R1

Increasing incidence of childhood type 1 diabetes mellitus in Romania

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Introduction: Romania is a country having a low/intermediate incidence of type 1 diabetes mellitus (T1DM) in children.
Aims: To assess the time trends in the incidence of childhood T1DM and to reveal some characteristics according to gender and ethnicity.
Methodology: Data were obtained from two sources: (i) Romanian Childhood Diabetes Registry, developed since 1995 by ONROCAD (Romanian acronym for 'Romanian National Organization for the Protection of Children and Adolescents with Diabetes') and (ii) Medical records from Clinical Center 'Cristian Serban' Buzias, where children with T1DM from Romania are treated.
Results: Table 1 presents the incidence of T1DM in children (0–14 years) from Romania, between 1996 and 2005. Several remarks can be made: (i) The general incidence increased with 61% between 1996 and 2005. A plateau was registered between years 2001 and 2004; (ii) The incidence was higher in girls between 1996 and 1999 and in boys thereafter and (iii) The incidence in Romanians was lower than in Hungarians, the only explanation being the genetic differences. Starting year 2002, data from age group 0–18 years were also collected. The same trends were noted.

	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
General*	3.91	4.02	4.10	4.97	5.05	5.66	4.88	5.47	5.36	6.30
G*	3.96	4.68	4.34	5.23	4.94	5.04	4.34	5.41	4.93	6.21
B*	3.88	3.39	3.72	4.56	5.15	6.15	5.34	5.52	5.78	6.39
R*	–	–	3.90	4.57	4.82	5.53	4.64	5.23	5.38	6.30
H*	–	–	7.02	8.98	7.88	7.19	5.91	11.63	9.77	8.84

* = no. of cases/100,000; G = girls; B = boys; R = Romanians; H = Hungariansa.

Conclusions: The incidence in T1DM in Romania showed an increasing trend over the past 10 years, being higher in girls in the first half of the decade and in boys thereafter. Children from the Hungarian minority are more frequently affected than those from the Romanian majority.

R2

Very early onset diabetes

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Background: Very early onset diabetes is an unfrequent entity. Some authors define neonatal diabetes as the hyperglycaemia that ocurrs in the first 30 days of life, while for others diagnosis is extended up to 3 months of life. Neonatal diabetes can be either permanent or transient.
Objectives: (i) To evaluate the proportion of very early onset-diabetes among diabetic patients in a Diabetes Paediatric Unit, their treatment and evolution and (ii) To describe their characteristics in terms of birth weight, gestacional age, age at onset in days, and affected first degree relatives.
Methods: All patients's clinical registries from 1/1/80 to 12/31/05 were analyzed. Children < 3 months with hyperglycaemia who received insulin treatment during at least 2 weeks were included. Birth weight, gestational age, age at onset in days, treatment, transient or permanent evolution and affected first degree relatives were collected.
Results: From 2062 children,15 patients with 3–90 days of age were included. Mean age was 37 days (IC 95% 20–54), and median age was 35 days. Male cases were the most (73.3%). Median gestacional age was 40 weeks, and only two cases were < 37 weeks. Median birth weight was 2462 g. (range 1650–3750). Low birth weight frequency was 53.3%. There were two cases in twins. Two children had infectious disease, and six (40%) an affected first degree relative with type 2 diabetes mellitus, and only two cases with type 1 diabetes mellitus. Ten children (66.7%) had permanent neonatal diabetes and only five (33.33%) were transient. Mean duration of insulin treatment was 115 days in transient form with a median of insulin treatment of 124 days.
Conclusions: Very early onset diabetes is a rare entity, with an observed proportion of 0.72% in our unit. All the children in the transient form had low birth weight. Two children (13.3%) were twins without affection of the sibling. One third of cases had a first degree relative with type 2 diabetes mellitus and 10% with type 1 diabetes mellitus. All the patients older than 36 days had permanent diabetes.

R3

Prevalence of the type 1 diabetes mellitus in children aged 0–14 years in the Republic Bashkortostan, Russia

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Introduction: In most world countries a rise of prevalence of the type 1 diabetes mellitus (DM) in children has been observed.
Aim: To evaluate prevalence of the type 1 diabetes mellitus in children aged 014 years in the Republic Bashkortostan, Russia, for 14 years (between 1992 and 2005).
Methodology: Data about all cases of the type 1 diabetes mellitus were recorded in the State Registry of diabetes mellitus. In this Registry, the following data were recorded for each case: patient's name, address, date of birth, date of first insulin injection, insulin dose, auxological characteristics, results of laboratory analyses, complications of the disease. The source of information about the diabetic children was data from Endocrinology Department of the Republican Children Clinical Hospital, from local practicing pediatricians, and from State Epidemiology Statistical institutions. Prevalence of the type 1 diabetes mellitus as well as 95% confidential interval (CI) were calculated per 100 000 children aged 0–14 years.
Results: Prevalence of the type 1 diabetes mellitus in 1992 amounted to 33.91 (CI 95% 30.41–37.71), in 1993–34.53 (31.00–38.36), in 1994–35.38 (31.79–39.27), in 1995–36.79 (33.11–40.77), in 1996–38.15 (34.38–42.21), in 1997–43.70 (39.66–48.04), in 1998–48.16 (43.83–52.80), in 1999–48.30 (43.90–53.02), in 2000–52.08 (47.42–57.07), in 2001–45.84 (41.39–50.64), in 2002–49.62 (44.88–54.72), in 2003–50.73 (45.85–55.99), in 2004–49.11 (44.20–54.41), in 2005–52.42 (47.24–58.02) per 100 000 children. For the last 3 years, prevalence of the type 1 diabetes mellitus in children has not changed. Prevalence of the type 1 diabetes mellitus rose with age. In 2005, it amounted to 14.33 in the 0–4-year old children, to 56.61 in the 5–9-year old children, and to 79.33 in the 10–14-year old children per 100 000 children of the corresponding age.
Conclusion: Prevalence of the type 1 diabetes mellitus in children in the Republic Bashkortostan, Russia, for 14 years rose 1.5 times (from 33.91 cases per 100 000 children in 1992 to 52.42 cases in 2005).

R4

Incidence of type 1 diabetes mellitus in children's population in Russian Federation during 2001–2004

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Introduction: The incidence of type 1 diabetes mellitus (DM1) annually increases in children's population in Russian Federation (RF). The territory of RF is large and subdivided into seven Federal districts (FD), located in various geographically-defined areas: Northwest, Central, Volga, Southern, Urals, Siberia, Far East.

Aims: To estimate the incidence of DM1 among the children's population of RF during 2001–2004 years.

Methodology: The information was received from national Register of DM and annual statistical reports from endocrinologists. The incidence was calculated on 100 000 the children's population. The confidential interval was 95%. The age standardized incidence was obtained using the direct method with a standard population consisting of equal members of children in each of three subgroups (0–4, 5–9, 10–14 years of age).

Results: During 2001–2004 years an average incidence of DM1 among children in RF was 9.9/100 000 (95% CI: 8.7–11.0), age standardized incidence was 9.8/100 000 (95% CI: 8.4–11.3). An incidence has been increased with age and was the greatest in 10–14 years age group (16.1/100 000). Significant distinctions in incidence were marked between FD. The highest incidence was constantly registered in Northwest district. It has reached 15.1/100 000 in 2004 year. Incidence rates were considerably below in Siberia and Far East districts: 7.5/100 000 and 5.8/100 000 accordingly. An incidence was similar to an average level in RF in Central, Volga and Urals districts. The annual incidence gain in Ural district was 45% in year. In South district an incidence was in the middle between incidence levels in Central and Siberia districts: 8.9/100 000.

Conclusion: In 2001–2004 years the average and standardized incidence of DM1 in children's population in RF were similar to most European countries. The decrease of incidence was observed in a direction from northwest on a southeast of RF.

R5

Postinitial remission in children with type 1 diabetes mellitus

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Introduction: Type 1 diabetes mellitus is characterized by post-initial remission (R), following the resistant phase after onset of the disease.

Aim: The aim of our study was to analyze demographic, metabolic and immunological factors determining the outcome and intensity of the remission phase.

Methodology: Follow up investigation of children diagnosed with T1DM at our department, between 1995 and 2004 was carried out. R was defined by stable metabolic state with insulin requirement ≤0.5 U/kg body weight.

Results: R has occurred in 92 patients out of 194 (47%). There was a significant ($p < 0.01$) correlation between R and HbA1c, C peptide and age at onset. Significant negative correlation ($p < 0.05$) was found between markers of autoimmunity (ICA and other auto-antigens) and duration of R. Blood glucose and acid base status at manifestation of D did not influence R.

Conclusions: According to our studies postinitial remission in children with T1DM is mainly determined by the duration and intensity of hyperglycaemic period before onset ('hyperglycaemic load') characterized by HbA1c at and C peptide (reflecting endogenous insulin reserve capacity) at onset.

R6

Changes in the epidemiology of childhood and adolescent diabetes in Singapore

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We report demographic and epidemiological data on 310 Singapore citizens and residents with Type 1 and Type 2 diabetes from the KKH Diabetes registry, which has grown from 80 to 365 patients since 1997. Patients were classified as T1DM or T2DM on the basis of positivity for GAD and ICA antibodies, c-peptide and insulin levels at diagnosis or at a later OGTT, and factors such as DKA at diagnosis, relevant family history and treatment modality (eg insulin or OHA).

Singapore Residents	Type 1 DM	Type 2 DM
Total Number	211	99
Age Range	0.75–16.5	8.2–17.5
Mean age at Diagnosis (SD)	7.9 (4.0)	13.0 (1.5)
Male:Female Ratio	1:1.30	1:1.25
Percentage presentng in DKA	53%	7%
Mean age at Diagnosis–DKA (SD)	8.1(4.1) years	13.0 (1.5) years
DKA +ve for GAD, ICA or both	72%	0%
NonDKA +ve for GAD, ICA or both	86%	0%
Family history of any DM:T1DM	51%:6%	75%:Nil

Distribution by Ethnic Group (%)	Chinese (%)	Malay (%)	Indian (%)	Other (%)
T1DM at KKH Registry	71.2	13.7	16.1	0.0
T2DM at KKH Registry	64.6	22.2	13.1	0.0
Singapore populaton	75.2	13.2	9.3	2.3

Almost half (45%) the T2DM patients needed insulin alone (12%) or in combination with oral agents (33%) and 46% were on metformin alone (46%) or metformin + other oral agent (4%), while a few T1DM also improved when metformin was added. A child aged 10–13 years not in DKA at first presentation of diabetes is 2.7 times (73% have T2DM vs. 27% with T1DM) more likely to have T2DM but careful and extended evaluation may be needed for the correct diagnosis and management. We report demographic and epidemiological data on 310 Singapore citizens and residents with Type 1 and Type 2 diabetes from the KKH Diabetes registry, which has grown from 80 to 365 patients since 1997. Patients were classified as T1DM or T2DM on the basis of positivity for GAD and ICA antibodies, c-peptide and insulin levels at diagnosis or at a later OGTT, and factors such as DKA at diagnosis, relevant family history and treatment modality (eg insulin or OHA). In some instances, classification was clarified only 1 year after initial presentation.

Almost half (45%) the T2DM patients needed insulin alone (12%) or in combination with oral agents (33%) and 46% were on metformin alone (46%) or metformin + other oral agent (4%), while a few T1DM also improved when metformin was added. Childhood diabetes in Singapore needs careful and extended evaluation for the correct diagnosis and treatment.

R7

Ketosis at first presentation of type 2 diabetes mellitus (T2DM)

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Background: Prevalence of Type 2 diabetes mellitus (T2DM) in childhood is increasing worldwide and children in developing countries are no exception. It is believed that ketosis/ketoacidosis at first presentation is rare.

Aim: To study the prevalence of ketosis/DKA and clinical profile of patients with T2DM at presentation.

Method: Children aged < 15 years with T2DM diagnosed at University Malaya Medical Centre (UMMC) from January 2001 to December 2005 were included. Diabetes was defined as random blood sugar (RBS) > 11.0 mmol/l and fasting blood sugar (FBS) > 7.0 mmol/l on two occasions. Diabetic ketoacidosis (DKA) is defined as heavy glycosuria (55 mmol/l), ketonuria, hyperglycaemia (blood glucose > 11 mmo/l), acidosis (pH < 7.3 and/or bicarbonate < 15 mmol/l) and dehydration (> 5% body weight) while ketosis as presence of ketonuria or ketonaemia without metabolic acidosis. Their demographic characteristics, laboratory results and treatment protocol were recorded and analysed.

Results: There were twenty-five patients with the diagnosis of T2DM, nine (36%) of whom had ketosis at presentation. They were four Chinese, three Indians and two Malays. Their mean age at diagnosis was 10.8 ± 1.9 years (range 7.9–13.2 years), male to female ratio was 7:2, mean BMI was 24.7 ± 4.9 kg/m^2. All had classical diabetic symptoms for 4.5 ± 2.7 weeks. Four of nine (44%) patients had acanthosis nigricans. Mean HbA1c at diagnosis was 13.0% ± 2.6%. Mean BG was 25.5 ± 7.6 mmol/l, serum osmolarity 308 ± 3.4 mosmol/kg and C-peptide 2.8 ± 0.8. All required insulin at presentation with two who had DKA needing insulin infusion. Patients presented with ketosis had a significantly longer duration of symptoms and higher HbA1c compared to those without ketosis.

Conclusion: Ketosis at initial presentation is not uncommon in T2DM. It is usually associated with a longer duration of classical symptoms and higher HbA1c at diagnosis.

R8

Type 2 diabetes in a tertiary center

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Objective: To investigate the prevalence, clinical and biochemical characteristics of type 2 diabetes in the national center for childhood diabetes.

Methods: The medical records of children and adolescents diagnosed with type 2 diabetes were reviewed for demographic characteristics, presence of concomitant illnesses, clinical and biochemical changes at onset of diabetes, mode of treatment and the clinical course.

Results: A total of 30 patients were categorized with type 2 diabetes. From 1996 to 2005, the proportion of diabetic children diagnosed with type 2 diabetes increased from 0.1% to 3%. The prevalence rate of type 2 diabetes among newly diagnosed children and adolescents was 2.7% in 2000, 1.2% in 2001, 3.8% in 2002, 4.4% in 2003, 4.4% in 2004 and 3.8% in 2005. Age at diagnosis was 15.2 ± 3.24 years (ranged 8.8–22 years), 2/30 (7%) of patients were prepubertal. The female/male ratio was 3:2. A first-degree relative with type 2 diabetes was identified for 73% of patients, 90% had family history of type 2 diabetes. There was no predominant ethnicity group. At presentation only 4/30 patients had ketosis and two presented with diabetes ketoacidosis. All were beta cell antibody negative with elevated c-peptide (775–2300 pmol/l). Mean HbA1c was 8.5 mg% (range: 5.9–12.9) at presentation. BMI was 31.2 ± 5.08 kg/m^2 (median 30.2), (range: 17.4–42). The current therapies consist of diet and exercise (27%), oral hypoglycemic (50%) and insulin (23%).

Conclusion: There is an increasing incidence of type 2 diabetes among children and adolescents referred to the national center for childhood diabetes. Affected children are usually overweight or obese, often female, pubertal, and have a family history of type 2 diabetes. The diagnosis is aided by demonstration of insulin resistance, and may include measurement of fasting C-peptide, and absence of ketones and autoantibodies against beta-cell components.

