

SP-1

Transplantation of neuroprotective choroid plexus epithelium prevents diabetes in the nod mouse

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Introduction: The islets of Langerhans are enveloped in Schwann cells which are the early target of islet auto-immunity. The islets also contain a profuse network of other neural elements. Neurotrophins are secreted by choroid plexus (CP) epithelium and we have demonstrated* that these secretions are able to prevent experimental neural damage *in vitro* (serum deprivation or malonate in culture) in a dose dependent fashion, and from quinolinic acid and hypoxic ischemia *in vivo*. *In vitro* we have demonstrated* the beneficial effect of CP culture supernatant on survival and function of porcine islets in long term culture. We therefore hypothesized that CP epithelial secretions might salvage islets subjected to a number of insults, including aggressive autoimmunity.

Methods: Female diabetic mice at the age of 30 days were transplanted IP with alginate encapsulated neonatal porcine choroid plexus epithelial clusters derived by collagenase digestion, and subsequent culture *in vitro* with frequent media changes for three days in groups of 6–7 animals given 3 different escalating doses (500, 1000, 2000). Litter mates were given empty microcapsules. Diabetes incidence (blood glucose consistently >15mM) was studied in all groups up to 250 days.

Results: There was a highly significant, dose independent protective effect on diabetes incidence of the CP transplants*. The control group reached the maximum diabetes incidence of 53% by day 156 of life, whereas the maximum diabetes incidence of 27% was not seen in the experimental group until day 230. CP transplants given after diabetes had occurred in the control group were ineffectual.

Conclusion: It is likely that the protection afforded by CP is capable of offsetting damage caused by immune attack of islets. CP intraperitoneal transplants could provide a novel, minimally invasive means of preventing Type 1 diabetes in humans, in those deemed to be at high risk. That neuroprotection is likely to be the mechanism of action of these cells casts new light on the possible pathogenesis of Type 1 diabetes.

*original data will be presented in detail.

SP-2

Birth size and postnatal growth in young offspring in European families with at least one family member affected by type 1 diabetes

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Introduction: Increased weight in infancy and rapid linear growth and weight gain subsequently have been shown to be risk factors for childhood type 1 diabetes (T1D). The highest incidence of T1D has been observed in Northern Europe (NE), whereas the rates are moderate or low in Central and Southern Europe (CSE) except for Sardinia. This study aimed at comparing birth size and postnatal growth between NE and CSE children.

Methodology: TRIGR is an international intervention study exploring whether weaning to a highly hydrolyzed formula decreases the cumulative incidence of preclinical and clinical T1D in young children at increased risk. The trial is running in 15 countries. This study cohort includes children born in NE (n = 78–363 at various time points) or in CSE (n = 24–278). Our analyses are based on growth data up to the age of 2 years.

Results: The newborn infants in NE were heavier (p < 0.001) but shorter (p = 0.007) than their peers in CSE. The NE children remained heavier than those from CSE at all time points (p ≥ 0.04) but at the age of 2 years. The former group was also taller than the latter group starting from the age of 3 months up to 18 months of age (p ≥ 0.03). The NE boys were heavier (p ≥ 0.04) at all time points during the follow-up, while that was true up to the age of 9 months (p ≥ 0.05) among girls. NE girls were marginally taller than their peers from CSE only at 6 and 18 months, whereas the NE boys were taller (p ≥ 0.05) at all time points but 6 months.

Conclusions: The young children in NE were shorter but heavier at birth than their counterparts in CSE. The NE children remained heavier over the first 18 months of life, and they became taller than their CSE peers already at the age of 3 months. These differences in early growth pattern may contribute to the high incidence of T1D in NE.

SP-3

Perinatal risk factors for childhood type 1 diabetes in western Australia – a population based study (1980–2002)

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Introduction: The relationship between perinatal factors and type 1 diabetes (T1DM) remains unclear, with several studies reporting inconsistent findings. No such studies have yet been performed in

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Western Australia (WA) where complete, population-based data are available on all children diagnosed with T1DM under the age of 15 years. Perinatal data collection on all births, including data on maternal health and socio-demographic factors, has been mandatory in WA since 1980.

Aim: This study aimed to investigate potential perinatal risk factors for childhood T1DM in WA, using a complete population-based cohort, from 1980 to 2002.

Methodology: Perinatal data were obtained from the Midwives' Notification System, on all live births in WA from 1980 to 2002 (n = 559,134) and record linkage performed to identify the cases. Cases born between 1980 and 2002 and diagnosed with T1DM, under the age of 15 years, in WA between 1985 and 2003 (n = 909), were identified using the prospective population-based diabetes register at Princess Margaret Hospital, which has a case ascertainment rate of 99.8%.

Results: After adjusting for year of birth, birth weight and gestational age, the incidence increased by an average of 9% for each 5 year increase in maternal age at delivery (Incidence rate ratio (IRR) 1.09 (95%CI: 1.03–1.17), $p = 0.005$). After adjusting for maternal age at delivery, gestational age and year of birth, the incidence increased by an average of 16% for every 500g increase in birth weight (IRR 1.16 (95%CI: 1.07–1.25), $p < 0.001$). After adjusting for maternal age at delivery, birth weight and year of birth, the incidence decreased with increasing gestational age [IRR 0.82 (95%CI: 0.75–0.90), $p < 0.001$]. Additional data on maternal medical history, pregnancy complications and socioeconomic status will be presented.

Conclusion: After adjusting for confounding variables, the incidence of T1DM increased significantly with increasing maternal age at delivery, higher birth weight and lower gestational age.

SP-4

Neighborhood genetic and environmental factors and number of newborns born with cord blood autoantibodies

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Introduction: Genetic factors are important in the development of islet autoimmunity and type 1 diabetes (T1D). HLA-DQB1*02 is associated with GAD65Ab and HLA-DQB1*0302 with IA-2Ab and IAA. The role of environmental triggers however is unknown but perinatal factors are considered important.

Aim: To examine whether prevalence of high risk T1D-HLA genotype and reported maternal infections in municipalities are independently related to frequency of newborns with autoantibodies.

Methodology: In all, 24732 newborns born to healthy mothers in the south of Sweden were included. Dried blood spots were prepared from the newborn and the address of the mother was obtained from a registration form. Prevalence of high risk T1D-HLA in municipalities was estimated from frequency of newborns with the high risk HLA-DQB1*02/0302 genotype. Reported maternal infections during pregnancy were taken from psychosocial questionnaires filled out by mothers. Poisson regression tested whether neighborhood factors were associated with frequency of newborns with autoantibodies.

Results: Neighborhood genetic and environmental factors were not related to frequency of GAD65Ab positive children. Frequency of IA-2Ab or IAA positive children however was positively associated with both prevalence of DQB1*02/0302 ($p = 0.006$) and mothers reporting gastroenteritis ($p = 0.01$). Number of younger mothers (<30 years) was also associated with increased autoantibody frequency ($p = 0.04$). Multivariate analysis showed both HLA and reported gastroenteritis to be significant ($ps < 0.01$).

Conclusion: High risk HLA and gastroenteritis in the neighborhood

are associated with an increased frequency of children born with IAA and IA-2Ab. Prospective analysis will determine whether these neighborhoods are also at increased risk for later development of T1D.

SP-5

Variation in physical activity lies with the child, not his environment. Evidence for an 'activitystat' in young children: the EarlyBird diabetes study

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Background: Children's physical activity (PA) is important in relation to diabetes risk, but there is little understanding of its control.

Aims: To establish whether a child's overall PA is greater where there is more provision or opportunity.

Methodology: Accelerometers recorded weekly PA in two groups of healthy children: Group 1: 215 9-year-olds from three schools (S) differing widely in timetabled physical education (PE) (S1 = 9.0 h/week, S2 = 2.2 and S3 = 1.8). Group 2: 300 of the EarlyBird cohort examined at 5y and again at 6y.

Results: Group 1: school-time PA was predictably higher in S1 (B: S1 = 18.6, S2 = 12.5, S3 = 11.0, G: S1 = 16.9, S2 = 9.7, S3 = 11.4 PA units/wk, $p < 0.001$). However, what PA the children from S2 and S3 lacked in school, they made up for out of school (B: S1 = 16.1, S2 = 26.6, S3 = 22.8, G: S1 = 13.6, S2 = 22.7, S3 = 22.6 units/wk, $p < 0.001$). Indeed, <1% of the variance in PA could be explained by the five-fold difference in timetabled PE. Group 2: weekday/weekend day and year-on-year correlations were high ($r = 0.43$ – 0.56). Furthermore, over 90% of the PA counts lost by car transport to school were 'recovered' during the rest of the day (walkers 37.56, car 37.60 units/wk, $p = 0.97$). Finally, the weekly PA recorded by Group 2 children in Plymouth was within 1% of that recorded by age-matched children in Glasgow.

