Ten diabetics (9%) and none of the controls had EMA, and 7 (7%) diabetics had GA compared to one of the controls. Two diabetics with previously diagnosed coeliac disease were known antibody negative on a gluten-free diet. Three diabetics and none of the controls had AA. An equal frequency of PCA were seen in the two groups.

Conclusions: Children with IDDM have a high prevalence of thyroid autoantibodies and of abnormalities by thyroid ultrasonography, though there was no significant relation between those markers of autoimmune thyroid disease. An increased frequency of EMA in diabetics suggests a high prevalence of coeliac disease in Danish diabetic children. The true prevalence of the disease are currently investigated by small bowel biopsy in the antibody-positive patients.

P31

Analysis of cytokine mRNA expression in pancreatic islets of nonobese diabetic mice

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Nonobese diabetic mice develop type 1 diabetes in an age-related and gender-dependent manner. Th1 (IFN- γ and TNF- β) and Th2 (IL-4 and IL-10) cytokine mRNA expression was analyzed in pancreatic islets isolated from female NOD mice with a high incidence of diabetes and male NOD mice with a low incidence of diabetes. The levels were measured at 5 time points from the onset of insulinitis until the development of overt diabetes, using a semi-quantitative reverse transcriptase PCR (RT-PCR) assay. IFN- γ mRNA levels were significantly higher in the islets obtained from females than those of males, from 10 weeks of age. TNF- β mRNA was expressed in both females and males between 5 and 15 weeks of age. However, TNF- β mRNA levels were decreased in males at 20 weeks of age. In contrast, IL-4 mRNA levels were lower in females than in males. These results suggest that islet β cell destruction and diabetes in female NOD mice depend on IFN- γ and TNF- β production in the islets, and that male NOD mice may be protected from autoimmune β cell destruction by down-regulation of these cytokines. Furthermore, our findings also suggest that insulinitis and β cell destruction are independently regulated: TNF- β is more important in forming and maintaining the insulinitis, while IFN- γ has more important role in β cell destruction.

P32

Social status and clinical predictors of hospitalization in childhood diabetes

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Background: In international studies predictors of hospitalization and especially the influence of the social status were

reported. The association between social status and morbidity was in part explained by differences in the specialization of diabetes care (Palta et al 1997, *Am J Epi*). Aim of this study was the evaluation of the influence of the social status and other relevant predictors on hospitalization in children and adolescents with diabetes within a structured treatment in Germany.

Methods: Based on the standardized longitudinal clinic documentation of a regional 'Quality in Childhood Diabetes Working Group', social status of the families (parents' school education level, 3 classes) was assessed, as well as sex, age, diabetes duration, and HbA1c as further predictors. Hospitalizations (frequency and duration) were admitted. Adjusted relative risks (RR's) were estimated using multivariate Poisson regression analysis.

Results: 430 children and adolescents (49% male, age 11.9 \pm 4.3 yrs, diabetes duration 4.6 \pm 3.8 yrs) were followed up to 3.5 yrs, resulting in 585 person years of follow-up. Adjusted RR's (CI_{95%}) of social status, lowest vs. highest class: 1.5 (1.1–2.1) for hospitalization risk, 1.6 (1.5–1.9) for hospital days. Higher HbA1c and pubertal age were significantly associated with higher hospitalizations.

Summary: A lower social status was associated with a significantly higher hospitalization risk and more hospital days, independent from age, diabetes duration, HbA1c, and treating clinic. The influence of the social status was as high as the influence of relevant clinical predictors. Also in a specialized structured treatment an association between social inequality and morbidity can be evaluated. This should be discussed in initiatives of quality management.

P33

Familial risk of type 1 diabetes mellitus in upper silesian children, Poland

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The aim of the study was to investigate the characteristics of the familial type 1 diabetes mellitus in a first degree relative for children diagnosed before age of 15 years.

Results: We analysed 528 diabetic children with onset of diabetes in period 1989–1997. 30 cases had a positive history of familial type 1 diabetes: 9 affected fathers, 6 affected mothers and 14 affected siblings. The prevalence of the family history of type 1 diabetes mellitus was following: Father's history 1.7%, mother's history 1.14% and sibling's history 2.65%. Fathers were more often affected than mothers. The tendency towards earlier onset of diabetes in children with positive familial history was observed. We found linear regression model and characteristic data for Silesian region similar to the other European children. **Conclusions:** Upper Silesian children demonstrate the same European trend of a positive association between the prevalence of familial type 1 diabetes and the population type 1 diabetes incidence rate, and the characteristic of familial type 1 diabetes (preferential transmission of disease from father to child).