R9

Diabetes after diarrhea-associated hemolytic uremic syndrome

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We report a 12 year old boy who developed diabetes while he was treated with betamethason 2 mg for 5 days for a sinusitis. His glycemia was 1500 mg/dl, his blood pH was 7.33. He was treated with insulin intravenously and the corticosteroids were ceased. After normalization of the glycemia the boy was started on a basal-bolus regimen with insulin aspart and insulin glargine. Twenty months later he still requires insulin (0.5 U/kg/day) and has a HbA1c of 6.8%. This boy was hospitalized with severe D + HUS when he was 6 years old. During his stay on the intensive care unit he developed hyperglycemia and was treated with insulin during 21 days. To differentiate between type 1 diabetes, glucocorticoid-induced diabetes and postHUS diabetes some additional bloodtests were done. Pancreatic autoantibodies, including islet cell, insulin, GAD65, and IA-2 antibodies were all negative. Insulin was 4 mU/l for a glycemia of 1453 mg/dl. Diabetes can develop during diarrhea-associated hemolytic uremic syndrome and can redevelop after initial apparent recovery. In the literature two cases who redeveloped diabetes 3 and 60 months after initial recovery are described. Our case is the third one with a relapse of diabetes after a long period of 82 months. In conclusion, survivors of D + HUS should have aggressive surveillance and treatment of hyperglycemia, not only in the acute phase but also in the long run.

R10

Psychological stress as a factor possibly contributing to the pathogenesis of type 1 diabetes mellitus

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Diabetes Mellitus type 1 (DM1) is an autoimmune disorder caused by genetic and environmental factors. The aim of this study was to assess the role of stress as an environmental factor that could be associated with the expression of DM1. The study group included 155 diabetic children and 153 controls, matched for age at diagnosis of DM1 (9.6 ± 3.2 years vs. 9.6 ± 3.4 years, respectively) and gender. The parents of the diabetics and the controls completed a questionnaire on family history of DM1, surgical operations and problems at school and home prior to DM1 presentation. Diabetic families mostly belonged to the lower social classes (44.8%), in comparison with the controls (36.4%) ($x^2 = 18.45$, $p = 0.001$). Severe life events (parental or grandparental death, divorce) and problems at home and school (poor school performance, less behavioral problems) were more frequently observed in the diabetic group, prior to DM1 presentation, than in the controls. The problems in the diabetic group were more frequent among children of the lower social classes in comparison with the controls and mostly occurred during the 2 years prior to DM1 presentation (grandparental death: diabetics: 61.5% vs. controls: 23.5%, $x^2 = 4.4$, $p = 0.035$). Moreover a higher percentage of diabetic children were operated during the 2 years prior to the diagnosis of DM1, in comparison with the controls (diabetics: 33.3% vs. controls: 5.9%, $x^2 = 22.1$, $p < 0.001$). A stepwise logistic regression analysis indicated that in the diabetic group, paternal loss (OR:1453.5, 95% CI = 0.0–2.68 (10^{16}), physical abuse by the parents (OR:9.7, 95% CI = 1.9–48.3) and quarrels among siblings (OR = 3.82, 95% CI = 1.0–1.19) were the factors potentially influencing the expression of DM1. Among the protective factors of DM1 presentation was higher parental education (OR = 6.68). In conclusion, an increased frequency of stressful events or situations was found in the lives of diabetic children prior to DM1 presentation and mostly in those of the lower social classes, in comparison with the controls. The above problems might induce chronic or acute stress to diabetic children, affecting immune response and possibly contributing to DM1 pathogenesis.

R11

Children diagnosed with diabetes between the ages of 2 months and 2 years have unique clinical characteristics

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Objective: To investigate the clinical and biochemical characteristics of children diagnosed with diabetes before age 2 years.

Methods: The medical records of 49 children diagnosed with diabetes aged 2 months to 2 years were reviewed for gender, ethnicity, family history, clinical signs at presentation, diabetic ketoacidosis, concomitant illnesses, HbA1c level, insulin dosage, and remissions. Findings were compared with those of 60 other diabetic patients diagnosed during the prepubertal or pubertal period.

Results: Children diagnosed at an early age had more symptoms of apathy, restlessness, failure to thrive, and hyperglyceamia during acute illness, and a lower rate of remissions, than the older group ($p < 0.001$). In addition, children diagnosed at 6–24 months of age had significantly more episodes of diabetic ketoacidosis at presentation (83%) than both children aged 2–6 months (29%) and the older group (40%) ($p < 0.001$). Infants aged 6–24 months had a higher rate of celiac disease than the older group (12% vs. 3%, $p = 0.046$). There were no between-group differences in the rate of other autoimmune diseases or family history of type 1 and 2 diabetes.

Conclusions: We have found that patients with diabetes presented before the age of 6 months have unique clinical characteristics which are associated with fewer metabolic derangements than diabetes diagnosed later. We have also shown a high rate of celiac disease in patients with diabetes diagnosed at the age of 6–24 months. Our findings suggest that diabetes presented before age 2 years might have a different clinical pattern. Understanding the nature and course of diabetes in this age group is a crucial step in any planning of an interventional program of therapy or prevention.

R12

Type 1 diabetes mellitus prediction in the families of diabetes patients

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Introduction: The risk of type 1 diabetes mellitus (T1DM) development is determined by specific HLA-haplotypes presence, titers, frequency of specific autoantibodies (AA) to ß-cells, and insulin secretion impairment extent.

Aim: Prediction of early preclinical stage of T1DM.

Methodology: Predisposing and protective haplotypes (HLA-DRB1, genes DQ) together with immunological markers (ICA, GADA, IAA) have been studied in 148 discordant families, in normal sibs. Groups with different genetic risk of T1DM, development have been recognized.

Results: Among all the persons studied high risk DQ2/DQ8 (DQA1*0501–DQB1*0201\DQA1*0301–DQB1*0302) genotype was detected in 13% sibs of patients with T1DM. Moderate risk genotypes (DQ2/not DQ8 and DQ8/not DQ2) were revealed in 50.3% of subjects studied. It is worth nothing that in the high risk group one autoantibody type occurs rarely than in the moderate risk group (14.3% vs. 25.9%, respectively, $p = 0.2$), and consequently for multiple AA it is higher (33.3% vs. 9.9%, $p < 0.05$; 4.8% vs. 2.5% respectively, $p > 0.5$). In addition, it was revealed that GADA have been identified significantly more frequently in the group having DQ2/DQ8 genotype comparing with the group having genotype DQ2/not DQ8 and DQ8/not DQ2 (52.4% vs. 23.5%, respectively, $p < 0.02$). No significant differences have been observed in ICA and IAA prevalence in these groups (28.6% vs. 25.9%; 14.3% vs. 11.1%, respectively, p = NS). Besides it, was shown that haplotype DQ8 was determined significantly more frequently in GADA-positive sibs in comparison with GADA-negative ones (51.3% vs. 29.4%, respectively, $p < 0.05$). Haplotype DQ2 was observed in them in 35.9% vs. 29.4% of cases, respectively ($p < 0.2$). No significant differences in haplotypes have obtained in IAA-and/or ICA-positive subjects comparing with AA-negative ones studied.

Conclusion: The relationship of GADA with high genetic risk of T1DM suggests the important role of these immunological markers in insulitis preclinical diagnosis. Further prospective observations are under way.

R13

Autoimmune pathology associated with type 1 diabetes mellitus in the child

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Introduction: The frequent association between type1 diabetes mellitus (type1 DM) and other immune diseases is an argument for the autoimmune determinism of type 1 DM.
Aim: The study of the immune pathology encountered in type 1 DM children followed-up in our clinic, between 1995–2004.
Material and method: We studied 75 cases (45F, 30M) aged $1^{9}/_{12}$–$17^{9}/_{12}$ years and a duration DM evolution within 1 day and $15^{4}/_{12}$ years. Patients were evaluated completely clinical, biological including also thyroid hormones quarterly and antithyroperoxidase (TPO), antithyroglobulin (TG) antibodies in patients with goitre. The thyroid gland was evaluated by echography. Intestinal mucosa biopsy was performed in one case.
Results: Two cases presented vitiligo and one case alopecia areata already from the onset of DM. After 5 years of DM evolution, one case (F) prepubertary, presented abdominal distension, hepatomegaly, decreased growth velocity. The intestinal mucosa biopsy confirmed celiac disease. In seven cases (F) with a DM evolution longer than 10 years, we found diffuse goiter. All these patients previously presented brittle glycemic control, clinical signs of hypothyroidism (six cases) or hyperthyroidism (one case). Nine cases presented increased TSH: in six cases with goiter and clinical signs of hypothyiroidism, with FT4 below normal and significant antiTPO and TG titres, while the other three cases presented slightly increased TSH but with normal FT4. The case with clinical signs of hyperthyroidism had positive antiTPO and anti TG titres, decreased TSH and increased FT4. Thyroid echography revealed morphological abnormalities only in the seven cases with goiter.
Conclusions(i) Autoimmune diseases may occur in children with type 1 DM even from the onset and (ii) Our results are concordant with the literature data showing that thyroid disease represent the most frequent autoimmune pathology associated with type 1 DM and, in our patients, occured peripubertary.

R14

L-Aspariginase induced diabetes in acute lymphoblastic leukaemia (ALL)

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Background: Acute lymphoblastic leukaemia (ALL) is the commonest haematological malignancy in childhood. L-Aspariginase(L-Aspa) is one of the chemotherapeutic agents used and it is known to cause secondary diabetes.
Aim: To study the incidence, patients' characteristics and outcome of L-Aspa induced diabetes.
Method: Children aged <15 years treated for ALL at University Malaya Medical Centre (UMMC) from January 2001 to December 2005 were identified. Diabetes was defined as random blood sugar (RBS) >11.0 mmol/l or fasting blood sugar (FBS) >7.0 mmol/l on two occassions. Diabetic ketoacidosis (DKA) is defined as heavy glycosuria (55 mmol/l), ketonuria, hyperglycaemia (blood glucose >11mmo/l), acidosis (pH <7.3 and/or bicarbonate <15 mmol/l) and dehydration ($>5\%$ body weight). Their demographic profiles, treatment and outcome of disease were recorded and analysed.
Results: Five of 235 children with ALL had L-Aspa induced diabetes, three presented clinically with DKA, while two were detected incidentally by glycosuria. Male:female ratio is 1:4, age range of 5–15 years. Three patients developed diabetes during induction chemotherapy, of whom two had DKA. Another two developed diabetes while on relapse protocol, one of whom had DKA with clinical and biochemical evidence of acute pancreatitis. One patient had an elder brother with type 1 diabetes. All needed insulin to maintain normoglycaemia, two for only 6 weeks while the rest ($n = 3$) longer than 6 months. Two of them (one with pancreatitis) died of recurrent relapse ALL while still on insulin. One is still on insulin at 12 months of diagnosis.
Conclusion: The incidence of L-Aspa induced diabetes among ALL patients in UMMC is high at 1:47 patients. L-Aspa induced diabetes could either be transient or permanent, thus all patients need long term blood glucose monitoring.

R15

Kearns-Sayre Syndrome (KSS). Diagnostic delay in one case

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Kearns-Sayre Syndrome (KSS) is a mitochondrial myopathy that demonstrates the following: chronic progressive ophtalmoplegia (CPEO), onset before age 20 and pigmentary degeneration of the retina. In addition, KSS may include cardiac conduction defects, cerebellar ataxia, and raised cerebrospinal fluid (CSF) protein levels (>100 mg/dl). KSS may affect many organs and systems (e.g. diabetes, growth retardation/short stature, hypoparathyroidism, myopathy, bilateral sensorineural hearing loss, cataracts, dementia, dystonia, and proximal renal tubular acidosis). KSS occurs secondary to deletions in mitochondrial DNA that cause a particular phenotype. We report a 15-year-old boy with short stature, external ophtalmoplegia, palpebral ptosis, myopathy, sensorineural hearing impairment, cerebellar ataxia, cardiac conduction defect, diabetes mellitus, hypoparathyroidism, hyperaldosteronism and chronic renal failure. The patient initially presented with endocrinological abnormalities: growth hormone deficiency, hyperaldosteronism and hypoparathyroidism. Despite his palpebral ptosis and his progressive encephalomyopathy with cerebellar ataxia, the initial diagnosis was different than KSS. The diagnosis was delayed for 3 years.
Results: The final diagnosis was established when he developed diabetes mellitus and was admitted in our department. Southern blot analysis and PCR amplification revealed the presence of a deletion in the mitochondrial DNA. Echocardiography revealed prolapse of the anterior mitral leaflet without mitral regurgitation. Patient exhibited cardiac conduction disturbances: left anterior hemiblock The ECG recorded 2 years before showed complete right bundle branch block with left anterior hemiblock and Mobitz type 2 second-degree AV block. He improved by implantation of a permanent pacemaker.
Conclusion: Despite of his rarity, the diagnosis can be easily made in the presence of the classical triad: external ophtalmoplegia, pigmentary retinopathy and onset in persons younger than 20 years.

R16

Comparison of polymorph alleles association of genes HLA-DRB1, HLA-DQA1, HLA-DQB1 with DM type 1 in Moscow and Yakut populations

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The main genes contributing to DM type 1 susceptibility are located in HLA locus and this association may differs between population with various level of incidence.

Objective: To perform a comparative analysis of polymorph associations of genes alleles HLA-DRB1, HLA-DQA1 and HLA-DQB1 with DM type 1 in Moscow and Yakut populations.

Materials and methods: Genes alleles HLA-DRB1, HLA-DQA1 and HLA-DQB1 was identified in 51 patients with DM type 1 and 51 healthy persons in Yakutia (Incidence 1.6/100 000 person), as like as 204 patients with DM type 1 and 600 healthy persons in Moscow (Incidence 11.9/100 000 person).

Results: See Table.

Comparison of DM type 1 risk development in Moscow and Yakut populations

	Yakut population		Moscow population	
Alleles	OR		OR	
DRB1*4	4.27	0.0001	5.96	<0.00005
DRB1*8	1.00	*	1.62	0.3
DRB1*17	8.47	0.0001	4.33	<0.00001
DQA1*0501	1.70	*	1.04	1
DQA1*0401	0.79	*	1.65	1
DQA1*0301	2.38	0.004	5.70	<0.00002
DQB1*0201	3.28	0.001	2.06	0.0001
DQB1*0302	3.95	0.0001	7.10	<0.00003
DQB1*0304	-	*	8.94	0,05

Conclusions: This data indicates in different association susceptibility alleles with DM type 1 in Moscow and Yakut populations.

R17

HLA alleles in children and adolescents with type 1 diabetes mellitus in northern Greece

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Type 1 diabetes (DM1) is one of the most frequent chronic disease in children. Although it is an autoimmune disorder, the etiology of DM 1 remains unclear. However, it is accepted that both genetic and environmental factors are major determinants.

Objective: Determine the frequency of HLA class II alleles (DRB1 and DQB1) in DM 1 patients from a northern Greek population.

Methodology: HLA typing was performed on DNA extracted from peripheral blood of 68 DM 1 patients (age 13.1 + 3.7 years) and 181 healthy control subjects using PCR-SSP. The significance of the difference in distribution of alleles between patients with DM 1and healthy control subjects was determined by χ^2 methods. Statistical significance was defined as $p < 0.05$.