Conclusions: The data point to consistency in PA among young children, irrespective of daily routine or culture. Further, almost all the variation in PA lies with the child, rather than his/her environment, which may have important implications for plans to increase provision. The correlations in PA within groups over time and the similarities between groups, despite differing opportunity, suggest that PA is under biological, rather than environmental, control.

SP-6

Parental body mass index (BMI) is closely related to the BMI in children and adolescents with type 1 diabetes

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Introduction: The excessive weight gain of children and adolescents with type 1 diabetes is a frequent finding.

Aim: We tested the hypothesis that there is an influence of parental BMI and analyzed the contribution of further diabetes and non-diabetes related factors.

Methodology: The association between the age and gender adjusted SDS of BMI of children and adolescents with type 1 diabetes treated in a regional referral center, clinical data, and the parental BMI were examined in a retrospective cross-sectional analysis by logistic multiple regression statistics.

Results: A representative sample of 251 patients (3–21 ys) with a mean diabetes duration of 5.4 ± 3.3 ys (mean \pm SD) exhibited a significant increase of body weight of 0.9 ± 0.9 SDS. A tendency towards higher SDS (0.9 ± 1.0) in girls (n = 119) compared to boys

(0.8 ± 0.8 $p = 0.2$) was observed particularly in pubertal girls ($n = 86$, SDS: 1.0 ± 1.0) compared to prepubertal girls (0.7 ± 0.8 $p < 0.05$). In contrast, the pubertal boys ($n = 80$) demonstrated a lower SDS (0.8 ± 0.8) compared to prepubertal ones (0.9 ± 0.8). Fathers who were overweight (BMI > 25 kg/m² $n = 167$) increased the odds ratio for obesity in children by 1.8 (95%CI: 1.06–3.1 $p < 0.05$). Maternal obesity (BMI > 30 kg/m² $n = 40$) increased the odds ratio even to 2.9 (95%CI = 1.42–6.11 $p < 0.05$). We found a direct positive correlation of maternal BMI to the BMI of their diabetic children in both sexes, while the paternal BMI increased the risk only for prepubertal girls ($p < 0.000$). Diabetes related factors such as diabetes duration, glycaemic control or mode of therapy showed no association. Furthermore, it had no influence on the results if the children were living in urban or rural regions.

Conclusion: The risk of overweight and obesity in children and adolescents with type 1 diabetes is primarily dependent on familial factors and particularly maternal obesity. Methods to prevent an excessive weight gain in pediatric diabetes patients should focus also on the parents.

SP-7

Higher body mass index at diagnosis of type 1 diabetes in younger children

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The accelerator hypothesis states that overweight in childhood brings earlier the diagnosis of type 1 diabetes. It may also suggest that younger children may be more overweight than older children at diagnosis.

Aim: To determine whether BMI standard deviation score (SDS) was higher in younger children at diagnosis and if so, whether that continued after five years of diabetes.

Methods: We analyzed the baseline weight and height measurements at 1–12 months post diagnosis to allow for the regain of any lost weight prior to diagnosis; and at five years duration. Weight, height and BMI SDS were compared between three age categories. SDS for age and gender were derived from CDC 2000 growth data.

Results:

Age at Diagnosis	2 ≤ 5 years (n = 149)	5 ≤ 10 years (n = 393)	10 ≤ 15 years (n = 307)	p-value
Baseline				
Height SDS	0.66	0.44	0.28	0.0005
Weight SDS	0.84	0.65	0.34	<0.0001
BMI SDS	0.95	0.66	0.37	<0.0001
5 years				
Height SDS	0.39	0.44	0.23	0.19
Weight SDS	0.66	0.77	0.79	0.43
BMI SDS	0.69	0.73	0.71	0.82
SDS change				
ΔHeight SDS	-0.27	-0.006	0.05	<0.0001
ΔWeight SDS	-0.27	0.06	0.40	<0.0001
ΔBMI SDS	-0.30	0.03	0.27	<0.0001

After 5 years of diabetes, the BMI SDS fell significantly in the youngest group ($p = 0.0004$), but had increased significantly in the older groups ($p = 0.032$, $p < 0.0001$).

Conclusions: At diagnosis BMI SDS was higher in younger children but after five years diabetes duration BMI SDS was not significantly different between younger and older children. This suggests the younger children had a relative deceleration in growth possibly following an acceleration prior to onset of diabetes.

SP-8

Free fatty acids level at onset of type 1 diabetes: further evidence supporting the accelerator hypothesis

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Introduction: Recent studies have reported that free fatty acids (FFA) affect insulin secretion by specific receptors, e.g. CD36 and GRP40. Moreover, in vitro studies have revealed that high FFA level may induce apoptosis of the pancreatic beta cells. On the other hand, the accelerator hypothesis suggests that adipose tissue and/or lipids metabolism may contribute to the pathogenesis of type 1 diabetes.

Aim: Thus, to determine whether the residual insulin secretion in children with type 1 diabetes is related to FFA serum level we recruited 178 diabetic patients (mean age 10.8 yrs; M/F 99/79).

Methodology: In all individuals the fasting C-peptide and FFA serum levels were measured at the onset and after 6 months of the diabetes duration.

Results: 34 (19.1%) of the patients had the C-peptide level above lower limit of normal range (>0.28 pmol/ml) at both time-points. FFA level at onset was significantly higher as compared to the level after 6 month of follow-up (38.4 ± 29.4 vs. 28.9 ± 23.1 mg/dl; $p = 0.0003$). However, both values were positively correlated ($r = 0.31$, $p = 0.0008$). Interestingly, negative correlation was found between FFA and C-peptide measurements at 6th month ($r = -0.19$, $p = 0.01$ and $r = -0.18$, $p = 0.02$ for FFA at onset and at 6th month, respectively). Moreover, when the C-peptide level was treated as a binomial variable (above and below 0.28 pmol/ml) higher levels of FFA were observed in children with C-peptide deficiency at both time-points (41.1 vs 29.9 mg/dl, $p = 0.03$ and 31.0 vs 23.7 mg/dl, $p = 0.1$). No relation of FFA with age at onset, gender, insulin requirement and HbA1c were revealed.

Conclusion: Obtained results, which link the FFA acids with residual insulin secretion in type 1 diabetes, may serve as further evidence supporting the accelerator hypothesis.

SP-9

TRMA, a novel aetiology to diabetes in childhood

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Introduction: In Denmark most children with diabetes have type 1 diabetes, but other more rare types of diabetes also exist. Thiamine Responsive Megaloblastic Anaemia (TRMA) is a rare autosomal recessive condition, including megaloblastic anemia, non-autoimmune diabetes mellitus and sensorineural deafness. We describe 3 cases of TRMA in children from two consanguineous Pakistani families, who were apparently not related.

Aim: To raise the awareness of other more seldom types of diabetes which especially occur in immigrant, consanguineous families.

Methodology: In our clinic 3 cases of TRMA have been diagnosed. Two children, who were cousins, came from the same consanguineous family from Pakistan. Their parents were siblings, and married to their first cousins. The last child came from another consanguineous family, not related to the first family, but coming from the same area in Pakistan.

All children were diagnosed at a young age, 10 months, 12 months and 8 weeks, and all had diabetes, severe megaloblastic anemia, failure to thrive and sensorineural deafness. Due to the complex of symptoms TRMA was suspected, and a genetic evaluation was performed.

Results: All children were homozygous and the parents heterozygous for a previously reported mutation 196G > T, leading to a premature stop (E66X) in the SLC19A2 gene. The gene is located on chromosome 1q23.2–23.3 and encodes a high-affinity thiamine transporter. The result is an abnormal thiamine transportation. Thiamine in high doses (100–200 mg/day) reversed the anemia in

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all patients. After a short treatment period two of the patients stopped insulin treatment, while the third remained on insulin treatment, but had a 50% reduction in daily insulin requirement. All children remained deaf, and have received a cochlea implant.

Conclusion: TRMA is a rare, autosomal recessive disease, including megaloblastic anemia, diabetes and deafness. The disease should especially be suspected in immigrant consanguineous families.

SP-10

CSII and MDI treatment of type 1 diabetic children under the age of 10: 5 years follow up

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Introduction: Continuous subcutaneous insulin infusion (CSII) is an alternative method of insulin administration in patients with type 1 diabetes. The guidelines of its use in young children are still being discussed.

Aim: The aim of this study was to evaluate and compare the outcome of type 1 diabetic children under the age of 10 treated with CSII therapy with a control group treated with multiple daily injection (MDI) for a period of 5 years.

Methodology: The study was conducted during years 2000–2004. 234 patients (128b, 108g) of an outpatient clinic of Medical University Department of Diabetology in Warsaw, with a history of type 1 diabetes for at least 6 months were followed. This group treated with CSII included 163 subjects (81b, 83g) with mean age – 7.46 ± 2.4 (2.3–10ys), mean duration of diabetes – 3.26 ± 1.7 (0.5–9ys) and mean duration of CSII therapy – 1.96 ± 0.3 (0.5–4.2ys). The group treated with MDI therapy included 71 subjects (37b, 25g), mean age – 8.57 ± 2.24 (2.3–10ys), mean duration of diabetes – 3.21 ± 2.35 (0.5–9ys).

Results: The average HbA1c values were significantly lower in CSII vs MDI patients (2000: $8.07 \pm 1.21\%$ vs $8.49 \pm 1.36\%$; 2001: $7.78 \pm 1.21\%$ vs $8.66 \pm 1.67\%$; 2002: 7.53 ± 1.03 vs $7.81 \pm 0.98\%$; 2003: $7.38 \pm 0.96\%$ vs $7.8 \pm 1.28\%$, 2004: 7.23 ± 0.94 vs 7.86 ± 1.23 p < 0.005). The overweight in pumps users was not observed and the average BMI in both groups was 16.2 ± 1.3 kg/m². No statistically significant difficulties were noted in mean insulin requirement between CSII and MDI groups during follow up period (2000: 0.5 ± 0.22 j/kg/d vs 0.58 ± 0.27 j/kg/d, 2001: 0.55 ± 0.2 j/kg/d vs 0.6 ± 0.29 j/kg/d, 2002: 0.6 ± 0.22 j/kg/d vs 0.65 ± 0.3 j/kg/d, 2003: 0.64 ± 0.22 j/kg/d vs 0.71 ± 0.49 j/kg/d, 2004: 0.71 ± 0.19 j/kg/d vs 0.77 ± 0.25).

Conclusion: The pump therapy is more effective than pen therapy in young diabetic children, provides good and sustained metabolic control without increasing of body mass index.

SP-11

Under dosage of insulin seems to be an important reason for not reaching treatment goals for Norwegian children with diabetes

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Introduction: Twenty-three percent of the patients in a nationwide benchmarking study of children with diabetes obtained the goal for glycemic control (HbA1c $\geq 7.5\%$).

Aim: To identify patients who managed to get significantly better glycemic control from 2003 to 2004 and characterize them.

Methodology: Data concerning treatment, acute and chronic complications in children with diabetes are collected yearly from the

treating hospitals. Patients who had an HbA1c value $>7.5\%$ in 2003 and managed to reduce it with 1% point in a year were selected for the study. All HbA1c values used in this study were measured at the same laboratory with the DCCT standard.

Results: The benchmarking was based on 1129 patients in 2003, 1417 patients in 2004. In 2004 mean HbA1c for the total group was 8.1%. 152 patients with a mean age of 13.4 years (3.7–20.4) were included in the study according to the inclusion criteria. Further results are given in the table.

Conclusion: Insulin dose, BMI and the proportion of patients using an insulin pump were significantly raised in 2004 compared to 2003. Higher insulin dosages and increased use of pumps were the main factors we could identify having importance for better glycemic control in this group of patients.

Clinical characteristics

Variable	Mean 2003	Mean 2004	p-value @ = 0.05
HbA1c	9.3	7.85	<0.0001
BMI kg/m ²	19.2	20.7	<0.0001
Insulin pumps	0.17	0.34	<0.0001
Total insulin dose units/kg	1.0	1.12	0.015
LDL-Cholesterol mmol/l	2.62	2.67	0.41
Episodes with hypoglycemia/4 weeks	0.17	0.28	0.21
Number of episodes DKA/year	0.13	0.08	0.25
Visits at clinic/year	3.72	3.91	0.16
Number of blood glucose measurements/week	27.8	28.6	0.053

SP-12

Treatment with insulin glargine (Lantus) of children and adolescents with type 1 diabetes

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Objectives: New therapies for treatment of type 1 diabetes should improve control without increasing the number of hypoglycemic episodes which are a significant cause of psychological and physical fear in patients. Previous studies suggested that hypoglycemia may be closely linked to the high variability observed with traditional basal insulin preparations such as NPH insulin. Further, NPH insulin is often administered twice daily and patients with dawn phenomenon need additional injection with short acting insulin at 3 a.m.

Aim: The aim of the study was to determine if the addition of insulin glargine (Lantus) could improve glycemic control and avoid an additional injection at 3.00 a.m. in children and adolescents with type 1 diabetes.

Materials and methods: 83 patient with type 1 diabetes (41 F and 42 M) mean age of 14.45 years (5–18.8) and diabetes duration of 5.85 years (0.5–12.9) were transferred from NPH insulin to Lantus and maintained the treatment for at least six months. The starting dose of insulin glargine at bedtime was 80–100% of the previous total dose of basal insulin. The doses of glargine and prandial insulins were adjusted according to fasting, postprandial glycemia and glycemia at 3.00 a.m.

Results: Mean HbA1c levels at baseline, after 3 and 6 months were 8.3%, 7.99% and 7.5% (p < 0.05 vs. baseline) respectively. The dose of glargine insulin was 0.24 IU/kg (27% of daily insulin dose). Episodes of severe hypoglycemia were not registered. The incidence of nocturnal hypoglycemia and early morning hyperglycemia tended to decrease. We also observed that patients with dawn phenomenon (78%) did not need additional insulin injections at 3.00 a.m. to have good fasting glycemia (almost 50% of them) or doses of short acting insulin were significantly lower. BMI did not change (19.88 kg/m² at baseline vs. 19.42 kg/m² after 6 months).

Conclusion: These results show that treatment with a basal bolus insulin glargine is effective and well tolerated in type 1 diabetic patients. Insulin glargine significantly improves metabolic control, reduces nocturnal hypoglycemic and hyperglycemic episodes and is not associated with weight gain. The insulin analogue glargine

(Lantus) is a valuable tool to obtain a basal insulin supplementation in patients with type 1 diabetes.

SP-13

The use of insulin glargine in pre-pubertal children on 3 × daily insulin regimen – a randomized cross-over trial

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Introduction: Insulin glargine is increasingly used in children with type 1 diabetes mellitus (T1DM) on multiple injection therapy (4 + injections/day) to reduce nocturnal hypoglycemia and to improve blood glucose control. However many younger children will only accept less intensive insulin regimens.

Aim: We investigated the effects of glargine on hypoglycemic events and glucose control in pre-pubertal children when combined with various insulin combinations given 3 × daily (morning/pre-tea/pre-bed).

Methodology: 17 pre-pubertal children with T1DM (7 girls), median age 10.2 years (range 6–12.4), HbA1c 8.8% (6.8–11.5) took part in an open-label, randomised, cross-over study. After a 2-week run-in period (with NPH pre-bed), every child received 3 different 3-week treatment blocks in randomised order. All the treatment blocks included: insulin aspart pre-tea, and glargine pre-bed. The different morning insulins were: Block 1: actrapid only, Block 2: actrapid + NPH, Block 3: aspart + NPH. A continuous glucose monitor (CGMS, Minimed) was applied at the end of the run-in and each 3-week glargine treatment block.

Results: Mean pre-breakfast glucose levels were lower in the 3 glargine blocks ($p < 0.05$), and showed lower variance ($p < 0.05$) compared to the run-in period. Mean day-time blood sugars and number of day-time hypoglycemia episodes did not differ significantly between treatment blocks and run-in. Night-time prolonged hypoglycemic episodes ($< 3.5 \text{ mmol/l}$ for $> 60 \text{ mins}$) were less common in Block 3 (14.9% of 47 nights) than in the run-in (33.3%; $p < 0.05$); Block 1 (21.9%) and Block 2 (38.3%) did not differ compared to run-in. Total daily insulin doses were 8–15% lower on each of the 3 glargine treatment blocks compared to the run-in period ($p < 0.05$).

Conclusion: In pre-pubertal children on a 3 × daily insulin regimen, insulin glargine (pre-bed) is as effective as conventional insulin, and results in lower and less variable morning glucose levels. When taking insulin glargine pre-bed, the morning insulin combination of a short-acting analogue + NPH was associated with reduced nocturnal hypoglycemia.

SP-14

The effect of insulin glargine and nutritional model on metabolic control, behavior, self-esteem and quality of life in type 1 diabetes mellitus

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Introduction: Nutritional model and the type of insulin used affect the metabolic control, quality of life, behavior problems and self-esteem of diabetic children.