Results: The phenotypic frequency of high risk determinants for DM 1, DRB1*03, DRB1*04 and DQB1*02 was significantly higher in patients with DM 1 than in control subjects ($p < 0.001$). The frequency of protective allele DRB1*15 was significantly higher in healthy control than in patients ($p < 0.05$). In contrast, there was no significantly difference in the other protective allele (DRB1*16) between patients and control subjects. However, there was 8/68 patients without any susceptibility alleles.

Conclusion: The results of our study are consistent with the international bibliography, in which the genes of the HLA region are accepted as alleles that predispose to DM 1. The statistically significant difference of the HLA DRB1 *03,*04 and DQB1*02 alleles from the respective percentages in the healthy control subjects, indicates these alleles as predisposing factors for diabetes type 1 in the northern Greek population. Nevertheless, the fact that, in our study, some persons without any predisposing alleles where found to have DM 1 indicates the role of other genetic factors in the phenotypic expression of the disease that needs further research.

R18

Insulin gene polymorphism may affect BMI, insulin secretion and lipid level in healthy children born with hypo- and hypertrophy – 6–9 years of follow-up study

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Introduction: Ambiguous results, which concern an association of insulin gene polymorphism with low body weight and insulin resistance (IR), have been published recently.

Aim: The aim of the study was to evaluate an influence of -23 A/T (HphI) polymorphism in insulin gene promoter on BMI-SDS, WHR, insulin and glucose level during oral glucose tolerance test (OGTT) as well as serum lipids and IGF-I in 6–9 years old children born with hypo- or hypertrophy.

Patients and methods: The analysis comprised 62 healthy children, aged from 6–9 years (7.1 ± 1.6 years), born with hypotrophy (body mass < 3 centile for gestational age; n = 49) or hypertrophy (body mass > 97 centile for gestational age; n = 42). For each child actual body mass index (BMI-SDS) and waist to hip ratio (WHR) were evaluated, lipids and IGF-I concentration in plasma were measured and OGTT was performed. Based on insulin and glucose concentrations during OGTT insulin sensitivity (QUICKY) and insulin resistance ($IRI_{Belfiore}$) was assessed. Genomic DNA was extracted from peripheral blood leukocytes. The -23 A/T polymorphism in insulin gene promoter was genotyped using PCR methods followed by digestion with HphI restriction enzyme.

Results: Considered BMI SDS and WHR values, serum lipids, IGF-I and glucose and insulin during OGTT, as well QUICKY and $IRI_{Belfiore}$, we did not find any statistical differences between group of children born with hypotrophy and hypertrophy. Genotype distribution was similar in both groups, however, minor T-allele frequency was slightly higher than in general Polish population showed in our previous report (0.26 vs. 0.17, respectively, p = 0.14). We did not observe any statistical differences between mentioned above parameters within the groups stratified by genotype.

Conclusions: We did not find an influence of the insulin gene polymorphism on BMI and WHR values as well on lipids, IGF-I and glucose and insulin levels during OGTT in 6–9 years old, healthy children born with hypotrophy or hypertrophy. However, our study may be underpowered and need to be verified on the larger sample size.

R19

Clinical characteristics of our patient suffering from BETA2/NeuroD1 genetic malformation

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BETA2/NeuroD1 gene is essential for the development of the pancreas and the brain. It is expressed in the endocrine pancreas and has a pivotal role: encodes transcriptional factor for the insulin gene and ???cell differentiation. The pancreatic islet cells in the BETA2/NeuroD1 null mice are not properly maintained and undergo apoptosis. Morphogenesis of the islet itself is also defective in the null. Its deletion results in neonatal diabetes secondary to islet defects. The loss of BETA2/NeuroD1 affects the cerebellar development. The granule cells of the cerebellum and hippocampal dentate gyrus fail to differentiate properly and are present in greatly reduced number. BETA2/NeuroD1 is also a critical gene for development of the auditory and vestibular systems. Phenotypically the null mice are completely deaf and suffer from severe deficiencies in balance and coordination. In addition, both the secretin- and cholecystokinin-expressing entero-endocrin cells are missing in the null gut. Animal and cell-culture studies have shown that BETA2/NeuroD1 influences the fate of retinal cells in culture. Null mice that survive into adulthood were completely devoid of photoreceptors. BETA2/NeuroD1 plays an important role in age-related degeneration of both rods and cones. Loss of BETA2/NeuroD1 leads to severe defects in these systems. We would like to describe our patient, who is suffering from permanent neonatal diabetes mellitus due to loss of BETA2/NeuroD1 gene. Among the above described phenotypical characteristics we found permanent neonatal diabetes mellitus, Dandy-Walker syndrome, impaired hearing, ataxia, unexplained diarrhea, developmental delay. On examination we did not find visual or retinal abnormalities. The family is not yet investigated. The father has mild glucose-abnormality on OGTT, the twin-sisters of the father both had GDM at pregnancy. Their genetic studies are not yet performed.

R21

Effects of switching basal insulin to glargine from NPH in children and adolescents with type 1 diabetes

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Introduction: Insulin glargine is a long-acting insulin analogue increasingly used instead of NPH in young subjects with type 1 diabetes.

Aims: We evaluated the clinical course of diabetes in children and adolescents who were switched to insulin glargine from NPH.

Methodology: Seventy-six children and adolescents with type 1 diabetes were changed to insulin glargine from NPH (0 months). All the subjects had received insulin NPH as basal insulin and their serum C-peptide levels had been nondetectable for at least 1 year. Twelve months after the change (+12 months) 69 patients continued with glargine, five had switched back to NPH and two started with insulin pump therapy. Data on HbA1c, hypoglycaemias, weight, height, insulin doses and number of injections was collected retrospectively. At +12 months aspects of treatment and quality of life were asked using a questionnaire.

Results: Data for 62 subjects (35 boys) were available. At 0 months the mean age was 12.7 years (range 5.1–17.5), mean duration of diabetes 6.7 years (range 1.8–14.3), and mean HbA1c 9.2% (95% CI 8.8–9.6). At +12 months the mean HbA1c was 9.2% (95% CI 8.8–9.7); $p = 0.938$ vs. 0 months, proportion of long-acting insulin was lower [47.7% (95% CI 46.0–49.5) vs. 58.1% (95% CI 55.9–60.2); $p < 0.001$], and total daily insulin dose was lower [0.97 IU/kg (95% CI 0.93–1.01) vs. 1.05 (95% CI 1.00–1.11); $p < 0.001$] than at 0 months. Number of insulin injections was lower at +12 months than before the change (17.7% with >5 injections vs. 64.5%; $p < 0.001$). No differences were found in weight for height or number of severe hypoglycaemias. At +12 months most subjects (n = 54; 87.1%) considered insulin glargine better than NPH.

Conclusions: Switch to insulin glargine results in similar HbA1c, lower proportion of basal insulin, lower daily insulin dose, and fewer daily injections than treatment with NPH.

R22

To compare the glycemic control and changes in body mass index in children with type 1 diabetes, on multiple daily insulin injections and continuous subcutaneous insulin infusion

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Introduction: Management techniques and goals of diabetes management have changed tremendously in the last few years. The DCCT and UKPDS trials highlighted that tight metabolic control of diabetes significantly reduced the risk of micro-vascular complications. This was only possible with multiple injections and frequent monitoring. Multiple needle pricks lead to poor compliance and quality of life for insulin dependent diabetic children. Sophisticated insulin delivery systems such as insulin pumps have resulted in good metabolic control and quality of life for children with Type 1 diabetes.

Aim: To compare the glycemic control and change in BMI on continuous subcutaneous insulin infusion (CSII) and multiple daily insulin injections (MDI) in children with Type 1 diabetes.

Method: We compared the glycemic control and change in body mass index (BMI) in six children and adolescents, 5 males and 1 female, aged 7–18 years, on MDI and on CSII. The duration of diabetes in the subjects ranged from 6 months to 9 years. All the subjects were initially on MDI with glargine once daily and regular insulin before meals and later opted for CSII for better control and quality of life. The duration of CSII varied from 6 months to 1.5 years. Glycemic control was assessed by measuring the average HbA1C.

Results: The glycemic control (average HbA1C) was better on CSII compared with MDI (7.5% vs. 10.3%). The improvement in the mean HbA1C on CSII was present in five of the six children. Slight increase in the body mass index (BMI) was found in all the subjects (19.5 vs. 21). This may be due to better control or overeating.

Conclusion: CSII results in better glycemic control compared to MDI although it is associated with an increase in BMI, which may result from better control or excessive eating or both.

R23

Children with DM type 1, treated by insulin glargine and aspart, while good glycemic control achieved

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Background: Basal insulin Glargine helps to achieve a appropriate glycemic control in children with Diabetes Mellitus type 1. However, achievement of target glycemic level increases a risk of hypoglycemia.

Objective: To determine frequency of hypoglecemia (blood glucose lower 4.0 mmol/l) in diabetic patients with HbA_{1c} <9% using Glargine (once in bedtime) and Aspart as a basal-bolus regime.

Materials and Methods: Measured 22 patients with Diabetes Type 1, age 6–17 years (13.1 ±3.4) and HbA_{1c} 5.8-8.9% (7.5 ± 0.9%). The patients was divided in two groups: with HbA_{1c} <7.6% (11 individuals) and >7.6% (11 individuals). The both groups had not significant differences for age and duration of diabetes. The Continuous Glucose Monitoring system (CGMS, Medtronic MiniMed, Sylmar, CA) was used for performing of this study. Glycemia was monitored 72 hours. Re-monitoring was repeated after the 3 months.
Results: A total of 18% of patients did not have hypoglycemia events during 72 hours of monitoring. 36.4% of patients did not have nocturnal hypo. There was no difference in hypoglycemia between the two groups with optimal and suboptimal metabolic control (63.6%). During 3 months patients had no severe hypoglycemia. The results of re-monitoring was received in 10 patients. The amount of patients without noctural hypo increased from 30% to 70%. The duration of noctural hypo had a trend to decreasing from 2.2 ± 2.6 hours to 1.3 ± 2.8. The glycated hemoglobin HbA_{1c} had not a significant changes in 3 months (7.6 ± 1.0 vs. 7.9 ± 1.3%).
Conclusion: Diabetic children could not have hypoglycemia, especially in night, while target glycemic control achieved, using of basis-bolus insulin therapy (glargine and aspart).

R24

Autoimmune polyglandular syndrome type 2 in 14-year old boy with diabetes mellitus type 1 cured by personal insulin pump therapy

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The autoimmune polyglandular syndrome (APS) type 2 is rare, especially in children, endocrinological disorder characterized by co-occurrence of several autoimmune endocrine diseases. The most frequent are: autoimmune thyroid disease, primary adrenal insufficiency and type 1 diabetes mellitus. We describe 14-year old patient who had been suffering from type 1 diabetes mellitus for 2 years. The intensive insulinotherapy by continuos subcutaneous insulin infusion (CSII) was applied during last year. He was admitted to the hospital because of mild nausea and periodically occurred abdominal pains observed for app. 6 months. The physical examination revealed hypotension (92/57 mmHg) and weight loss without any other abnormalities. HbA1c level was 5% (n: <6.3%). The total daily insulin requirement in CSII was also decreased upto 0.33 U/kg/day (with basal insulin rate–3.4 U/day). Several days later his clinical state become worse–vomiting and weakness had appeared. Further biochemical and hormonal determination led to the proper diagnosis of APS. Thyroid hormonal levels: hTSH-5.74 uIU/ml (n: 0.3–4.7), fT4-0.74 ng/dl (n: 0.7–1.9), fT3-3.14 pg/ml (n:1.64–3.45) indicated hypothyroidism. Thyroid antibodies were also detected. Serum sodium level was slightly decreased (132 mmol/l) and potassium concentration was normal. Synacthen stimulation test revealed baseline and 30 minute stimulated serum cortisol values: 0'–1.8 ug/dl, 30'–0.4 ug/dl (normal stimulated value >18 ug/dl), serum ACTH level was 1821 pg/ml (n: 10–60) and serum aldosterone level was <7.0 pg/ml (n: 42–201). Hipogonadism and celiac disease were ruled out. ASMA Ab -against smooth muscle antibodies–were determined. He was started to be treat with hydrocortison, fluorocortisone and L-thyroxine. All symptoms disappeared quickly. CSII was very helpful to adjust correct insulin doses to increased insulin requirements. The diabetic patients with unexplained changes in insulin requirements and glyceamic control, particularly with a family history of thyroid and/or Addison's disease, need careful follow-up.

R25

High level of antiinsulin antibodies – indication for insulin pump therapy?

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Background: High level of anti-insulin antibodies (>5.5) makes assessment of good metabolic control of diabetes difficult, especially in patients of pubertal and adolescent age. Insulin pump therapy is excellent mean for achieving optimal metabolic control of diabetes but because of its price it is not available to all patients who need it according general indications.
Aim: A total of 6 monts following of clinical and therapeutical parameters in four diabetic patients with high level of anti-insulin antibodies after starting of insulin pump therapy.
Metodology: Therapy with available four insulin pumps we introduce to diabetic patients with high level of anti-insulin antibodies and different problems because of this finding. Our four patients (F 3, M 1) were mean 13.5 years old, with average duration of diabetes 3 years. Their mean HbA1c level was 8.5%, C peptide level <25 (total diabetes) and average level of anti-insulin antibody 35.6 at the start of insulin pump therapy.
Results: Six months after introduction of insulin pump therapy mean HbAlc in our patients was 7.0% (range 5.5–8.5); daily insulin dose of insulin decreased from mean 1.41 IU/kg to 0.71 IU/kg ($p < 0.0001$); start BMI was 19.8 and after 6 months 20.2; level of insulin antibodies decreased to 14.1 ($p < 0.001$). Incidence of hypoglycaemia was 34.2/yearly before and 14.1 after introducing pump therapy ($p < 0.0001$).
Conclusion: By insulin pump therapy we significantly reduce daily insulin dose, number of hypoglycemic episodes and consequently improves metabolic control of diabetes in our patients. Level of anti-insulin antibodies significantly decreased, so circulus viciosus of bed events they produced was stopped. Although our sample was small we can suggest that high level of anti-insulin antibodies must be one of indications for introducing insulin pump therapy in pediatric and adolescent diabetic patients.

R26

Patients, practitioners and professional education: A tripartite approach to insulin pump therapy in children

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Introduction: The advent of Continuous Subcutaneous Insulin Infusions (CSII) has shown them to be more effective than multiple injection regimens in reducing HbA1c in persons with Type 1 diabetes, and thus more effective in minimizing the risk of diabetes related complications. To be able to offer CSII to children, it was clear that more knowledge which could be evidenced was needed. This resulted in the development and delivery of an accredited, post-graduate module in insulin pump therapy.
Aims: To enhance clinical practice through the development and delivery of an accredited, post-graduate module in insulin pump therapy using a tripartite approach.
Methodology: A multiprofessional curriculum development team was identified which included representatives from clinical practice, higher education and service user and carers. Inclusion of all the key stakeholders was essential to ensure different knowledge skills and experiences were reflected within the module.
Results: The first delivery of the module attracted students from around the United Kingdom and from a range of professional

disciplines. Patients, practitioners and educators were involved in the delivery and assessment of the module. In evaluating the module students specifically commented on the effectiveness of the tripartite approach and they felt confident and competent to provide an effective, quality insulin pump service.
Conclusions: Increased numbers of healthcare professionals are now able to develop and enhance their skills in CSII which will lead to more children having the opportunity of treating their diabetes via an insulin pump. This should result in a reduced level of diabetes complications, increased quality of life for the child and family and a decrease in long term health costs. It is through an effective tripartite approach to curriculum development and delivery that this has been truly achievable.