Aim: To evaluate the effects of glargine insulin and nutritional model on metabolic control and quality of life.

Methodology: Thirty eight children (19 girls, 19 boys) with type 1 diabetes were included. The patients were assigned to 2 groups according to their nutritional model. First group ($n = 14$) were changed to carbohydrate counting and the second group ($n = 24$) stayed with the same nutritional model as before (calories). Both groups started to use insulin glargine and rapid acting insulin. At

the beginning of therapy and on the 6th month Childhood Behavior Check List (CBCL), self-esteem and quality of life scoring were evaluated. Hb A1c, height SDS, BMI, BMI SDS and insulin dosages were evaluated at delta Hb A1c, the beginning and on the 3rd and 6th month.

Results: Mean age of the patients was 15.2 years (6.3–22.3 years) and the mean duration of diabetes was 7.1 years (1.2–18 years). There was no difference in BMI, BMI SDS, the total insulin dosage and basal insulin dosage at the beginning and on the 6th month of therapy in the two groups. There was a significant decrease in HbA1c in both of the groups on the 6th month of therapy ($p < 0.05$) but no difference was found between delta Hb A1c at the end of the 62.37 $p = 0.78$). Self-esteem of ± 2.72 ; group 2: -0.46 th month (group 1: -0.58 the patients did not show any difference between the two groups but there was a significant difference in the behavioral issues of the patients at the beginning and at the end of the 6th month. CBCL scores decreased in both of the groups at the end of the sixth month but not statistically significantly. There was no difference in the self esteem of the two groups at the beginning and on the 6th month. Anxiety of the patients decreased in the first group at the end of the sixth month ($p = 0.049$) according to quality of life scale.

Conclusion: As a result, glargine insulin helps to provide a better metabolic control albeit nutrition and the difference in behavioral issues is statistically significant and carb counting helps to decrease the anxiety about diabetes.

SP-15

Impact of regular physical activity on metabolic control and cardiovascular risk factors in children with type 1 diabetes – a large multicentre study

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Introduction: Physical activity has been shown to have a positive effect on glycaemic control in type 1 diabetes.

Aim: To evaluate the influence of the frequency of regular physical activity on HbA1c, BMI, plasma lipids and blood pressure in a large cohort of children with type 1 diabetes.

Methodology: Anonymous data of 18.392 pediatric patients (age 0.2–19.9 years; 8828 girls) with type 1 diabetes were provided by the Pediatric Quality Initiative (DPV), including data from 179 centers in Germany and Austria. Patients were grouped by the frequency of their regular physical activity per week (FRPA) as follows: FRPA0 = none, FRPA1 = 1–2×/week, FRPA2 = >2×/week.

Results: Frequency of regular physical activity was 0–9 (mean 1.26) times/ week. Multiple regression analysis revealed that FRPA was one of the most important factors influencing HbA1c, LDL, HDL, triglycerides (TG) and diastolic blood pressure. High FRPA correlated with low HbA1c ($p < 0.0001$) in both sexes and in all age groups. In the FRPA1 group HbA1c was lower than in the FRPA0 group, but in the FRPA2 group HbA1c was not lower than in the FRPA1 group. We found a significant negative correlation between Cholesterol, LDL, TG and diastolic blood pressure and FRPA and a significant positive correlation between HDL and FRPA. In girls, but not in boys, high FRPA was associated with low BMI-SDS ($p < 0.0001$). Rate of severe hypoglycemia (defined by unconsciousness or seizures) did not correlate to FRPA.

Conclusion: Regular physical activity represents one of the most important factors influencing the metabolic control and cardiovascular risk factors in children with T1DM. Frequency of the regular physical activity has an important impact on lipid profiles and diastolic blood pressure. Concerning the HbA1c, regularity of physical

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activity seems to be more important than frequency. The risk for severe hypoglycemia is not elevated even in children frequently performing regular physical activity.

SP-16

What is the relationship between the frequency of self-monitoring of blood glucose (SMBG) and metabolic control? Effects of age, gender, mode of insulin therapy

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Introduction: Repeated daily blood glucose measurements and appropriate dose-adjustments are considered a major part of modern intensified insulin therapy. However, few studies have addressed the question whether more frequent SMBG is actually related to better metabolic control in pediatric patients with type-1 diabetes.

Aim: Evaluate the relationship between SMBG and metabolic control.

Methodology: The DPV-Science-Database is a multicentre documentation initiative as a basis for quality management in routine care. Data are recorded locally by a dedicated computer software program, anonymized and transferred for central analysis. This report is based on pediatric patients (age <18 years) with type-1 diabetes. By March 2005, 17940 patients from 166 centers in Germany and Austria were available for analysis (mean age at onset: 8.0 years, mean chronological age: 12.8 years, 48% female). HbA1c was mathematically standardized to the DCCT normal range based on local reference ranges.

Results: On average, patients measured 30.9 blood glucose values per week. The frequency of SMBG increased during recent years (1995: 23, 2004: 34), was higher in younger patients (<5 years: 39, 15–18 years: 27) and in patients on intensified insulin therapy (4+ injections/day, 32 versus 28), and girls measured slightly more BG values compared to boys (all $p < 0.0002$). A multiple regression model (GLM) was used to evaluate the relationship between the frequency of glucose testing and metabolic control. Overall, HbA1c averaged 8.4%. After correction for age, gender, duration of diabetes, injection frequency, dose and preparation of insulin, year of observation and center, there was a highly significant relationship between the frequency of SMBG and better metabolic control ($p < 0.0001$). One additional BG measurement per day improved HbA1c by 0.27%. This effect was more pronounced in older subjects and in patients on intensified insulin therapy or insulin pump therapy. In contrast, the rate of severe hypoglycemia did not improve with more frequent blood glucose testing.

Conclusion: This observational study on a large cohort of subjects demonstrates that under real-life conditions patients who measure blood glucose more frequently display better metabolic control, especially in older subjects on intensified insulin therapy.

SP-17

Does the addition of pioglitazone to insulin improve metabolic control in youth with type 1 diabetes and insulin resistance? A randomized placebo-controlled trial

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Introduction: Insulin resistance (IR) during puberty may cause deterioration of metabolic control in adolescents with type 1 diabetes

(T1D). We and others have shown that adjunctive therapy with metformin moderately improves A1c in these subjects. The objective of this study was to determine if the addition of a potent insulin sensitizer, the thiazolidinedione pioglitazone (PIO), to standard therapy also leads to improved metabolic control in pubertal T1D patients with IR.

Methodology: We conducted a 2 site, randomized, placebo-controlled, double-blind 6 month trial of 30 mg PIO versus placebo (PLAC) in 38 adolescents with T1D, high insulin requirements (>0.9 U/kg/day) and suboptimal metabolic control (HbA1c > 7.5%). We contacted each subject by telephone at least weekly to adjust insulin doses to target blood sugars of 4–8 mmol/L.

Results: There was 1 dropout. 2 subjects withdrew [severe hypoglycemia (PIO); elevated hepatic enzymes (PLAC)].

Baseline characteristics of patients who completed the study

	Pioglitazone (9F/9M)	Placebo (9F/8M)
Age (years)	14.3 ± 1.9	14.7 ± 2*
Duration of diabetes (years)	5.7 ± 3.1	7 ± 3.9*
BMI SDS	0.8 ± 1.1	1.3 ± 0.6*
Injections T1D/Q1D/pump	9/6/1	14/3/2
Insulin dose (U/kg/day)	1.3 ± 0.4	1.4 ± 2*
A1c (%)	8.8 ± 0.9	8.8 ± 0.9*

Data are expressed as mean ± SD; ns*

After 6 months both groups had significantly lower A1c levels ($p < 0.05$); (mean change in A1c in PIO group -0.4 ± 0.9 vs $-0.5 \pm 1.2\%$ in the PLAC group), without significant differences between groups. Insulin dose was unchanged. The PIO group demonstrated a small decrease in cholesterol and LDL, compared to an increase in the PLAC group ($p < 0.05$). BMI SDS increased by 0.3 in PIO group, and remained unchanged in the PLAC group ($p = 0.01$).

Conclusion: Unlike previous studies using metformin, adjunctive therapy with PIO was not effective in improving metabolic control in adolescents with T1D. The effect on lipid profile, despite increased BMI SDS, in these patients may suggest potential antiatherogenic benefit.

SP-18

Glimepiride (GLIM) vs metformin (MET) as monotherapy in pediatric subjects with T2DM: a single blind comparison study

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Introduction: Glimepiride (GLIM) with its favorable efficacy and safety profile in adults may be an appropriate alternative for initial therapy in pediatric patients with T2DM.