R27

Insulin pump uses in patients with diabetes mellitus type 1: the results of 2 years follow-up.

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The improvement of glycemic control is a real problem for patients with Diabetes Mellitus type 1, especially for children and adolescents. Even intensive scheme of insulintherapy is not always available to reach the target levels of glycemia and glycohemoglobin (HbA_{1c}). Insulin pump is a new approach for patients which can help to improve glycemic control.
Objective: To compare the data of metabolic control before and after the start of using insulin pump and to assess the possibility of glycemic control improvement with the help of this method.
Materials and Methods: A total of 30 patients (15 M/15 F) with diabetes type 1 aged 5–37 years (14.45 ± 6.32 years) and duration of disease 0.5–24 years (6.7 ± 5.32 years) took part in this study. The insulin pumps 'Minimed 508' and 'MiniMed 712' (Medtronic MiniMed, Sylmar, CA) was used. For correction of insulin doses 18 patients stayed in hospital for 10–15 days and 12 patients visited doctor 3–5 times during 5–7 days. HbA_{1c} level before and in 3, 6, 12 and 24 month after the start of insulin pump usage, the frequency of severe hypoglycemia and diabetic ketoacidosis, convenience of pump usage were analyzed.
Results: HbA_{1c} level before insulin pump was 6.1–4.7% (9.92% ± 0.24%); in 3 months of insulin pump usage HbA_{1c} was 5.8%–13.1% (9.03 ± 1.92%); in 6 months 4.9%–13.3% (8.95 ± 2.21%); in 12 and 24 months 5.4%–11.9% (8.75% ± 1.62%) and 5.4%–10.2% (8.61% ± 1.59%) respectively. None of patients suffered from episodes of severe hypoglycemia during the evaluation period. Diabetic ketoacidosis occurred in two patients.
Conclusion: Insulin pump therapy significantly helps to improve the metabolic control. Insulin pump can be the effective alternative vs. multiple daily injection.

R28

Transition from MDI (multiple daily injections) to CSII (continuous subcutaneous insulin infusion) treatment in children and adolescents with type 1 diabetes: differences in insulin doses of various paediatric age groups.

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Introduction: There are few and controversial data examining the transition from MDI to CSII in paediatric patients with type 1 diabetes.
Aims: To investigate the difference in insulin doses during the transition from MDI to CSII in various age groups paediatric patients with T1D.
Methodology: We analyzed with a retrospective study the insulin treatment of 38 patients with T1D (duration 5.2 ± 2.4 years) regrouping in group: A 13 (34%) prepubertal subjects (Tanner stage I), B 13 (34%) pubertal subjects (TS II-IV), C 12 (32%) postpubertal subjects (TS V); who were switched from MDI to CSII. Data regarding insulin doses were collected before (MDI treatment) and 1 month after the start of CSII treatment.
Results: During MDI treatment the patients used regular/rapid anologue insulin before meals and NPH insulin at bedtime (41% of total daily insulin). During CSII treatment all patients used rapid-acting analogue insulin. Compared to pre-CSII treatmen the insulin requirements on CSII (U/day) decreased significantly in all age groups (13–20%). On CSII, basal insulin dose comprised respectively 55% of total daily insulin (57% in group A and 54% in group B, C). There is not difference between age groups ($p < 0.05$) regarding the mean number of basal rates/day (4.8 ± 1.1 4.8 ± 0.9 and 4.5 ± 1.3); the nocturnal basal insulin (29%, 32% and 30% of total daily basal dose). During the night, prepubertal patients required more insulin from 24.00 to 2.00 h, while pubertal and postpubertal patients required more insulin between 2.00–7.00 h. There is not difference ($p < 0.05$) between gruops regarding mean HbA1c levels at the start of CSII.

	MDI treatment	CSII treatment	Change (%)	p
Total daily insulin (U/day) Group A (9 males; mean age 6.2 ± 2.1 years)	29.5 ± 8.4	24.1 ± 7.4	Decr 19 ± 2%	0.01
Total daily insulin (U/day) Group B (11 males; mean age 12.6 ± 2.0 years)	48.2 ± 11.6	38.3 ± 10.9	Decr 20 ± 4%	<0.001
Total daily insulin (U/day) Group C (6 males; mean age 16.1 ± 1.3 years)	55.4 ± 24.5	48.4 ± 14.3	Decr 13 ± 3%	0.02
Total daily insulin (U/day) Total patients	44.0 ± 19.6	35.6 ± 14.7	Decr 17 ± 3%	0.01

Conclusions: A decreased of total daily insulin doses is necessary during the transition from MDI to CSII in all age groups of pediatric patients, especially in prepubertal and pubertal patients. At the start of pump treatment, age-related differences exist in insulin basal dose, and nocturnal basal profile of paediatric patients.

R29

To determine the impact of continuous subcutaneous insulin infusion (CSII) with insulin pump, on the Quality of Life in children and adolescents with Type 1 diabetes.

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Introduction: The availability of CSII with insulin pump has improved the quality of life in children with Type 1 diabetes. This has been primarily due to reduction in the number of needle pricks, flexibility in eating and better metabolic control.
Methods: Quality of life was assessed in six children and adolescents with Type 1 diabetes on CSII by means of written questionnaires. The subjects comprised of five boys and one girl. Age of the children ranged 7–18 years. The duration of diabetes ranged from 6 months to 9 years and duration of CSII was 6 months–1.5 years, at the time of answering the questionnaire. The questionnaire measured quality of life in the four subscales: convenience (sleeping, playing, dressing), local factors (pain, skin infection, hyperpigmentation), Control (avoidance of hyper and

hypoglycemia and overall satisfaction (physical and psychological). Answers were graded from lack of satisfaction to complete satisfaction.

Results: In response to convenience of CSII, pain and skin infections, all the subjects were very satisfied to completely satisfied. Hyper pigmentation at the infusion site was reported in one subject. Embarrassment in school due to insulin pump was felt by one child (female). Interference with dressing up and sleeping was reported in three (50%) children. In response to avoiding hyper and hypoglycemia and keeping good control, the response was good to excellent in all the subjects. The response to overall satisfaction with the pump was very satisfied in four (66.6%) children and completely satisfied in two (33.3%) children. None of the six children wanted to switch back to MDI therapy.

Conclusion: CSII is an effective means of managing type 1 diabetes. It results in satisfaction regarding good control, avoiding severe fluctuations in blood glucose, convenience, over all satisfaction and better quality of life

R30

Assessment of the practicality of intensive therapy in a standard adolescent diabetes clinic

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Background: The increasing incidence of Type 1 Diabetes in childhood has been mirrored by its increasing intensity of management. The DCCT demonstrated that intensive therapy is associated with better glycaemic control and a subsequent reduction in microangiopathic complications. Side-effects of intensive therapy include increased risk of hypoglycaemia and weight gain. Newer insulin analogues allow a more targeted approach to insulin delivery and are potentially less likely to cause hypoglycaemia and weight gain.

Aim: To assess the feasibility and success of implementing intensive therapy in a routine adolescent diabetes service and to compare clinical and metabolic outcomes between intensive (IT) and conventional (CT) treated patients

Methods: Retrospective longitudinal descriptive study of adolescents attending a single secondary centre. Conventional patients were age and sex matched to their intensive counterparts. Main outcome measures include HbA1c, number of hypoglycaemic and DKA episodes, and weight change (BMI and BMI SDS) measured at defined time intervals including baseline, 3, 6 and 12 months.

Results: A total of 32 patients in the intensive group (4+ injections/day) and 46 in the conventional group (2 injections/day). There was no significant difference in mean HbA1c (8.97 CT vs. 9.0 IT), number of hypoglycaemic or DKA episodes or BMI SDS between the different treatment groups at any time interval. There was a statistically significant difference ($p < 0.001$) in the difference in mean BMI SDS at 12 months minus baseline (conventional +0.18 BMI SDS and intensive group – 0.26 BMI SDS)

Conclusion: Intensive management is sub-standard in routine clinical practice. There is no difference in glycaemic control and number of hypoglycaemic episodes between CT and IT patients. Intensive therapy is less likely to cause weight gain than conventional therapy. Greater resources are needed for successful delivery of intensive diabetes management.

R31

Results from an audit of paediatric diabetes services in Leeds, UK

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Background/Aims: The National Diabetes Audit (NDA) was established to replace that previously administered by Diabetes UK. An NDA requirement is for every diabetes clinic in England to submit electronic patient information. We aimed to examine the profile of patients attending two paediatric diabetes centres in Leeds, UK by interrogating data submitted as part of the NDA.

Methods: We extracted data from hospital notes for every patient attending the two paediatric diabetes clinics in Leeds between January 2004 and April 2005. Data was input electronically into a bespoke database and uploaded via the NHSnet to the NDA directly. Interrogation of the data was carried out using the PIANO toolkit available through the Open Exeter system.

Results: Information on 282 patients was extracted. Over half of patients were aged 11–15 years, with females comprising the majority of attendees (54%). 66% (185/282) of patients had been diagnosed within the last 5 years. Only 12% of individuals achieved a target HbA1c of 7.5% or below; there was no consistent pattern by age group although patients were less likely to reach this target the longer they had been diagnosed. The majority of patients had all their care processes monitored, with virtually all having BMI, HbA1c, blood pressure, eye and foot exams recorded.

Conclusions: Analysis of the paediatric diabetes dataset for Leeds has been useful for monitoring and comparing clinical performance indicators across the two paediatric clinics in Leeds. Although we were unable at the time of analysis to provide a comparison with UK data, in the future we hope to compare our results to other centres across England with a view to improving service provision both locally and nationally.

R32

Clinical and laboratorial profile of children and adolecents with type 1 diabetes from São Paulo, -Brazil

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Introduction: Type 1 diabetes mellitus is a chronic illness with incidence around 10% in the Brazilian population. Due to the risk of long term complications rigorous laboratory and clinical control is necessary:

Objective: Evaluate the laboratory and clinical profile of infants and adolescents in two university hospitals from São Paulo state of Brazil

Methodology: Cross analysis of diabetics in follow up at the university service of São José do Rio Preto (FAMERP) and of Campinas (UNICAMP) with type 1 diabetes, with rescue of the distribution by sex, age, period of diabetes, daily insulin dose, number of insulin shots and glycated hemoglobin (HbA1c), by HPLC , normal range between 4.6–6.5%

Results: Of the 218 (100 male and 118 female) diabetics, with ages varying from 1 to 26 years and time of diabetes varying from 1 to 18 years were evaluated. The daily insulin doses varied between 0.1 to 1.6 units/kg (M = 0.8). 17 diabetic patients (7.7%) used an unique insulin shot by day, 176 (80.7%) two doses and 25 (11.4%)

three doses. The glycated hemoglobin ranged from 4.6% to 17.6% (M = 10)

	Media	Variation
Ages	13.2 years	1–26 years
Time of diabetes	6.9 years	1–18 years
Dose of insulin/day	0.8 μ/Kg	0.1–1.6 μ/Kg
Number of shots by day	2.0	1–3
HbA1c	10%	4.6–17.6%

Conclusion: In despite of those two reference hospitals for diabetes follow up, from two of the five biggest cities of the state more developed in the country, the metabolic control measured by the glycated hemoglobin, was not adequate. The majority of the diabetics use two daily shots of insulin. These facts show that despite of efforts from the team, we still have big challenges.

R33

HbA1c in relation to some clinical parameters

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Background: The risk of late complications increases with poor metabolic control. There are no clear explanations to why patients at some clinics seem to get lower HbA1c than at other clinics. This study aimed to explore differences in HbA1c between paediatric departments and the relation between HbA1c and insulin regimen, duration of diabetes, age, gender, BMI in a homogenous population within one country with similar treatment traditions.

Material and methods: Clinical data collected prospectively at 18 719 clinical examinations (1565 girls, 1698 boys) at 22 centres during 2002 and 2003, from the national registry for children with diabetes in Sweden (SWEDIABKIDS), were analysed. Swedish HbA1c-values are ca 1.1% lower than DCCT-values.

Results: HbA1c was <7% (target value) at 40% of the visits, 7–7.99% at 30%, 8–9.99 at 25%, >10% at 5%. HbA1c was significantly higher in adolescents ≥13 years compared to younger children (7.6% ± 1.6 (SD) and 7.1% ± 1.26 (SD) resp. $p < 0.001$). Girls had higher mean HbA1c compared to boys especially during late adolescence (7.9% ± 1.76 (SD) and 7.5% ± 1.56 (SD) resp. at 17 years of age). Higher mean HbA1c correlated to higher mean insulin dose ($r = 0.413$, $p < 0.001$) and longer duration ($r = 0.311$, $p < 0.001$). Centre mean HbA1c varied between centres from 6.6% ± 1.33 (SD) to 8.0% ± 1.6 (SD). Only two centres reported centre mean HbA1c below target value.

Conclusions: Although we find correlations between HbA1c and certain clinical parameters, there is still a centre difference, which needs to be further investigated. We need more focus on adolescents with high insulin dose and long duration, especially girls.

R34

Factors affecting body mass index from onset of diabetes to age 18

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Introduction: The Danish Childhood Diabetes Register was founded in 1996. It is a nation-wide register collecting data from all Danish paediatric diabetes centres treating type-1-diabetic patients aged 0–15 years. Weight and height is measured at onset of the disease and yearly thereafter.

Aim: The aim of the present study was to describe the factors affecting body mass index (BMI) from onset to age 18.

Methodology: Weight and height is measured by health professionals at each centre. Weight is measured in kilogram, height in m. Weight and height measured less than 30 day after onset were excluded. BMI was calculated as weight/height^2 In the model BMI was entered as sds-score. Standard deviation score (SDS) was defined as (observed – expected)/standard deviation for age and sex. General linear modelling was used to estimate the association between the different risk factors and the BMIsds.

Results: There are 2906 children in the register, and 13310 year reports with height and weight data. There was a significant increase in BMIsds with length of diabetes ($p < 0.01$) and older age of onset ($p < 0.01$). There was a significant interaction between diabetes duration and sex. Girls tended to start on a lower level, but had a more steep increase in BMI ($p < 0.01$). The BMIsds were the same for boy and girls after approximately 2 years of diabetes, thereafter the girls tended to have a higher BMIsds. There were a significant association between BMIsds and HbA1c and centre. There was a significant increase in BMI with year of onset.

Conclusion: BMI differed between centres and were associated with diabetes duration, sex, HbA1c, year of onset and age at onset.

R35

To describe the main reasons for hospitalisation and the average length of hospital stay for children with diabetes-type 1 in Germany and Austria

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Introduction: In general, length of hospital stay has decreased under the enormous economic pressure on health care systems in recent years. Efforts to reduce the rate of hospital admissions and the length of hospital stay require exact data on the duration and the main reasons for admission. For children with diabetes-type 1 in Germany, exact data are not yet available.

Aim: To describe the main reasons for hospitalisation and the average length of hospital stay for children with diabetes-type 1 in Germany and Austria.

Methods: Anonymous data of paediatric patients (n = 25,847; age 0.1–19.9 years; 50.1% girls) with diabetes-type 1 were provided by the Pediatric Quality Initiative (DPV), including data from 152 centres in Germany and Austria. Data from 1995–2005 were analysed and a multivariate analysis has been performed.

Results: Main reasons for hospitalisation were adjustment of metabolic control and teaching (44.5%), diabetes onset (27.4%), diabetic ketoacidosis (8.9%), and severe hypoglycaemia (4.2%). Average length of stay has decreased from 10.4 days in 1995 to 8.2 days in 2005 ($p < 0.0001$). Factors influencing the length of stay were age, distance to place of residence, and reason for admission ($p < 0.0001$ each). In the age-group <5 years, average length of stay was 12.1 days compared to 7.7 days in the group 15–20 years. A longer distance to place of residence was associated with a longer stay in hospital. In 2005, the average length of stay was 13.2 days at diabetes onset, 7.5 days for ketoacidosis, 6.3 days for adjustment of metabolic control, and 5.1 days for severe hypoglycaemia.

Discussion: In children with diabetes-type 1, length of hospital stay has decreased in recent 10 years in Germany. In addition to medical decisions, the choice for inpatient versus outpatient

treatment is closely related to the available structure of diabetes care and the accountancy system.

R36

Factors influencing glycemic control in children with type 1 diabetes mellitus

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Introduction: HbA1c is an important tool in estimation of glycemic control in young patients with type 1 DM and greatly contribute to optimisation of diabetes treatment. Maintenance of adequate HbA1c level helps to reduce the risk of late complications.
Aim: To estimate glycemic control in children with type 1 DM and analyse factors influencing HbA1c level.
Methodology: The study involved 131 children with type 1 DM: M/F 95/79 (54.6%/45.4%), mean age 13.5 ± 0.29 years (2–18), mean diabetes duration (MDD) 4.5 ± 0.28 years (0–17). There was no statistical difference between males and females. HbA1c was estimated at Hitachi device (N 4.8–6.0%).
Results: Mean HbA1c level was 9.6 ± 0.2%. Ideal glycemic control with HbA1c less 6% was recorded in 7 children (5.4%). 24 children (18.3%) had optimal compensation with HbA1c 6.1-7.5%. Hypoglycemic events of different degree were detected in that group 1–2 times per week. 50 children (38.3%) had suboptimal control with HbA1c 7.6–10.0% and 50 children (38.3%) had inadequate glycemic control with HbA1c >10.0%. The table shows HbA1c level depending on age and MDD:

HbA1c, %	Number (%)	Mean age, years	MDD, years
<6	7 (5.3%)	10.6 ± 1.65	1.7 ± 0.29
6.1–7.5	24 (18.3%)	11.2 ± 1	3.2 ± 0.87
7.6–10.0	50 (38.2%)	13.7 ± 0.43	4.7 ± 0.5
>10.0	50 (38.2%)	14.5 ± 0.4	5.5 ± 0.53
Mean 9.6 ± 0.2	Total 131	Mean 13.5 ± 0.29	Mean 4.5 ± 0.28

The results demonstrate that the higher HbA1c level was associated with age and diabetes duration.

Conclusions: The results underline the necessity of optimization of insulintherapy and continuing re-education in children with type 1 diabetes especially in groups with longer diabetes duration. Re-education is also advisable in group with optimal control to decrease the risk of hypoglycemia.

R37

Exploring centre differences in HbA1c levels without prejudice: Redefinition of 'conventional' and 'intensive' insulin treatments

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The principal aims of therapeutic management of the child, adolescent and adult with type 1 diabetes are to allow good quality of life and to avoid long-term complications by maintaining blood glucose concentrations close to the normal range and an HbA1c level under 7%. The number of daily insulin injections, 2 or ≥4, by itself does not necessarily give better results, but the 4-injection regimen allows greater freedom, taking into account that the proper insulin adjustment is difficult before adolescence[1]. Successful glycaemic control in young patients depends mainly on the quality and intensity of diabetes education. Any dogmatism must be avoided. The term 'intensive' and 'non-intensive' refers to the long-term glycaemic goals, not to the model of insulin replacement (number of injections, pumps), diet, blood glucose monitoring, education, etc.[2] The 'conventional' and 'intensive' insulin treatments proposed by the DCCT[3] are no longer acceptable.[2] Dietary recommendations issued over the last few years are the same for diabetic and non-diabetic individuals in order to avoid degenerative diseases. In the twice-daily injection regimen, the allocation of carbohydrates throughout the day is essential.[4] Due to their pharmakokinetic characteristics, rapid-acting and long-acting insulin analogues have specific indications in both the twice-daily injection regimen and the basal-bolus insulin therapy. They improve quality of life, without necessarily reducing HbA1c. Because recent multicentre studies, even those performed in developed countries without financial restriction (cf the results of the three Hvidoere surveys 1995–2005 exploring centres differences), show that treatment of childhood diabetes is inadequate in general and that levels of HbA1c are very different, diabetes treatment teams should individually explore the reasons for failure, without any prejudice or bias.

Refereces:

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R38

Diabetes care from a diabetes nurse perspective – the Swedish experience

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Introduction: A current picture of the diabetes outpatient clinics on a national level can give valuable information, hints and ideas for progress in the further development of diabetes care.
Aim: In order to promote new, effective strategies the Pediatric Society of Endocrinology and Diabetes collected information and experiences from nurses working with diabetes care in Sweden.
Methodology: A questionnaire was sent to all diabetes outpatient clinics in Sweden, both for adult and pediatric patients. It was performed during March–April 2006 in collaboration with Swedish Society for Diabetology. The questions on different issues as resources, staff education and teamwork were answered by the local diabetes nurse. Mediation of viewpoints of care given and possible improvements were encouraged.
Results: Answers were received from 35% of the pediatric clinics, representing the diabetes care of 2608 children and adolescents with T1DM, 15 with T2DM and two with MODY. Most clinics offer four visits/year to a diabetologist and nurse. A dietician is always included in the team and nearly all have a psychologist and almoner available. The level of specific diabetes education of the nurses is in general high and insulin pumps are available at all clinics with a frequency differing from 12–48% of the patients. All clinics offer CGMS when needed and group education for teenagers and other groups. Time and staff resources differ significantly between clinics but screening procedures are performed everywhere. The nurses were satisfied with the team work, collaboration with inpatient care units, information given to school and day-care centre but have a wish for more time and resources. Collaboration with the adult clinics during transition of patients was desired.
Conclusion: The result of the investigation elevated the imbalance of resources between clinics, possibly leading to different results of diabetes care. There is however a high compliance to National Guidelines on diabetes care which are well accepted.

R39

Journey to the Earth's centre: a new experience with a group of diabetic children and adolescents

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Many sport activities are not suggested for diabetic children.
Objective: Demonstrate that type 1 diabetic children can play spelaeology and use physical activity as educational experience. We selected 20 boys and 10 girls (8–18 years) in good metabolic control in MDI. Staff was composed by 10 spelaeologist, two doctors and one nurse. We chose as method a progressive increase of technical difficulties and time spent in grotto. For this reason, only the best 15 children could participate at second and third expeditions. The climate in grotto was: humidity (98–99%) and temperature (2–4 °C). For a correct management of diabetes, we produced a water resistant bag containing a glucometer, sugar and bottle of water and insulin was carried in a dedicated, water resistant and anti-crash bag. The first grotto 'Europa' is characterised by 20 m of subterranean passage and a big chamber with a water-fall, the second 'Forgnone' by a long tunnel with stream and some narrow passages and the third 'Bus di Tacoi' by bottleneck and shafts. We went down until – 200 m from entrance and we reached a green lake at this point. In total we spent 14 h inside the grotto and we ate two meals. We reduced basal insulin the night before, during and the night after the days of expeditions. All participants measured capillary glycaemia before starting physical activity and every 2 h at fixed points in grotto. All children started expedition with glycaemia >150 mg/dl and ate 18 g of complex CHO every 2 h. Only four mild hypoglycaemia were detected and two patients had >300 mg/dl (ketones negative) before starting and corrected by insulin. We confirm that spelaeology could represent a possible sport for children with diabetes and a useful situation for teaching diabetes-related sport management.

R40

Coping with diabetes control at home

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Introduction: Coping with diabetes control is difficult for newly diagnosed and experienced patients alike; the former because of the complex technical requirements they face suddenly; the latter because of constant repetition of testing, insulin administration, dietary vigilance and careful adjustment of every aspect of living. Some of our patients have stored insulin inappropriately, measured it incorrectly and done inadequate home blood glucose monitoring. Some children have to give their own insulin or do home blood glucose monitoring without help or supervision at an age when they cannot be developmentally expected to cope with such complex tasks.
Aims: To establish whether insulin is appropriately stored in the home, and whether paediatric patients are adequately supported by their family in terms of giving injections and doing monitoring.
Methodology: Patients attending the paediatric and the young adult diabetic clinics at the hospital were interviewed. Permission was granted by the Ethics Committee, and informed consent was obtained.
Results: Forty subjects were interviewed; the age varied between seven and 31. Insulin was stored in the refrigerator overnight by 80%, and in the day by 47.5% while 33% carried it with them during the day. Only one family did not own a fridge, and no one stored insulin in the freezing compartment. The four children ≤10 years old, had their insulin measured by their mothers, but one administered the injection himself. Eight of the nine between 11 and 15 years, measured and administered the insulin themselves; but in only two were the dosages checked by an adult.
Conclusion: The fact that only one patient does not have access to a fridge, in a lower socio-economic area, is gratifying. However, 20% of the patients never store insulin in the fridge, in this area of the country where day temperatures are frequently above 30 °C in summer.

R41

Quality of life of children and adolescents with type 1 diabetes in northern Greece

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Type 1 diabetes (DM1) is one of the most frequent chronic disease in children. Although it is an autoimmune disorder, the etiology of DM 1 remains unclear. However, it is accepted that both genetic and environmental factors are major determinants.
Objective: Determinate the frequency of HLA class II alleles (DRB1 and DQB1) in DM 1 patients from northern Greek population.
Methodology: HLA typing was performed on DNA extracted from peripheral blood of 68 DM 1 patients (age 13.1 + 3.7 years) and 181 healthy control subjects using PCR-SSP. The significance of the difference in distribution of alleles between patients with DM 1and healthy control subjects was determined by x^2 methods. Statistical significance was defined as $p < 0.05$.
Results: The phenotypic frequency of high risk determinants for DM 1, DRB1*03, DRB1*04 and DQB1*02 was significantly higher in patients with DM 1 than in control subjects ($p < 0.001$). The frequency of protective allele DRB1*15 was significantly higher in healthy control than in patients ($p < 0.05$). In contrast, there was no significantly difference in the other protective allele (DRB1*16) between patients and control subjects. However, there was 8/68 patients without any susceptibility alleles.
Conclusion: The results of our study are consistent with the international bibliography, in which the genes of the HLA region are accepted as alleles that predispose to DM 1. The statistically significant difference of the HLA DRB1 *03, *04 and DQB1*02 alleles from the respective percentages in the healthy control subjects, indicates these alleles as predisposing factors for diabetes type 1 in the northern greek population. Nevertheless, the fact that, in our study, some persons without any predisposing alleles where found to have DM 1 indicates the role of other genetic factors in the phenotypic expression of the disease that needs further research.

R42

Experience in transitional care clinic – a user group perspective

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Background: A transitional clinic for adolescent diabetics in the local hospital was set up just over 18 months back, for smooth transfer of adolescent diabetics' medical care from paediatric to adult team
Aims: This study was carried out to ascertain the effectiveness of this service against patients' satisfaction and NICE guidelines.
Methodology: Retrospective study covering the period of 18 months involving 38 patients. A list of user group was

populated from our database and individual patient was given a unique number. A carefully designed questionnaire was sent to the user group. After the response time, the data was collected and analysed by our Clinical Effectiveness Unit.
Results: The mean age of study group was 16 years 3 months at transition. All the patients were satisfied with the information received about the service before transition, understood the purpose of clinic and liked the site of the clinic. 93% were satisfied with the timing of clinic (4–6 PM) 79% found the information given about the clinic being adequate. 93% were satisfied with the clinic setup (two teams: (i) an Adult Diabetologist was paired with a PDN, (ii) a Paediatrician was paired with an ADN). 14% wanted the physician from the adult team to be present at all consultation. 79% felt their physical needs and 64% felt their emotional needs were being assessed during transition. 64% were given the choice for age of transfer. Clinic attendance rate was 86.8%.
Conclusion: The key factors for the success of a Transition Clinic being: prior preparation of the patients, prior consultation with patients and parents regarding the services available, the availability of members from both the team, input from CAMHS team, and lastly a convenient time and place of the clinic for user group.

R43

'Don't let an insulin pen plus needle change your life – you are just the same as you were before'. Children's management of their chronic illness – diabetes as a case study

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Introduction: In the light of the call for improved patient-centred care set out in the Children's and Diabetes NSFs and the NHS modernisation agenda, this study uses systematic review and ethnographic methods to describe the experiences of children with diabetes.
Aims: Using type 1 diabetes as a case study, the study aims to identify levers and barriers to person-centred care with children in multi-cultural settings.
Methods: A review to identify existing data on the views of children on their care
A comparison of findings across illnesses to explore whether findings from children with type 1 diabetes might be extrapolated to other paediatric populations
In-depth qualitative fieldwork work to explore the views of children on managing their care. This comprises 2–4 interviews/observations at home, plus clinic observations with each child from a self-selecting sample of approximately 25 children drawn from the population of approximately 140 3–10-year old children receiving care for type 1 diabetes at two clinics in East London. Interviews with the paediatric endocrinologist and diabetes specialist nurses
Results: The review identified 15 relevant studies involving approximately 450 children aged 10 years and younger. Preliminary analysis of these, and early findings from fieldwork, indicate children's perceptions of their illness in terms of disruption, restriction, and difference from others in their day-to-day lives; their understandings of their illness; and the over-riding importance of 'being normal'. Interviews with clinicians, further analysis, and feedback from local dissemination of children's views in the final year of the study will identify implications for practice.
Conclusions: Evidence cited in the Diabetes NSF included little qualitative work to capture patients' views, and none with young children. This study brings together and builds on what is known to date about children's preferences for care, and the implications of these for practice, both for child patients generally and specifically for those with type 1 diabetes.

R44

Group interventions in children and young people with diabetes

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Introduction: This literature review was undertaken to examine more closely the move towards group based interventions in children and young people with diabetes despite a lack of evidence for their effectiveness. With the UK national average HbA1c results exceeding 9% the need to find a more effective way of educating patients and families is clearly necessary.
Aim: The purpose of this review was to identify whether group interventions work in children and young people and if so, why?
Methodology: A transparent, systematic and reproducible review of the literature identified eleven studies which met the inclusion criteria. In order to critically analyse the studies a data extraction summary table was used and level of evidence categorised. Three systematic reviews from the UK were included. Four studies were non randomised controlled trials and four were randomised. Six of these studies were carried out in the US and two in the UK.
Results: Synthesis of these studies suggests the theoretical framework should be based on self efficacy, empowerment, self management and family involvement thorough separate but concurrent sessions. Elements of a successful group intervention involve the need for additional preparation of facilitators, structured education, a maximum of 2–7 per group, a maximum of 3 years age range and for groups to be a part of routine care. Groups may be more effective than one to one interventions as young people of a similar age have the opportunity to interact with each other, generate a number of possible solutions for issues relevant to them and then more confidently put them into practice.
Conclusion: Group based interventions can be as effective as one to one interventions and therefore add to the repertoire of skills available to the paediatric diabetes team for improving health outcomes.