Methodology: A 26 wk randomized, single blind, parallel-group, forced-titration study compared the efficacy and safety of GLIM and metformin (MET) therapy in 263 T2DM pts age 9 to 17 inadequately controlled (A1C > 7.1% but <12.0) with diet & exercise only &/or failed oral monotherapy. Pts were randomized to GLIM 1 mg qd & titrated every 4 wks to 2 mg, 4 mg, and 8 mg qd, respectively to achieve FBG <7.0 mmol/L (126 mg/dL) or MET 500 mg bid titrated to 1000 mg bid if mean SMBG > 7.0 mmol/L (126 mg/dL). **Results:** Baseline demographics were similar: mean age 13.8 yrs; 66% female; >50% tanner stage ≤3; mean A1C 8.5%; median BMI GLIM 30.4 kg/m² (range 14.5–70.5) & MET 31.2 kg/m² (range 17.2–62.9). Mean last dose of GLIM was 3.8 mg & 1408 mg for MET. At wk 24, mean A1C was 7.99% & 7.83% and mean SMBG was 9.0 mmol/L (161 mg/dL) & 8.4 mmol/L (152 mg/dL) for GLIM & MET groups, respectively. Similar percentage of pts achieved A1C <7% (42% GLIM vs 48% MET, $p = 0.3468$). Incidence of

ADRs was low with headache, diarrhea, & nausea occurring most frequently in the MET group. Incidence of hypoglycemia [<2.8 mmol/L (50 mg/dL)] was similar in each group [4.9% (7/142) pts GLIM vs 4.2% (6/142) MET, $p < 0.7464$]. One severe hypoglycemia event [<2.0 mmol/L (36 mg/dL)] occurred in each group. Lipid profile was similar between groups.

Conclusion: GLIM & MET are safe and effective for the treatment of pediatric pts with T2DM.

	GLIM*		MET*		Between Group Difference P
	Baseline	Δ from Baseline	Baseline	Δ from Baseline	
A1C, %	8.47 \pm 0.24	-0.70 \pm 0.3	8.49 \pm 0.23	-0.85 \pm 0.30	0.5420
SMBG, mmol/L (164.3 \pm 10.11)	9.13 \pm 0.56 (-15.1 \pm 9.05)	-0.84 \pm 0.5	8.79 \pm 0.55 (158.2 \pm 9.93)	-1.15 \pm 0.49 (-20.6 \pm 8.91)	0.4485 (0.4499)
(mg/dL)					
Weight, kg	65.71 \pm 3.46	2.21 \pm 0.66	67.48 \pm 3.39	0.73 \pm 0.64	0.0036

*Adjusted means from analysis of covariance (ANCOVA)

SP-19

Oxidative stress, DNA damage and DNA repair capacity in children with type 1 diabetes mellitus and Crohn disease

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Introduction: Oxidative stress (OS) occurs in conjunction with diabetes mellitus (DM) and chronic inflammatory state represented by Crohn disease (CD). OS results in damage to lipids, proteins and DNA.

Aim: To study the intensity of oxidative stress, degree of DNA damage and DNA repair in a group of children with diabetes mellitus type 1 (T1DM) and CD. These results were compared with those derived from healthy children.

Methodology: 20 T1DM children (8 girls, 12 boys, average age 13.26 \pm SD 2.98 years, average T1DM duration 2.94 \pm 2.72 years, mean HbA1c 9.50 \pm SD 2.52%-DCCT) and 17 CD children (7 girls, 10 boys, average age 14.29 \pm SD 2.52 years, average disease duration 3 \pm 1.43 years, PCDAI index 35.69 \pm 16.60) were randomly chosen from a list of those treated at the Department of Pediatrics, University Hospital in Plzeň. Investigated markers of OS were: superoxide dismutase (SOD), glutathione peroxidase (GPx), plasma antioxidant capacity (AOC), reduced glutathione (GSH) and malondialdehyde (MDA). Breaks in DNA chains due to OS were investigated within peripheral lymphocytes using comet assay technique (DNAsb). Lymphocyte capacity to repair damaged DNA (DNArC) was also assessed using the modified comet assay. DNRI index expressed the relationship DNRI = DNArC/DNAsb. Results were compared with a group of 11 healthy children of similar age and sex (5 girls, 6 boys, average age 13.73 \pm SD 3.80).

Results: There were no significant differences between children with T1DM and CD in terms of disease duration and examined parameters. Children with T1DM compared with healthy children had lower SOD ($p < 0.001$), lower GSH ($p < 0.05$) and higher DNArC ($p < 0.05$), CD children had only SOD significantly lower ($p < 0.05$) than healthy controls.

Conclusion: Children with T1DM demonstrated more intensive oxidative stress compared with healthy children than the CD group. Comparison of T1DM children versus CD children did not show important differences.

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SP-20

Effects of rosiglitazone on intracellular antioxidant enzyme production in adolescents and young adults with early diabetic angiopathy

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Introduction: Defective intracellular antioxidant enzyme production (IAP) has been recently demonstrated in adults with diabetic angiopathy.

Aim: The objective is to evaluate the effects of rosiglitazone, one of the thiazolidinediones, on IAP in adolescents and young adults with type 1 diabetes mellitus (T1DM) and early signs of retinopathy and nephropathy.

Methodology: Prospective, matched case-control study conducted between November 2003 and December 2004 among 16 adolescents (age 16–21 years) with T1DM and early signs of angiopathy, 16 patients (age 16–22 years) with T1DM, without diabetic angiopathy and 13 healthy volunteers (age 17–23 years). Skin fibroblasts were obtained by skin biopsies from the anterior part of forearm and cultured in Dulbecco's modified Eagle's medium. Activity of CuZnSuperoxide-dismutase (SOD), MnSOD, catalase (CAT) and glutathione-peroxidase (GPX) and mRNA expression were measured before and after 6 months of treatment with rosiglitazone; in both occasions antioxidant enzyme activity was evaluated at different glucose concentrations (5 mmol/l and 22 mmol/l). Adolescents and young adults with diabetic angiopathy were treated with rosiglitazone (4 mg daily) for 6 months.

Results: In normal glucose concentrations, CuZnSOD (0.56 \pm 0.23 U/mg protein; 4.7 \pm 1.5 mRNA/GAPDH), MnSOD (0.32 \pm 0.08; 0.9 \pm 0.4), CAT (0.39 \pm 0.12; 4.6 \pm 1.4), and GPX (0.53 \pm 0.15; 2.6 \pm 0.9) activity and mRNA expression were not different among the three groups (values of diabetics with angiopathy). In high glucose concentrations, CuZnSOD activity and mRNA expression increased similarly in all groups (in angiopathics: 0.99 \pm 0.32; 10.0 \pm 3.4). CAT and GPX activity and mRNA did not increase in high glucose conditions only in the adolescents with diabetic angiopathy (0.39 \pm 0.11; 4.7 \pm 1.3 and 0.55 \pm 0.16; 2.7 \pm 0.9, respectively). MnSOD did not change in any group. Treatment with rosiglitazone in adolescents with diabetic angiopathy was able to restore CAT and GPX activity and mRNA expression after exposure to high glucose concentrations. Markers of oxidative stress (MDA, FPLP, MCP-1 and 8-isoprostanes PGF2 α) were significantly reduced after treatment with rosiglitazone.

Conclusion: Adolescents and young adults with early signs of diabetic angiopathy have defective intracellular antioxidant enzyme production and activity; treatment with rosiglitazone is able to substantially improve activity and production of these enzymes in skin fibroblasts.

SP-21

Risk factors of prehypertension in type 1 diabetic children and adolescents

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Introduction: The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents 2004 includes the new term – prehypertension. Prehypertension is an indication of increased risk for developing hypertension and requires therapeutic lifestyle changes.

Aim: The aim of the study was to evaluate the selected factors influencing the prevalence of prehypertension in T1DM children and adolescents.

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Methodology: 82 T1DM patients (46 male), aged 12–18.9 years, with diabetes duration of 0.5–17.2 years, without evidence of arterial hypertension were recruited. In patients 24-hour automatic blood pressure (BP) monitoring was performed. The individuals with >40% of systolic BP (SBP) and/or diastolic BP (DBP) \geq 95th percentile were defined as hypertensive, >40% of SBP and/or DBP \geq 120/80 mmHg but <95th percentile – as prehypertensive. BMI and daily dose of insulin (DDI) were calculated. Insulin resistance (M index) was estimated by using euglycemic-hyperinsulinemic clamp. Power spectral analysis of heart rate variation was performed.