R45

Influence in the adult quality of life having attended diabetic camps in their childhood

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Introduction: It's useful group children to teach them. Summer time is the best period.
Aims: The aims of the study, after having attended summer camps, were (i) to evaluate psychological support; (ii)
to evaluate effect of their attendance (i) and (iii).
to observe which aspects of the quality of life are more affected.
Methods: We sent 2 types of questionnaires. (i) Made by us. (ii) Questionnaire of quality of life specific for diabetes mellitus (EsDQOL) is a questionnire containing 46 items. four subescales. The responses are rated according Likert scale. Satisfaction from one (very satisfied) to five (very disatisfied). Impact and Worry scales from one (no impact or never worried) to five (always impacted or always worried).
Results: 145 answered, 112 had attended and 33 hadńt. Age average 26.22 years.

	Very good	Good	Regular	Bad	Very bad
Memories camps	69.60%	23%	2.51%	5%	0%
Support knowledge	32%	55%	13%	0,1%	0%
Liberty	41%	44%	13%	1%	1%
Live with diabetes	44%	46%	7.30%	1%	1.60%

Apprenticeship	Yes	Not
Self-Injection	78.40%	21.60%
Self-Analyse	81.50%	18.50%
Self-Dosage	86.70%	13.30%
Modification insulin with exercise	92.60%	7.30%
Negative things	40,6%	59,3%

	Attend	Not attend	Attend men	Not Attend men	Attend women	Not attend women	Atte. 1 year	>1year	Rural population	Not Attend rural	Urban	Not Attend urban
Satisfaction	36(2)	29(2)	29(2)	22(1)	36(2)	24(2)	36(2)	24(2)	30(2)	29(2)	36(2)	22(1)
Impact	27(1)	28(1)	26(1)	24(1)	27(1)	28(1)	28(1)	27(1)	27(1)	32(2)	28(1)	19(1)
Worrysocial	7(1)	9(1)	12(2)	12(2)	9(1)	12(2)	12(2)	14(2)	14(2)	10(1)	9(1)	9(1)
Worrydiabetes	8(2)	7(2)	8(2)	8(2)	8(2)	7(2)	8(2)	8(2)	8(2)	8(2)	8(2)	7(2)

Conclusions: It's useful as transference of children to Endocrinology adults, and in the continuity of treatment.
Answers suggest an improvement on psycological adaptation.
All diabetics screened are satisfied with their quality of life, although they are worried with general problems of Diabetes.
We haven't found influency between the attendance and not attendance to the camps in the quality of life.

R46

An innovative, interactive way to engage and educate young people with diabetes

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Introduction: The Children's Diabetes Team aim to provide high quality seamless care for all young people with diabetes and continually strive to improve the service. Currently using group education sessions, a patient-held record incorporating educational literature, patient clinic letters, text messaging and e-mails to assist with this.
Aim: To engage the service users, reinforce the education and allow interaction with the Children's Diabetes Team and other young people with diabetes.
Methodology: An interactive website was launched in October 2005 and is constantly evolving in response to feedback and to keep up to date with new developments. It is in a format which is designed to be attractive to young people and allows them to share experiences (e.g. about using insulin pumps), contribute articles and ideas, as well as enter the quiz. Any questions can be answered by the team and there are links to various relevant websites for more information. The website contains details of latest developments and device/drug alerts. The educational leaflets are all available, including guides to insulins, top tips, sport/exercise and carbohydrate counting tables. There are details of social activities and events, and suggestions from the young people are actively encouraged. The teenagers section contains information about diabetes and complications as well as alcohol, sex, drugs, smoking, driving and employment. These subjects also contain information which is not diabetes specific such as health promotion and interview technique.
Results: The website has been a success with the young people as shown by their comments on the service user questionnaire and their use of the website.
Conclusion: The website could be replicated in other areas and be made relevant to the needs of the local population. It requires no extra funding, but is reliant on the enthusiasm and experience of the medical secretary, the Children's Diabetes Team and the young people themselves.

R47

Diabetic children's camp session medical and psychological outcomes

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We studied 51 campers from the Georgian Diabetic Camp Summer Session 2005, 23 boys and 28 girls. Mean age was 13.9 ± 1.6 years; the duration of Diabetes Type 1 was 4.2 ± 1.9 years. All the campers get 4 insulin shots daily and 3 meals +3 snacks diet. Standard blood glucose profiles (BGP) have been recorded daily (before meals and at bedtime) during 10 day session. We used Spielberger's State Anxiety and Buss-Durkee Hostility Inventories for the psychological assessment of campers reaction on the camp session. In nine campers BGP-s was within normal range (70–120 mg/dl) from the first day and till the end of the camp session (group #1). Situational anxiety level significantly increases and became adequate to personal anxiety level in this group. In 25 cases BGP-s remain elevated during the first 4 days of the session and lowered to normal starting from 5th day and remain so till the end of the session (group #2), Situational anxiety level significantly decreases in the group #2 at the end of the camp session, as well as personal anxiety level. In 17 cases BGP-s never reached normal values (group #3). Personal anxiety level significantly decreases in this group. Diversity of the situational anxiety changes reflects that not all the campers can equally adjust to the camp session. No significant hostility changes have been observed in campers during the camp session. Comparative analysis between the groups shows that in the group #1 the level of verbal hostility was high. In the group #3 physical and indirect hostility remains low, the same as negativism. In conclusion, camp session might have a positive reflection on the camper's medical and psychological state, but depends on the individual dispositional parameters.

R48

Psychological and social attitudes to diabetes in children and youths in Poland – cross-sectional study

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Introduction: Psychological attitudes toward diabetes seem to play major role in future treatment success. Social support is essential to change disadaptative attitudes.
Aim: Diagnose post prevalent attitudes toward diabetes in children and youths with recent diabetes diagnosis.
Materials and methods: The mean age of children: 10.0 ± 8.61 years, 47% males. Most of subjects 40.4% came from small cities (< 100000). Respectively 24.5% and 35.1% came from bigger cities and villages. None of the subjects reported diabetes in brother or sister, however 6% of subjects reported diabetes history in parents. Demographics and socio-psychological questionnaires were filled by parents in subjects below 12. The cross-sectional study was performed in 2005 in pediatric centers in Poland. 550 questionnaires were analyzed.
Results: The reaction to the diagnosis of diabetes was measured in questionnaire where subjects were to grade the concordance with statements being answers to the question: 'How would you agree to the description of your reaction to the diagnosis of diabetes': Most of respondents (69.3%) perceived the diagnosis as a new challenge that can be dealt with. As unjustifiable (unfair) and upsetting the diagnosis was perceived by 34.4%. Less respondents saw the diagnosis of diabetes as catastrophe (disaster) (14.1%),

"punishment coming from bad fortune 'fate' (13.6%). Diabetes in general was perceived as "condition I know a lot about, I know how to deal with" (50.2%) however it was cause of sadness and worry for 55.2% respond. 44.7% found their diabetes to be mainly problem of their parents and doctor (23.6%). Minority of subject rejected to answer that question (12.7%). Youths show less awareness of sadness than the adults.

Conclusion: Diagnosis of diabetes leads to crisis situation in youths and parents of younger children. Whatever the emotional status is, the diabetes is still frequently perceived as a challenge. Youths usually seeks help from their parents.

R49

Group visits: a new and challenging approach in the medical checkups of children with diabetes

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Aims: (i) To achieve a better communication between the paediatric diabetes team and children with diabetes and their parents. (ii) To increase productivity and efficiency in the outpatient attendance of these patients.

Methods: A total of 8-10 children with diabetes and their parents are seen all together by the diabetes team (consultant paediatrician, diabetic nurse, dietician, child psychologist and medical receptionist) during 1½ hour in the outpatient department: (i) The group visit (GV) is chaired by the child psychologist; (ii) The paediatrician does the medical checkup of each patient in front of the group (an eventual physical examination is done in a private side room); (iii) The dietician keeps records and advises if necessary on diet issues and (iv) The medical receptionist makes the new appointments. Half an hour before the start of GV the medical receptionist registrates weight, height and blood pressure. The diabetic nurse controls the injection places. The child psychologist summarizes questions of patients and parents on a flip chart. All patients have to sign a form of confidentiality. Before starting with GV's all members of the diabetes team followed an intensive 2-day course led by E. Noffsinger, the founding father of GV's in the U.S.A. On the basis of this training we developed a detailed plan of action on how to organise GV's with our diabetic patients.

Results and conclusions: So far we have done eight GV's: 70–80% of the patients and their parents are satisfied about this new kind of collective checkup : they get better information from the members of the diabetes team, they learn from experiences of other patients and parents and they overall spent less time in visiting the paediatric outpatient department. Our pediatric diabetes team is enthusiastic about the gain in productivity and efficiency.

R50

Telemedicine in pediatric endocrinology and in the prevention of childhood obesity

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Telemedicine is used for the evaluation and treatment of Pediatric Endocrine disorders and obesity at distant sites. Using several I.S.D.N. (Integrated Services Digital Network) lines or I.P. (Internet protocol) over a dedicated T1 line and a compact video camera and receiver combination at each end, this method can eliminate travel time for both medical team and family alike. History is obtained during discussion online and the use of wide angle or close up views allow inspection of general status as well as details such as skin lesions. Local medical personal performs palpation if necessary and heart and lung sounds can be transmitted using specialized apparatus. Preordered laboratory testing, such as Hg1AC is sent by fax or communicated at the time of the telemedicine visit and blood sugar readings can be downloaded locally and transmitted to the specialty site. With medical personnel, such as the local physician or nurse practitioner, in the patient's room, subspecialty consultation serves as a one on one educational experience. A specialty team of nurse educator, dietician and pediatric endocrinologist can be utilized for such a visit when such teams are not locally available. On the other hand, local medical teams dealing with less technical areas can be educated via the telecommunication connection by the specialty team so the providers at the distant site can ultimately become more self sufficient: this approach is used as an approach to the prevention of type 2 diabetes and childhood obesity using a curricula developed at our center. Family, patient and referring physician report a high degree of acceptance for the program. Lastly, the telecommunication setup may be used for access to didactic conferences such as Grand Rounds. These methods all allow access to high quality specialty care and education at remote sites of low population density.

R51

Improving diabetes treatment for children: experiences from a participatory action research

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In a qualitative research, with children with diabetes between the ages of seven and fourteen, we explored the perspectives of children on their illness and its treatment, and the consequences for their daily life. The study is an illustration of the agency and competence of children with diabetes in their dealing with and thinking about their disease. Children with diabetes perform acts that resemble the work of doctors, which contrasts sharply with their position as a child and care receiver. The study reveals that parents and medical professionals are dependent on the cooperation of the children to achieve their goals. Based on these results we started a second study. Characteristic of the project is that children act as co-researchers; they define the main problem concerning their diabetes, analyse this and develop an intervention for it. Children will also do the evaluation. Parents and medical professionals are involved, but are not the main focus of the project. The children have defined lack of understanding in their surroundings as their main problem. This lack of understanding concerns three issues: (i) a misunderstanding about the disease itself, (ii) a misunderstanding about the impact the disease has for the daily life of children, and (iii) adults do often not acknowledge the knowledge and competence of children. Together with the children we developed three interventions: a book, a rap, and a TV-campaign. Besides a problem definition from the child's point of view, and educational material that children think is best, the study resulted in knowledge about how children with diabetes actually live their life, about their competence in balancing treatment with daily live, and about conditions and barriers that work against or for child participation, in healthcare and in research.

R52

Non pharmacological management of painful diabetic neuropathy in paediatric patients

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Management of pain is a difficult task in children with painful diabetic neuropathy. The drugs available are limited in efficacy and

tolerability. There is a need, therefore, to study non-pharmacological methods of pain relief in this population. This paper studies the effect of transcutaneous electrical nerve stimulation (TENS) on painful neuropathy in pediatric patients of diabetes mellitus. 15 pediatric diabetic patients receiving five sittings of TENS on daily or alternate day basis were compared with 15 age-matched, disease – matched patients who were given daily oxcarbamazepine and five sittings with sham electrodes. Glycemic control was maintained with insulin as per protocol. Pain scores reduced significantly in both groups, but much more so in the TENS group (from 4.60 ± 0.54 to 2.40 ± 0.54) than the sham electrodes + oxcarbamazepine group (from 4.40 to 0.54 to 3.60 ± 0.54). A significant change was seen in health distress and disease intrusion scores in the TENS group. This study demonstrates the beneficial effect of low dose TENS in pediatric patients with painful neuropathy due to diabetes mellitus.

R53

Renal hypertrophy as the driving dysfunction in the pathogenesis of diabetic nephropathy

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Introduction: Renal hypertrophy and hyperfiltration characterize the early phases of diabetes and precede the development of microalbuminuria. Whether it is hypertrophy or hyperfiltration to came first is presently still unknown.

Methods: We evaluated, during the same day, kidney volume and glomerular filtration rate in 146 individuals affected by type 1 diabetes for more than 4 years and normal urinary albumin excretion. All the individuals were then monitored for the development of microalbuminuria. Kidney volume and glomerular filtration rate were revaluated in a subset of 68 individuals who remained normaoalbuminuric 4 years after baseline.

Results: During follow-up, microalbuminuria developed in 27 of 146 individuals considered for the study. At baseline kidney volume (312 ± 52.S6 vs 281 ± 46.6 ml (1.73 m^2)-1, $p < 0.05$), but not glomerular filtration rate, was increased in patients predisposed to develop microalbuminuria. Altogether, the risk of progression to microalbuminuria was higher in patients with increased kidney volume, $p = 0.0058$. In the subset of 68 patients that repeated the evaluation, kidney volume remained stably elevated in patients destined to develop microalbuminuria ($p = 0.003$). In parallel, rate of decline of glomerular filtration rate was faster in patients predisposed to develop microalbuminuria ($p = 0.01$).

Conclusion: Our results support the hypothesis that in the early stages of diabetic nephropathy renal (tubular) hypertrophy is primary dysfunction and that GFR adjusts accordingly. Altogether these findings suggest that by normalizing kidney volume at the onset of diabetes it should be possible to prevent the development of diabetic nephropathy.

R54

Lipid composition of serum in children with type I diabetes mellitus

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Lipid disorders play important role in pathogenesis of atherosclerosis and vascular complications in diabetic patients.

Aim: To study the qualitative and quantitative composition serum lipid in children with type 1 diabetes mellitus (T1DM) and to investigate correlations between lipid levels and postprandial hyperglycemia (PPH) level, duration of diabetes, and degree of its compensation.

Objects and methods: A total of 100 children with T1DM and 100 healthy children (control group) aged 6–16 year. were investigated. Levels of total cholesterol (LDL, low-density lipoprotein), high-density lipoprotein (HDL, alpha-cholesterol), triglycerides, atherogenic coefficient (AC) (AC = (LDL-HDL)/HDL), $HbA1_c$, and postprandial glycemia were measured. Statistic analysis: ANOVA, Spearmen's correlation (r_s).

Results: Lipid disorders (LD) was found in 39% children with T1DM and 23% healthy children ($p = 0.01$). Hypercholesterolemia was diagnosed in 33 (33%) patient with T1DM and in 8 (8%) healthy children ($p < 0.01$), decreased HDL and elevated AC – in 39 (39%) and in 8 (8%) children respectively ($p < 0.01$). High triglyceride levels were diagnosed in 13 (13%) and 5 (5%) children ($p = 0.04$) respectively. There was a positive correlation between lipid concentration and duration of diabetes ($r_s = 0.65$, $p = 0.02$) and with PPH ($r_s = 0.9$, $p = 0.01$). There was no correlation between the lipids and HbA1c levels. LD has been associated with vascular diabetic complications: retinopathy (28%), nephropathy (17%) and hayropathy (9%).