Results: None of the study patients had hypertension. In 30 individuals (36.6%) prehypertension was diagnosed. In the table we compared selected risk factors of the patients with normal and elevated BP. Normal blood pressure Prehypertension p Age (years) 16.1 ± 0.24 17.2 ± 0.33 0.013 Duration of diabetes (years) 5.2 ± 0.5 6.4 ± 0.7 0.19 BMI (SDS) 0.48 ± 0.14 0.68 ± 0.19 0.40 DDI (U/kg) 0.80 ± 0.03 0.87 ± 0.04 0.2 HbA_{1c} (%) 7.9 ± 0.20 7.4 ± 0.26 0.14 HDL-cholesterol (mg/dl) 58 ± 2 55 ± 3 0.30 M index (mg/kg/min) 6.68 ± 0.41 6.35 ± 0.5 0.63 LF/HF ratio 0.77 ± 0.05 1.03 ± 0.07 0.005

Conclusion: Prehypertension is common in T1DM children and adolescents. The prevalence of prehypertension is connected with the shift of the sympathovagal balance toward sympathetic activation.

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SP-22

High prevalence of cardiovascular risk factors, as defined by ADA in 2005, in Norwegian children and adolescents with type-1 diabetes

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Introduction: The risk of dying of CVD before the age of 40 is 20 fold increased in patients with type-1 diabetes compared to non-diabetics.

Aim: To evaluate the CVD risk factors in Norwegian children and adolescents with type-1 diabetes according to the new ADA definitions [Diabetes Care 28 (suppl 1): 21–24].

Methodology: CVD risk factors were examined in a national prospective quality study. All diabetic children in Norway are treated at the pediatric clinics of the government hospitals. In 2004, 23 clinics (of 25) participated with 1417 patients.

Results: The HbA_{1c} was >7.5% in 64% of the patients. The LDL-cholesterol was >2.6 mmol/l in 42% and the HDL-cholesterol was <1.1 mmol/l in 5%. 3% reported smoking (8.8% of those \geq 15 years). The blood pressure (systolic and/or diastolic) was above the 90th percentile by age, gender and height in 7% and above the 95th percentile in 3%. 1% of the patients had persistent microalbuminuria. 0.2% of the patients got statin treatment and 0.3% anti-hypertensive treatment. About 55% reported watching TV more than 2 hours each day. Obesity was present in 4.4% of the patients. 29% had a positive family history (1. and 2. degree relatives) of one or more of the following: type-2 diabetes, heart attack and/or stroke before the age of 60. Dietary habits were evaluated in a group of 9–10 and 12–13 year old. Dietary fat was >30% of caloric intake in 82% and 85%, saturated fat >10% in 94% and 97% and fiber intake <25 g/daily in 94% and 92%, respectively.

Conclusion: Approximately 90% of the Norwegian pediatric type-1 diabetic patients had at least one of these CVD risk factors. Sys-

tematic screening is important and feasible. Early intervention should be considered in all patients at risk. So far few patients are treated with statins and anti-hypertensive drugs.

SP-23

Retinopathy in young adults with type 1 childhood-onset diabetes. A Spanish multicenter study

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Introduction: Diabetic retinopathy (DR) is the most frequent and an early-onset microvascular complication in type 1 diabetes. It is the main cause of blindness in western countries. Its detection using sensitive methods is relatively easy and it can be reversible in early phases. Quality of metabolic control and puberty have a great influence in DR appearance and progression (DCCT).

Objectives: To estimate DR prevalence in diabetic young adults whose evolution is controlled in 10 Spanish Pediatric Diabetic Units. Inclusion criteria comprised to have patients' recent data of their medical records (from our pediatric or adult units). To analyze metabolic control influence (HbA_{1c}) during puberty as well as evolution time until DR appearance.

Subjects and methods: A total of 474 diabetic young adults (218 males /256 females) with an average age of 22.3 ± 4.6 years; age at onset 9.3 ± 3.9 years and a mean follow-up of 13 ± 5.6 years were included in the study. Patients had to have regular ophthalmological examinations: funduscopy (83%), retinography (11%) and/or angiography (6%) with at least one exploration available in the last year. DR classification according to the ISPAD Consensus Guidelines (2000) was used in this study. Puberty HbA_{1c} values are expressed in mean SDS. Student t-test and logistic regression (OR) statistical analysis were performed.

Results: We have observed DR in 54 (11.4%) patients. Forty-six patients (85%), in an early stage and with a mean evolution time of 14 ± 42.3 years (10–17 years range). Patients who have DR, had a significant worse metabolic control (HbA_{1c} SDS: $+10.25 \pm 2.9$ vs $+7.05 \pm 2.76$; $p = 0.000$), with a clear influence of puberty (HbA_{1c} SDS: $+9.75 \pm 3.45$ vs $+7.07 \pm 3.36$; $p = 0.000$). There are no significant differences in prepubertal metabolic control (HbA_{1c} SDS: 7.35 ± 2.46 vs 6.39 ± 2.82 ; $p = 0.32$). Patients who have HbA_{1c} >9 SDS have 4.0 (OR) times more risk of suffering DR with 95% CI (2.23–7.24). Diabetes evolution time is significantly higher in patients with DR (17.9 vs. 12.1 years; $p = 0.000$).

Conclusions:

- We have found relatively low retinopathy prevalence in our population, clearly lower than in former studies of our own group, as well as in other experiences recently published.
- Poor metabolic control during puberty and disease evolution time are relevant factors in DR appearance. Thus, trying to reach the best possible metabolic control at this age in our patients has to be one of the main objectives of pediatric diabetologists.
- It is necessary to unify systematic ophthalmological examinations and HbA_{1c} laboratory technique validation in future studies to know the real prevalence of this complication and to assess its evolution in the future years.

SP-24

Risk factors analysis of diabetic polyneuropathy in children above 10 years of age

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Introduction: Pathogenesis of diabetic neuropathy is multifactorial, but the prevailing theory implicates persistent hyperglycemia as the primary factor.

Aim: The aim of the study was to establish the influence different factors have on risk of diabetic polyneuropathy development in children with type 1 diabetes.

Methodology: 97 children with type 1 diabetes (55 girls, 42 boys, mean age 15.4 ± 2.16 years, mean duration of diabetes 8.11 ± 2.9 years, mean age in onset 7.16 ± 2.96 years, mean HbA1c $8.58 \pm 1.06\%$) at least 10 years old and with at least 3 years duration of diabetes, were included in the study. Nerve conduction studies of the median, ulnar, tibial and peroneal motor nerves, and median, ulnar and sural sensory nerves were performed with standard surface stimulating and recording techniques. The sensory and motor amplitude, velocity and latency were detected. 24 children were diagnosed with diabetic polyneuropathy defined as impaired at least two parameters of conduction tests in at least two peripheral nerves (16 children with subclinical diabetic polyneuropathy, and 8 children with diabetic polyneuropathy with clinical signs). Influence of age, mean (for whole diabetes duration) and actual HbA1c, duration of diabetes, age at onset of diabetes, height, mean and actual BMI, treatment method (conventional, intensive, continuous subcutaneous insulin infusion), and hypoglycemic episodes in history. A model of logistic regression analysis was performed.

Results: The logistic regression analysis revealed that the statistical significant factors were mean HbA1c, duration of diabetes, height, hypoglycemic episodes in history and mean BMI [$\text{Chi}^2(5) = 23.12$]. In the population studied, the mean duration of diabetes (OR 1.36, $p < 0.005$, $\pm 95\% \text{CI } 1096\text{--}1697$), mean HbA1c (OR 1.91, $p < 0.05$, $\pm 95\% \text{CI } 1072\text{--}3411$), hypoglycemic episodes in history (OR 2.11, $p < 0.05$, $\pm 95\% \text{CI } 1005\text{--}4433$) were the most significant risk factors. In this population of children the height was statistically significant but seemed to be a factor of low impact (OR 1.06, $p < 0.05$, $\pm 95\% \text{CI } 1003\text{--}1123$).

Conclusion: Long-term metabolic control, duration of diabetes and hypoglycemic episodes in diabetes history were the strongest risk factors for developing polyneuropathy. The influence of hypoglycemic episodes on peripheral nerves function is very interesting and needs to be studied more.

SP-25

Prevalence of diabetic polyneuropathy in children with type 1 diabetes

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Introduction: Neuropathy is a common and serious late complication of diabetes mellitus in adults, but its prevalence in children is unknown.

Aim: The aim of this study was to establish the prevalence of clinical and subclinical polyneuropathy in children with type 1 diabetes, and identify the independent risk factors in the development of this complication.

Methodology: 97 children with type 1 diabetes (55 girls, 42 boys, mean age 15.4 ± 2.16 years, mean duration of diabetes 8.11 ± 2.9 years, mean age in onset 7.16 ± 2.96 years, mean HbA1c $8.58 \pm 1.06\%$) at least 10 years old and with at least 3 years duration of diabetes, were included in the study. Nerve conduction studies of the median, ulnar, tibial and peroneal motor nerves, and median, ulnar and sural sensory nerves were performed with standard surface stimulating and recording techniques. The motor and sensory amplitude, velocity, and latency were detected.

Results: Clinical signs were detected in 24 (25.5%) diabetic children (in 9, abnormality in sensory thresholds, in 13, reduced reflexes of

legs, in two subject reduced reflexes in legs and arms). Eight (8.2%) patients had diabetic polyneuropathy defined as abnormalities in nerve conduction tests in at least two nerves and clinical signs or symptoms. 16 (16.5%) patients had subclinical polyneuropathy defined as abnormalities in at least two nerves without signs or symptoms. Abnormalities in conduction tests in 27.8% of diabetic children in peroneal nerves, 22.7% in sural, 17.5% in sensory ulnar, 14.4% in median motor, 7.2% in ulnar motor, 6.2% in median sensory and 5.1% in tibial nerves were detected.

Conclusion: The study revealed clinical signs in a quarter of the studied population of diabetic children. The diabetic polyneuropathy was diagnosed in a quarter of the studied population. The percentage of sensory nerve abnormalities did not differ from motor nerves. The impairments in sural and peroneal nerves in legs were the most frequent. Poor metabolic control and duration of diabetes were significantly different in diabetic children with and without polyneuropathy.

SP-26

Subclinical hearing deficits in children and adolescents with type 1 diabetes

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Introduction: Hearing disturbances are one of the latest complications of type 1 diabetes, but electrophysiological methods gave the opportunity to detect subclinical defects early.

Aim: The aim of the study was to detect the early impairments of hearing, and to establish the risk factors of this dysfunction.

Methodology: 87 children with type 1 diabetes (mean age 15.46 ± 2.17 SD years, mean duration of diabetes 8.14 ± 2.75 SD years) at least 10 years old and with at least 3 years duration of diabetes, were included in the study. The following were done in the course of the study: otorhinolaryngologic examination, tonal, impedance, and verbal audiometry, auditory brainstem responses (ABR), DPOAE. In ABR latency of wave I, III, V, and intervals I-III, III-V and I-V were analyzed.

Results: In the studied population, abnormalities in ABR in 34.9% were detected. The results of ABR were not related with age, age at onset, mean and actual HbA1c. Wave latencies in ABR were significantly correlated with duration of diabetes (wave I latency $p < 0.01$, wave III latency $p < 0.005$, wave V latency $p < 0.05$). Significant differences between subgroups of different treatment methods in interpeak latency III-V ($p < 0.05$) were detected. More intensive method of treatment had a positive influence on the decrease in latencies of evoked potentials. When analyzing the presently used method of treatment, significant differences in interpeak latencies I-III and III-V between the subgroups were observed.

Conclusion: Abnormalities in ABR were diagnosed in over one third of the studied population. The increase of ABR latency depends on longer duration of diabetes. The study revealed that auditory evoked potentials in the subgroups that were treated with more functional methods (intensive, and CSII) had a more normal shape than those in the subgroups treated with conventional and multiple injection, even though there weren't any differences in metabolic control between the subgroups. The authors consider it a favorable result of the applied method.

SP-27

Prevalence of type 2 diabetes and MODY in children and adolescents. A state-wide study in Baden-Wuerttemberg (Germany)

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Short Poster Presentations

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Introduction: In contrast to North America, Japan and few European countries, prevalence data for childhood type 2 diabetes and maturity onset diabetes of the young (MODY) have not been available for Germany up to now.

Aim: To estimate the prevalence of childhood type 2 diabetes and MODY for the age group 0–20 years in Baden-Wuerttemberg (BW) (Germany).

Methodology: In 2004, we conducted a state-wide survey of all children's hospitals in BW (n = 32), all diabetologists (n = 122) and all departments of internal medicine (n = 164). In addition, in the district of Tuebingen, all family doctors (n = 121) were included in the inquiry.

Results: 530 institutions were surveyed, responses of 445 were suitable for analysis. Our findings showed that in 11.0% (49/445) of all institutions, patients aged 0–20 years are treated for type 2 diabetes or MODY. 55 patients with type 2 diabetes (mean age 15.8 years) and 57 patients with MODY (mean age 14.0 years) were registered. Most of these patients (56/112) were treated in pediatric departments or by diabetologists in private consultancies. In the data from the district which we used as a random sample, we found that none of the type 2 patients in this age group had been treated by any of the 121 general practitioners; and only 1 patient with MODY had been treated in a private practice. Prevalence of type 2 diabetes was calculated as being 2.36/100 000; and the prevalence of MODY was calculated as 2.45/100 000, respectively, for the studied age group.

Conclusion: The calculated prevalence figures indicate the lower limit for the prevalence of type 2 diabetes and MODY in childhood and adolescence. At present the frequency of these diabetes types is lower than in North America, they are, however, more frequent than in other European countries. This epidemiological study is the first population-based survey for type 2 diabetes and MODY in Germany.

SP-28

Metabolic remodeling in pre-pubertal children – testing the lipid flux hypothesis

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Introduction: The behavior of insulin resistance (IR) and its metabolic correlates in response to changes in body fat has not been well characterised in children. Frayn's lipid flux hypothesis proposes that adipose tissue buffers the flux of fatty acids in circulation by 'trapping' them, thus increasing triglyceride clearance.

Aim: To test this hypothesis by examining trends in adiposity, IR and metabolic risk in healthy pre-pubertal children.

Methodology: EarlyBird is a prospective, non-intervention cohort study documenting physical, metabolic and lifestyle development of 300 children from school entry at 5 yrs. Data were obtained from 230 children (130 boys, 100 girls) who attended at 5, 6, 7 and 8 yrs. Measures included adiposity (sum of skinfolds), IR (HOMA-IR), triglycerides, HDL cholesterol (HDL-C), beta-cell function (HOMA-beta).

Results: In both genders, adiposity rose progressively and significantly from 5–8 yr (+18%, p < 0.001), while IR unexpectedly fell (–24%, p < 0.05). Consistent with falling IR, HDL-C rose (+17%, p < 0.001) and triglycerides fell (–8%, ns). Fasting glucose rose (+12% or 0.5 mmol, p < 0.001), while HOMA-beta fell (–35%, p < 0.001).

Conclusion: Weight gain is normally associated with rising IR – but only when existing adipocytes are further filled, losing their buffering capacity. Frayn's lipid flux hypothesis, on the other hand, envisages that if the increase in adiposity is due to new adipose cells,

triglyceride buffering capacity will paradoxically increase, with falling rather than rising IR. The rise in adiposity, fall in IR and rise in HDL-C reported here are consistent with the hypothesis. The rise in glucose was unexpected, and possibly related to an independent loss of beta cells. These observations are novel, represent substantial metabolic remodeling in pre-pubertal children, and need explanation to establish whether they are physiological and programmed, or pathological and ultimately harmful. They should also be taken into account when interpreting the response to childhood interventions designed to reduce IR.

SP-29

Pediatric prevention of metabolic syndrome and type 2 diabetes in obese children and adolescents – when to start?

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Introduction: The risk of type 2 diabetes mellitus is correlated with BMI positively. There are natural steps in progress of obesity in young patients: a) overweight, b) simple obesity, c) obesity with insulin resistance, d) with insulin resistance and impaired glucose tolerance, e) metabolic syndrome, f) type 2 diabetes.

Aim: 1) To evaluate the prevalence of metabolic syndrome and diabetes type 2 in obese children. 2) To compare the stage of obesity and the insulin secretion in relation to age, gender and sexual maturation.

Methodology: Study comprises 140 obese, 12 overweight and 14 nonobese children, aged 4 to 18 years. BMI-SD and Tanner stage were estimated in all patients. OGTT, insulin measures, HOMA-IR and QUICKI indexes were performed. Triglycerides, cholesterol and blood pressure results were adjusted for age and sex. ANOVA test and Pearson's correlations were applied in statistics.

Results: Fasting glycemia was found as dependent on age (p < 0.02) and Tanner's stages (p < 0.013), without gender and obesity influence. Fasting insulinemia depended on age (p < 0.004), puberty (p < 0.009) and on the progress of obesity (p < 0.006) but not on sex. HOMA-IR and QUICKI were depending on age (p < 0.002, p < 0.001), puberty (p < 0.009, p < 0.001) and on the stage of obesity (p < 0.009, p < 0.001) respectively. BMI-SD correlated positively with fasting insulinemia (p < 0.006), glycemia after 2 hours of OGTT (p < 0.02), triglycerides (p < 0.018), systolic (p < 0.001) and diastolic (p < 0.003) blood pressure. 13.2% of patients had impaired glucose tolerance and 1.3% – diabetes type 2. The prevalence of the metabolic syndrome was 31% in obese subjects.