Conclusions: Children with TIDM (more frequently than healthy children) were found to have higher levels of atherogenic lipid fraction and lower antia-therogenic fractions. The changes in the lipid composition are associated with duration of disease, the postprandial hyperglycemia level and vascular diabetic complications.

R55

Lipid profile in children with type I diabetes mellitus according to glycemic control and disease duration

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Diabetes mellitus type I (DM) constitutes a major risk for atherosclerosis and cardiovascular disease in later adulthood. Altered lipid profile is an important aspect of this complication. The purpose of this study was to investigate total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein LDL and triglyceride (TG) levels in patients with diabetes mellitus as well as how those may be related to glycemic control (HbA1C) and illness duration. Our study group comprised 15 children (mean age11.75 ± 4.3years) with type I diabetes mellitus of variable duration (2 months–7.8 years). Subgroups consisted of children with disease duration < 3 years (group I- 9 children) or more than 3 years (group II- 6 children) and those with adequate (n = 5) (group I -HbA1C < 7%) or inadequate glycemic control (n = 10) (group II- HbA1C > 7%). Blood samples were drawn and TC, HDL, LDL and TG were determined. The Mann–Whitney test was employed for comparative purposes. Children with adequate glycemic control displayed similar lipid values compared to the other group (TC median = 174 mg/dl vs. 176.5 mg/dl, respectively, HDL median = 68 mg/dl vs. 62 mg/dl, LDL 95 mg/dl vs. 100 mg/dl and TG median 91 mg/dl vs. 78 mg/dl, Mann–Whitney $p > 0.05$). The same insignificant differences were found when results were classified according to the duration of the disease (group I -short duration vs. group II- long duration, TC median = 174 mg/dl vs. 88 mg/dl, HDL median = 62 mg/dl vs. 67.5 mg/dl, LDL median = 96 mg/dl vs. 110 mg/dl, TG median = 70 mg/dl vs. 61 mg/dl, Mann–Whitney $p > 0.05$). It can be deduced that in childhood in contrast to adulthood studies, DM duration and adequate glycemic control do not seem to have

an effect on the children's lipid profile. However, further studies with longer disease durations must be conducted to ascertain this.

R56

Growth changes in children and adolescents with type 1 diabetes mellitus

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Normal growth is a continuous process with some age, sex and pubertal variations. In DMT1 children additional factors like age of onset of diabetes, duration of diabetes, coexisting diseases and metabolic control of diabetes can potentially influence growth.

Aim: Evaluation of the growth and yearly growth rate in children with DMT1 in the time of the diagnosis, a year and 4 years after the diagnosis and evaluation of effect of glicemic control on growth and yearly growth rate in the same children.

Methods: Sixty-six children (35 boys and 31 girls) with type 1 DM, whose diagnosis was made 1994–2001 years, were studied over a 5-year period. Every 4 months glycemic control was assessed by measuring HbAlc. Height was measured with stadiometer, pubertal status was determined by physical examination. Growth was assessed at diabetes onset, one and 4 years later, and plotted on our own national standards.

Results: At the onset of diabetes (1995–1999 years) percentage of insulin-dependent diabetics at the diagnosis in each heigt-centiles group were as folows: 17% were below 25 centile, 58% between 25–75 centile, 25% above 75 centile. One year after diagnosis 20% patient have been below 25 centile, 57% between 25–75 centile, 23% above 75 centile. Four years after diagnosis 30% have been below 25 centile, 53% between 25–50 centile , 17% above 75 centile. During the first year of diagnosis 37% boys and 31% girls had a yearly growth rate below 25 centile, 38% boys and 47% girls between 25–50 centile , 25% boys and 22% girls above 75 centile. Yearly growth rate the fourth year after diagnosis was: 38% boys and 50% girls below 25 centile, 40% boys and 36% girls between 25–75 centile and 22% boys and 14% girls above 75 centile.

Conclusions: At the time of diagnosis diabetic children were taller than normal children of the same age and sex. Significant retardation of growth occurred after 4 years of diabetes. Growth of a younger subgroup was affected more by diabetes than growth of the older subgroup. Our study did not show any statistically significant association with metabolic control and growth velocity of children with diabetes.

R57

Predictors of persistence and progression of diabetic nephropathy in adolescents

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Introduction: Nephropathy is a serious complication of diabetes mellitus in adult, but predictors of progression of diabetic nephropathy in adolescents are poorly known.

Aims: To identify predictors of progression of diabetic nephropathy in adolescents with type 1 diabetes.

Methodology: We analyzed data from a prospective cohort study of type 1 diabetic adolescents with diabetic nephropathy. The study included 41 type 1 diabetic adolescents with diabetic nephropathy aged (mean ± SD) 16.0 ± 1.5 years, with duration of diabetes 11.4 ± 3.1 years, HbA1c 10.3 ± 1.7%. 22 out of 41 had microalbuminuria [urinary albumin excretion (UAE) – 30–300 mg/day] and 19 matched on age, duration of diabetes, sex patients had macroalbuminuria (UAE > 300 mg/day). Subject were monitored for a mean of 6 years (following parameters: age, age at onset of diabetes, duration of diabetes,initial HbA1c, sistolic and diastolic blood pressure, urinary albumin excretion). All patients were treated with angiotensin converting enzyme inhibitors during the study.

Results: After 6 years, of the 22 with initial microalbuminuria, 5 (22%) regressed to normoalbuminuria , whereas microalbuminuria was persistent in 15 (69%) and progressed to macroalbuminuria in 2 (9%). Of the 19 who had initial macroalbuminuria, microalbuminuria developed in 4 (19%), macroalbuminuria was persistent in 15 (79%). Multiply regression analysis showed that only baseline UAE (R^2 = 51%, $p < 0.01$) was significantly and independently associated with progression macroalbuminuria, whereas initial HbA1c (R^2 = 39%, $p < 0.02$) was independent factor of progression microalbuminuria.

Conclusion: The persistence or progression of diabetic nephropathy is influenced both by poor metabolic control and initial urinary albumin excretion in adolescents.

R58

Biliary sludge in a 5 year-old with recurrent ketoacidosis

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A 5 year old boy, weighing 14 kg with no family history of diabetes, presented in frank diabetic ketoacidosis. On examination, he had rachitic features, and abdomen was protuberant. There was mild epigastric tenderness. Ketosis was corrected within 24 hours with 58 units insulin, and the patient discharged after 72 hours on a 3-dose regime (Aspart-regular – premixed aspart) totaling 19 units/day. He returned after 3 days with moderate ketonuria, but no evidence of acidosis. The parents were adamant that he had followed the prescribed diet pattern and not missed any insulin dose. Two such episodes recurred within 2 weeks; each accompanied by severe upper abdominal pain, and treated successfully by IV insulin infusion over 12–24 h. On detailed investigation, ultrasonography revealed multiple gall stones. This finding was confirmed a week later. After initial difficulties for the first 2 weeks, the patient stabilized on 15 units/day of aspart insulin, in three divided doses. Frequent abdominal pain prompted a surgical referral for cholecystectomy, but a preoperative scan revealed no abnormality. The earlier finding was retrospectively thought to be biliary sludge. Adult patients of diabetes frequently get decompensated because of cholecystitis associated with cholelithiasis, and biliary sludge is a not infrequent finding on ultrasonography. This case reports highlights the occurrence of biliary sludge in paediatric patients of diabetes. Cholecystitis and cholelithiasis/biliary sludge should be ruled out in any type 1 diabetic patient presenting with recurrent ketosis.

R59

Differences between acidosis in diabetes mellitus associated with mitochondrial gene mutation and that in type I diabetes mellitus

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Introduction: Initial treatment for diabetic ketoacidosis is still controversial to prevent diabetic brain edema. It is crucially important to evaluate the type of acidosis for the appropriate initial fluid therapy.

Aim: An aim of this study is to compare the difference of diabetic acidosis between in patients associated with mitochondrial gene mutation and in patients with type I diabetes mellitus (T1DM).

Patients: Three patients ranging in age from 13 to 19 years old at the onset of acidosis showed MIDD (maternally inherited diabetes

and deafness) with mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS). Other five patients ranging in age from 1 to 12 years were T1DM with positive anti-GAD antibodies.

Results: Patients with MIDD showed blood sugar levels from 393 to 654 mg/dl, blood ketone body from 262 to 850 μmol/l, and pH from 7.05 to 7.287. Blood lactic acid levels in the respective patients were 76, 145, and 179 mg/dl. On the other hand, their values in five patients with T1DM were from 248 to 637 mg/dl, from 1069 to 3000 μmol/l or higher and from 6.94 to 7.27, respectively. Lactic acid levels were from 12 to 21 mg/dl. Type of acidosis were ketoacidosis in the patients with T1DM and lactic acidosis in patients with MIDD, respectively.

Conclusion: At the diabetic acidosis, type of acidosis should be clarified. Initial fluid therapy should be started with fluids not containing lactic acid in patients with lactic acidosis such as MELAS.

R60

Characteristics of Krasnoyarsk children with diabetic ketoacidosis

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Introduction: Diabetic ketoacidosis (DKA) is a frequent reason for hospital admission of children with newly diagnosed diabetes and the most frequent cause for rehospitalization of children with poorly controlled diabetes.

Aim: To evaluate the frequency of DKA hospitalization for pediatric patients and resources for its decrease.

Methodology: Subjects included children < 18 years who hospitalized with DKA in the pediatric diabetes care unit at the City Hospital from January 2003 to December 2005. The study entry criteria were venous pH < 7.30 and/or bicarbonate < 15 mmol/l, ketonuria. Patients were treated with fluid replacement and insulin infusion. The patients were analyzed according to demographic data, clinical and laboratory findings.

Results: One hundred and twenty four DKA patients (72 boys) were hospitalized during the study period. Pediatric DKA accounted for 1739 hospital days (median length of stay 14 days). 38 children (30.6%) were with new-onset diabetes. The frequency of DKA at onset of diabetes was equal 92%. The risk of presenting with DKA was the highest among patients < 5 years old. 86 DKA children were with established diabetes and duration of disease from 2 months to 12 years. Compared with single-episode DKA, recurrent DKA (46.2%) was highest among children with poorly controlled diabetes, peripubertal and adolescent boys, children with difficult family circumstances. Children with recurrent DKA may benefit from comprehensive care provided by a diabetes team including pediatric endocrinologists, diabetes educators, mental health professionals, and social workers to reverse the chain of events resulting in poor metabolic control.

Conclusion: The carried out research was shown high frequency of DKA at onset of diabetes, recurrent DKA among adolescent boys and children with difficult family circumstances. Opportunities exist to reduce DKA hospitalizations for children with diabetes with clinical and policy interventions targeted to this population.

R61

The occurrence and chosen risk factors analysis of DKA among children with new onset of DMT1 from Upper Silesia (Poland)

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Especially in children and in the subjects newly diagnosed DKA is still the potentially life-threatening complication of DMT1.

Aim: The aim of the study was the assessment of the DKA frequency and the analysis of chosen risk factors among children with the new onset of DMT1.

Material and methods: The group of 173 children hospitalised between 2004 and 2005 with the onset of DMT1 from highly urbanised region (Upper Silesia) were followed up. The following features of DM onset were analysed: clinical symptoms, the duration of symptoms, month of onset, diseases directly preceding the onset, the numbers of visits preceding right diagnosis and biochemical parameters: venous pH, glycaemia and HbA1c (HPLC).

Results: A total of 57 children (33%) present DKA at the onset of DM. The mean age at the onset of these children (8.4 ± 4.9 years) was significantly lower than mean age of the whole group (9.2 ± 4.9 years). The highest number of DKA episodes was observed in children below 4 years ($p < 0.001$). Apart from the classical symptoms of DM, nocturnal enuresis was the most frequent symptom reported at the onset (27% children aged 5–9). The correlation between duration of symptoms and venous pH has not been observed. The occurrence of DKA was constant in spite of seasonality of incidence of DMT1. The right diagnosis at the first visit received 17 subjects (32%), at the second 25 subjects (46%) and at the third or next visit 11 subjects (24%). There were no correlations between delaying of diagnosis and both severity of DKA and age of children.

Conclusions: At the time of diabetes initial diagnosis DKA episodes have been reported in 1/3 of cases. Among analysed risk factors of DKA only the young age has been evidenced as significant in newly diagnosed children.

R62

HLA-antigens and necrobiosis lipoidica diabeticorum in children with type 1 diabetes

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Introduction: Necrobiosis lipoidica diabeticorum (NLD) is a rare chronic cutaneous complication of diabetes mellitus.

Aim: To investigate whether HLA-antigen frequencies are different in diabetic patients with and without necrobiosis lipoidica diabeticorum.

Methodology: We studied 100 type I diabetics, six with and 94 without necrobiosis lipoidica diabeticorum and 150 normal control subjects. HLA antigens were determined in all 100 children (50 girls and 50 boys , aged 5.9 ± 2.3 years). The age of the onset of diabetes varied from 3 months to 6 years (mean 2.7 ± 1.1). Their mean glycosylated hemoglobin level was 9.9 ± 5.0% (7.3–16.6%) Standart microlympho-cytotoxical test with a broad spectrum of typing antisera to 59 HLA-antigens A, B, DR, DQ-locuses was used.

Results: Compared to controls type I diabetics had increased frequencies of B8, DR3, DR4 and DR3/4; decreased frequencies of DR2, DR5 and DR7. All diabetics with necrobiosis had DR3/4 phenocypes which associated with more expressed beta-cell destruction and severe course of diabetes. Diabetics with

necrobiosis differed from diabetics without necrobiosis only in that HLA-A2 was significantly less frequent in patients with necrobiosis.

Conclusion: The carried out research is suggested that the lack of major differences between patients with and without necrobiosis argues in favour of the role of metabolic and/or vascular rather than genetic factors in the aetiology of necrobiosis.

R63

Insulin secretory capacity and insulin resistance at diagnosis in Japanese children with type 2 diabetes mellitus

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Introduction: In patients with type 2 diabetes mellitus (T2DM), insulin resistance and insulin secretory abnormality are both present. It is known that hyperinsulinemia associated with obesity is initially present, and progresses to insulin secretory failure with aggravation of hyperglycemia. However, Japanese studies have demonstrated that Japanese adults with T2DM are not markedly obese and exhibit impaired insulin response to the elevation of blood glucose. We examined insulin secretory capacity and insulin resistance at diagnosis in Japanese children with T2DM to expand knowledge of the pathophysiology of this disease.

Methodology: A total of 110 patients with T2DM (M/F = 56/54, age 12.8 ± 1.7 years) were divided on the basis of % overweight at diagnosis, i.e. group A (n = 17): 20% >, group B (n = 37): 20%–39%, group C (n = 30): 40–59%, group D (n = 26): 60%≤. A total of 84.5% of the subjects exhibited obesity. Indicators of insulin secretion and insulin resistance were compared among the groups at diagnosis.

Results: (i) Average concentration of FPG was significantly higher in groups A and B than in group D (238 ± 80, 192 ± 65 vs. 184 ± 47 mg/dl). Average value of HbA1c was significantly higher in group A than in groups C and D (11.0 ± 2.2 vs. 8.8 ± 1.5, 8.9 ± 2.1%); (ii) Average fasting IRI concentration was significantly higher in group D than in groups A and B (42 ± 24 vs. 15 ± 10, 24 ± 12 μU/ml). Overall, 49.1% of the patients exceeded 25 U/ml in fasting concentration of IRI; (iii) Average value of HOMA-β was significantly lower in group A than in group D (43 ± 33 vs. 156 ± 117). Most obese patients exhibited hypersecretion of insulin and (iv) Average value of HOMA-IR was significantly higher in group D than in groups A and B (18.1 ± 10.9 vs. 8.8 ± 5.5, 10.3 ± 6.4). The overall frequency of patients with HOMA-IR < 3.0 was only 3.6%.