Conclusion: The prevalence of disorders in glucose metabolism, insulin secretion and metabolic syndrome is high among obese children and it increases in parallel to obesity. Biomarkers of an increased risk of metabolic complications are already present in the youngest patients. It suggests, that prophylactic intervention against type 2 diabetes should be started at the earliest stage of obesity and prior to sexual maturation.

SP-30

Commencement of gluten-free diet in children with type 1 diabetes mellitus and celiac disease increases body mass index and insulin requirement

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Introduction: The incidence of celiac disease (CD) is increased in children with type 1 diabetes Mellitus (T1DM). However, the benefit of a gluten-free diet (GFD) remains unclear.

Aim: To assess effects of GFD on growth, body mass index (BMI), glycemic control and insulin requirement in children with T1DM and CD.

Methodology: Retrospective study of the effect of GFD on height SDS, BMI SDS, mean HbA1c, mean insulin requirement and dietetic input was performed in children with T1DM and CD diagnosed following screening and intestinal biopsy.

Results: 350 children with T1DM were screened for CD. Twelve (3.4%, 5M) were diagnosed with CD and commenced on GFD within 4 weeks of diagnosis. We report data from 11 patients, 44.1 ± 12.3 weeks following introduction of GFD. Mean age of diagnosis of T1DM was 5.5 ± 4.5 years and for CD 10.7 ± 3.3 years. BMI SDS, insulin requirement and dietetic input were increased significantly after introduction of GFD but there was no change in height SDS or mean HbA1c.

Table 1. Characteristics of patients before and after introduction of GFD

	Before GFD	After GFD	Mean difference	95% Confidence interval	P-value
Height SDS	0.14 ± 0.90	0.14 ± 1.10	0.00 ± 0.43	(-0.30, 0.31)	0.98
BMI SDS	0.31 ± 0.68	0.82 ± 0.73	0.54 ± 0.68	(0.05, 1.03)	0.03*
HbA1c (%)	9.30 ± 1.01	9.26 ± 1.08	-0.04 ± 0.68	(-0.50, 0.42)	0.86
Insulin Requirement (units/kg/day)	1.05 ± 0.33	1.20 ± 0.34	0.15 ± 0.11	(0.07, 0.22)	0.001*
Dietetic reviews	1.25 ± 0.71	3.75 ± 1.39	2.50 ± 0.93	(1.73, 3.27)	<0.0001*

Conclusion: Our data do not demonstrate any short term clinical benefits of GFD. GFD may improve carbohydrate absorption resulting in increased BMI and insulin requirement.

SP-31

Beneficial long-term effects of motivational interviewing (MI) in adolescents with insulin dependent diabetes mellitus: a multicenter randomised controlled trial

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Introduction: MI is a counseling approach promoting behavior change. We have previously shown a non-significant ($p = 0.09$) trend to improvements in HbA1c after a one-year MI intervention with adolescents.

Aims: To evaluate the effect of MI on psychosocial variables at the end of the 12-month intervention and the long-term effects on HbA1c one year after the intervention was completed.

Method: We recruited 70 teenagers (mean age 15.3 years) to an RCT of an MI intervention versus counseling support. HbA1c and a range of psychosocial variables were measured at baseline, at the end of the one-year intervention and one year later.

Results: There were no demographic differences between the two groups at baseline. At 12 months the MI group had improved quality of life, lowered anxiety, more positive well being, placed higher importance in controlling their diabetes and had a more positive belief system that their actions would prevent complications (all $p < 0.01$). After 24 months there was a significant difference in HbA1c between the two groups over time, after adjusting for baseline ($F = 9.707$, $p = 0.003$).

Conclusion: MI produces a significant improvement in HbA1c one year after the end of the intervention. This was preceded by positive changes in quality of life, well-being and personal models of diabetes at the end of the intervention. The potential of MI as an effective and deliverable intervention in improving outcomes is promising.

SP-32

Mummy I feel invisible: living with a brother or sister who has diabetes

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Introduction: A diagnosis of Diabetes affects all family members, yet most attention has been given to the child with Diabetes. In contrast there has been very little research focusing on siblings. Siblings have very real concerns about their brother or sister with diabetes, often different concerns from their parents. This qualitative study represents an attempt to achieve a broad perspective and understanding of effects on the well child and family relations by conducting in-depth interviews with siblings and their parents.

Methodology: Qualitative data was collected to determine the impact for children when a sibling has been diagnosed with Diabetes. A semi structured interview guide was used to assist with data collection. A sample of 32 participants, including children and their parents were interviewed. This allowed for multiple data sources to be incorporated into the study design. The Non-Numerical Unstructured Data Indexing Searching And Theorising (NUDIST) program successfully facilitated data analysis.

Results: Earlier researchers relied on anecdotal reports, case studies and retrospective designs. In this study the qualitative data allowed the researchers to gain first hand knowledge regarding the actions and reactions of children to their siblings with Diabetes in the context of their daily lives. Findings suggest that children can have either enhanced or strained experiences from living with a sibling who has Diabetes. The in-depth interviews show well children can experience stress and a sense of being forgotten in comparison to their sibling with Diabetes. In contrast the study also uncovered that many children experience closeness, maturity and improved health.

Conclusion: The research findings have implications for how brothers and sisters are educated and strongly indicate the need for including all family members from the point of diagnosis.

SP-33

Art therapy groups for children with diabetes and their parents

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Introduction: Art Therapy is a therapeutic method which aids in connecting the child to his inner world through artistic creation. Through their drawings children can non-verbally express and work through emotionally problematic topics

Aim: 1. To renew the children's sense of control over their lives and to better process the emotions that the illness evokes. 2. To improve parents' quality of life by allowing them to express their feelings verbally and artistically in group sessions.

Methodology: 12 two-hour meetings, two groups, 4-6 participants in each group. A parents' group took place separately at the same time. Diabetes Quality of Life questionnaires were given to children and parents at beginning and end of complete sessions. Qualitative analysis was done of the children's artistic creations.

Results: The children's creative products revealed the 'emotional inner world' regarding daily handling of routine diabetes care, and provide an opportunity to vent these emotions. The simultaneous group sessions enabled a better understanding of each family's dynamics. Parents' Diabetes Quality of Life questionnaires revealed statistically significant areas: improved happiness quotient ($p = 0.01$); less frustration and restlessness ($p = 0.03$); more positive daily life experiences ($p = 0.01$) post group sessions.

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Conclusion: Art Therapy groups enable children with diabetes and their parents to express their inner feelings through non-verbal media in a secure and empathetic environment. The group process enables them to develop a more in-depth understanding of positive coping methods, and gives them a renewed sense of control over their lives. Enabling parents to meet and share their feelings and fears has been proven as being a contributing factor to the improved quality of their own lives. These groups are recommended as an integral part of care in childhood diabetes centers.

SP-34

Psychological reactions to type 1 diabetes in children

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Introduction: The incidence of type 1 diabetes is increasing in Kuwait. Treatment of the disease puts an enormous burden on both the child and his family and may put them at increased risk for psychological difficulties. Therefore it is important to deal with the effect of the disease on family function and the child's psychological well being.

Aim: To assess the psychological reactions to type 1 diabetes in children and the effect of metabolic control.

Methodology: Children (n = 240) with type 1 diabetes participated in the study. Trained psychologists interviewed the children and

their families in an out-patient setting, using a demographic questionnaire which included information about their disease as well. A behavioral check list for children and Arabic Childhood Depression Inventory (ACDI) were used. These are translated, validated and adopted for Kuwaiti culture.

Results: The mean age of the children was 9.1 years (SD 4.26), and their mean duration of diabetes was 7.4 years (SD 4.8). Sixty one reported mild depression. There was no sex difference, and no statistically significant relation to metabolic control ($p > 0.5$). Hyperactivity was found in 65.4% and was significantly increased in children with poor metabolic control ($p = 0.001$). Similar positive association was found with aggressive behavior ($p > 0.005$), concentration and attention ($p < 0.001$). Several somatic symptoms were reported; dizziness and abdominal pain were the commonest (62.1, 35.4% respectively). Duration of the disease was not associated with an increased risk for any abnormal reactions ($p > 0.05$).

Conclusion: This is the first study on the psychological consequences of diabetes in children in our community. High prevalence of depression, aggressive behavior, hyperactivity and poor attention were found. Poor metabolic control is associated as an increased risk for all, except depression. Further controlled studies are needed to confirm the direct effect of diabetes on these abnormalities.