Conclusion: Most children with T2DM initially had insulin resistance regardless of % overweight and insulin resistance gradually increased accompanied by increase in this percentage. The majority of obese children with T2DM had hyperinsulinemia at diagnosis, while some nonobese children with T2DM initially exhibited impaired insulin secretion. More severe glycemic decompensation at diagnosis in nonobese patients may be due to a combination of insulin resistance and insulin secretory abnormality.

R64

Can body mass index, waist circumference identify children with the metabolic syndrome?

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Objective: To determine in children the association between waist circumference (WC), body mass index (BMI) and insulin resistance determined by homeostasis modeling (HOMA-IR) and components of the metabolic syndrome, including lipid profile and blood pressure (BP).

Methods: A total of 279 subjects (184 boys) aged 6–18 years and matched for sex and age underwent a anthropometric measurements; 140 were obese; 33, overweight; and 106, nonobese. BMI, WC, BP, and Tanner stage were determined. An oral glucose tolerance test, lipid profile, and insulin assays were performed. Overweight and obese were defined according to BMI reference norm of Group of China Obesity Task Force.

Results: There was univariate association ($p < 0.01$) between WC and BMI (r = 0.96), Tanner stage (r = 0.458), systolic BP (r = 0.603), diastolic BP (r = 0.584), high-density lipoprotein cholesterol level (r = -0.340), triglyceride level (r = 0.377), total cholesterol level (r = 0.170), and HOMA-IR (r = 0.587). There was univariate association ($p < 0.01$) between BMI and Tanner stage (r = 0.449), systolic BP (r = 0.588), diastolic BP (r = 0.571), high-density lipoprotein cholesterol level (r = -0.363), triglyceride level (r = 0.369), total cholesterol level (r = 0.170), and HOMA-IR (r = 0.587). Multiple linear regression analysis using HOMA-IR as the dependent variable showed that BMI (β coefficient = 0.295) and triglyceride (β coefficient = 0.888) were significant independent predictors for insulin resistance adjusted for systolic BP, diastolic BP, WC, Tanner stage, cholesterol, high-density lipoprotein cholesterol level in total subjects. In the nonobese subgroup, however, WC (β coefficient = 0.047), triglyceride (β coefficient = 0.827) and cholesterol (β coefficient = 0.311) were significant independent predictors for insulin resistance adjusted for systolic BP, diastolic BP, BMI, Tanner stage, high-density lipoprotein cholesterol level. In the overweight and obese subgroup, BMI (β coefficient = 0.356) and triglyceride (β coefficient = 0.886) were significant independent predictors for insulin resistance adjusted for systolic BP, diastolic BP, WC, Tanner stage, cholesterol, high-density lipoprotein cholesterol level.

Conclusions: Waist circumference and BMI are predictor of insulin resistance syndrome in children and adolescents in different groups. In clinical practice, WC and BMI should be measured and calculated simultaneously to help identify children at risk.

R65

C-peptide levels in obese children

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Obesity in children is a growing concern for the physicians. The diagnosed insulin resistance may be a motivation for stating high risk for the health and also as an indication for the treatment. An aim of our study was to evaluate c-peptide levels in the group of obese children as a possible indication for the medical treatment. The study group consists of 19 children, 10 boys and 9 girls, mean age 9.9 ± 3.4 years. Height was in the range of 60–97 percentiles according to the National Growth Charts for the Georgian children. Weight in all cases far exceeded the normal range, starting from + 2.4 SDS and upto +3.9 SDS by the same charts. No health related problems has been stated in any patient. Familial history of Diabetes Type 2 has been documented in 7 cases and history of Obesity in 11 cases. C-peptide levels were measured in all patients fasting and 1 hour after the high carbohydrate breakfast, as well blood glucose, fasting, 1 hour and 2 hours after the meal. Blood glucose remains within normal range for all patients in all three points: 4.9 ± 0.4, 5.5 ± 1 and 5.4 ± 1.0, all numbers in mmol/l. Fasting C-peptide levels were normal in five cases–1.83 ± 0.09 ng/ml, and significantly elevated in 14 cases–5.57 ± 2.08 ng/ml. C-peptide levels in 1 hour after the breakfast were significantly elevated in all cases – 11.5 ± 5.12 ng/ml.

Significant correlation (r = 0.8) was stated for Weight and C-peptide fasting levels. We may conclude that children with severe obesity and elevated fasting C-peptide levels might be the first line candidates for the medical treatment.

R66

Characteristics of obese children who were referred to the pediatric endocrinologist for assessment

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Aim: To evaluate characteristics of patients who were referred to our pediatric endocrinology clinic for obesity.
Methods: The records of 374 (178 F, 196 M) patients referred between 2000 and 2006 were reviewed in this retrospective analysis. Body mass index(BMI) $>95^{th}$ percentile was defined as obesity. Only patient with primary obesity were included. History, family history, clinical and laboratory data were assessed from the medical records at the first endocrine evaluation.
Results: The mean age of 290 (136 F, 154 M) patients with primary obesity at the first endocrine visit was 9.5 ± 3.6 years ranging from 1–17.2 years. Forty-four percent of patients were prepubertal. Parental BMI values showed that 40% of mothers and 50% of fathers were obese (BMI > 30 kg/m^2). Family history was positive for obesity in 47.4%, diabetes mellitus in 51.6%, hypertension in 27.2%, and cardiovascular disease in 18.1%. Acanthosis nigricans was present in 17.1% of patients. Impaired fasting glucose was found 1.4% of patients, hyperinsulinism in 23.1% and impaired glucose tolerance 4.8%. Total cholesterol and triglycerides were elevated in 39.3% and 13% of patients, respectively. Age of patients with insulin resistance was significantly early in patients with family history of diabetes ($p = 0.001$) and obesity ($p = 0.008$).
Conclusions: Obesity starts early ages. Hyperinsulinemia and dyslipidemia are often present at younger ages. High prevalence of parental obesity and type 2 diabetes show that family based interventional programs are needed for management in childhood obesity.

R67

Incidence of glucose and lipid metabolism disturbances in overweight children and adolescents in Croatia

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Prevalence of obesity in children and adolescents is reaching epidemic proportions, and an increase in incidence of type 2 diabetes (DM2) is shown. In overweight population disorders of lipid metabolism are frequent too. Both disorders are risk factors in occurrence of cardiovascular complications.
Aim: The aim was to define incidence of impaired glucose tolerance (IGT), DM2, hypercholesterolemia and hypertriglyceridemia in overweight children in our population.
Subjects and methods: In 270 children (147 girls, 123 boys) BMI above 85%, age 5–19 years (11.97 + 3.0), a standard OGTT was performed. Cholesterol concentrations were determined with enzymatic CHOD-PAP method, triglyceride levels with enzymatic GPO-PAP method. Normal values were defined by LRCP, and values above 95. centile for age and sex were considered increased.
Results: IGT was found in 11 children (4.08%), eight boys and three girls, and DM2 in two boys (0.7%). Increased cholesterol levels had 56 children (20.7%) (33 boys, 23 girls). The proportion of the boys with increased cholesterol was significantly higher than of the girls ($p < 0.024$). Increased triglyceride levels were found in 83 children (30.7%) (41 boys, 42 girls). Increased concentrations of triglycerides and cholesterol were found in 28 children (10.4%, 14 boys, 14 girls).
Conclusion: Incidence of IGT in overweight children in our population was 4.08%. It is smaller than in USA (20–25%), and in Western Europe (6.3–11%), it resembles most to that of Southern Europe (4.5%). Incidence of DM2 in our sample was 0.7%, smaller than in USA (4%), Western Europe, and higher than in Southern Europe (0.2%). Data of increased cholesterol and triglyceride levels in overweight children (20.7%, and 30.7%), are close to those in literature. In overweight children performing of OGTT and determination of lipid levels in serum is indicated. By body weight reduction and dietetic regime, the risk of DM2 and cardiovascular complications would be reduced.

R68

Obesity is associated with increased risk of metabolic syndrome, an anomaly recognized mainly in adults

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Obesity is associated with increased risk of metabolic syndrome, an anomaly recognized mainly in adults. Its components include abdominal obesity, hypertension, dyslipidaemia, hyperinsulinism with insulin resistance, type 2 diabetes and coronary disease. The objective of the study was to assess metabolic disorders and occurrences of metabolic syndrome in obese children and adolescents as well as to analyze them in the aspect of family histories of such disturbances.
Material and Methods: The study included 95 obese children (BMI > 97%) at the age of 6–18. We evaluated their BMI, waist circumference, hip circumference, waist-to-hip ratio (WHR), mean systolic and diastolic blood pressures, concentrations of total cholesterol, HDL cholesterol, triglycerides, glucose and insulin in OGTT; apart from that fasting insulin to fasting glucose ratio (FIGR) was calculated. All those factors were analyzed in the aspect of positive family histories of obesity, type 2 diabetes, and circulatory disorders.
Results: We found an occurrence of at least one metabolic disorder in 65% of the study subjects, namely, abnormal lipids metabolism in 58.9% of the children, abnormal carbohydrate and insulin metabolism in 50%, hypertension in 14% and abdominal obesity in 82.1% of them. Metabolic syndrome was recognized in 22.1% of the children. The family histories revealed obesity in 80% of the cases, type 2 diabetes in 57.9%, circulatory disorders in 65%, and all the aforementioned components in 36.8% of them. Only 8.4% of the subjects had negative family histories.
Conclusion: Metabolic disorders occurring in children with excessive body mass, mainly with abdominal obesity, may lead to the development of type 2 diabetes and circulatory disorders in adulthood. Most of such children are familiarly loaded with complaints resulting from disorders in lipids and carbohydrate metabolism.

R69

Circulating nucleases and importance of nucleic acid 'danger motifs' in immune response of diabetics

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Foreign, infection-associated, synthetic or endogenously generated nucleotide motifs may represent the critical determinants for the

activation of the innate immune system with the polarization toward Th1 immune response. Introduction of double stranded (ds) RNA fragments into the cytoplasm may drive normal cells to become antigen-presenting (APC), with the increased expression of genes important for antigen persentation, activation of Janus kinase/Stat, NF-kB and MAPK kinase system, IFNα/β production, macrophage and dendritic cells activation, NK activity and B lymphocyte immunity. The oligonucleotides and oligodeoxynucleotides containing palindromic unmethylated cytosine-guanine (CpG) motifs can activate lymphocytes, redirecting the immune response from a Th2 to a Th1 fenotype, by inducing monocytic cells and other immune cells to produce Th1 cytokines, IL-12 and IFN-γ. The possible importance of circulating nucleases would be to protect against infectious agents by destroying unprotected or transiently revealed nucleic acids and oligonucleotides in the blood stream and during cell entry. This study was undertaken in order to examine if the nuclease activities vary in relation to the different substrates immune or nonimune response modifires, in relation to the types of diabetes, if the RNA differ in quantitative and qualitative fashion compared to corresponding healthy population and in relation to the different types of diabetes. The study included 36 patients with juvenile insulin-dependent diabetes, 20 adult patients with insulin-dependent diabetes, 19 adult patients with noninsulin-dependent diabetes and corresponding controls. The results of the decreased plasma enzyme activity obtained for the degradation of dsRNA forms, poly(I:C) and CpG showed inverse relationship with HbA1c level. In vitro results confirmed enzyme glycation. The amount of purified plasma RNA and oligonucleotides, (by using Sigma TRI Reagent), was significantly increased in diabetic patients. Our results may give a hypothesis that the increase of nucleic acid 'danger motifs', may be associated with Th1 immune stimulation.

R70

Impaired hGh-IGF1 axis in two adolescents with Alstrőm Syndrome

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Background: Alstrőm Syndrome is a rare genetic condition. The gene responsible for this syndrome has been recently localized on *chromosome 2p13*. A defective function of ALMS1 in the target tissues of insulin action, as well as in central nervous system is probably responsible for the clinical features of Alström Syndrome. We present two patients with Alstrőm Syndrome. The first sign noted during infancy was the presence of nystagmus. They developed early loss of central vision, due to a severe infantile retinal distrophy. Associated findings: blindness, diabetes mellitus (insulin-resistant), dilated cardiomyopathy, and several metabolic abnormalities are discussed. Because growth hormone deficiency and Alström Syndrome share some clinical and metabolic features, we studied the GH-IGF1 axis, using MRI techniques, dynamic tests (such as insulin tolerance test, ITT), and several metabolic disturbances related to GHD in two adolescents with Alström Syndrome. We found a *severe GH deficiency in both patients*, defined by a peak response to insulin-induced hypoglycemia <3 ng/dl and IGF1 concentrations less than –2SDS. We used Re-hGH in one patient for 12 consecutive months.
Results: *Echocardiography* has shown that left ventricular mass index, fractional shortening and fiber shortening velocity improved after 12 month of low-dose therapy. No lipid metabolism improvement was noted. The total body fat mass decreased after 1 year, most significant in visceral trunk location as revealed by DEXA (body composition), the bone density *increased with 5% after 6 months*.
Conclusions: In patients with Alström Syndrome the GH-IGF1 axis is impaired, demonstrating a severe GH deficiency. Further studies are needed to demonstrate if, hGH administration in children with Alström Syndrome is beneficial and also long-term follow-up data are required to assess the impact of GH replacement on cardiovascular morbidity and mortality rates in adults with GHD and AS.

R71

The induction of peritoneal dialysis in a child with insulin dependent diabetes with hypoparathyroidism, deafness, renal dysplasia (HDR) syndrome

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Introduction: The experience of peritoneal dialysis in the childhood diabetes was few. We report the induction of peritoneal dialysis in a child with inslin dependent diabetes with HDR syndrome. GATA3 haploinsufficiency was detected in this case. The effect of dialysis on insulin resistance, adsorption of glucose from dialysate and diabetic control were reported.
Case: The patient was 12-year-old girl. Body height 120 cm (-5.1 SD), body weight 21.7 kg (-3.0SD), BMI 14.6 kg/?. She has three cardinal symptom (hypoparathyroidism, sensorineural deafness, renal dysplasia) of HDR syndrome. She was suffered by polydipsia, diuresis and loss of weight at 3 years old. She was diagnosed as diabetes mellitus by hyperglycemia, urine sugar positive. She started insulin injection. She was suffered by the aggravation of renal function at 8 years old and introduced peritoneal dialysis at 12 years old. Before a dialysis start, she injected regular insulin 3~6 units six times a day. Her Total Daily Dose was 14.3 unit/day (0.68 unit/kg/day), HbA1c 11.1%, mean of fasting blood glucose 250 mg/dl. After a dialysis start, Total Daily Dose was decreased to 11.8 unit/day (0.59 unit/kg/day), HbA1c was improved to 6.2%, and the mean of fasting blood glucose was decreased to 121 mg/dl.
Conclusion: After peritoneal dialysis induction, the diabetic control was remarkably improved. Insulin antagonist may decrease by peritoneal dialysis, and insulin resistance improved. In an adult diabetic, dextrose absorbed from peritoneal made glycemic control worse. However, the dextrose absorption protected from hypoglycemia in this patient.

R72

Serum sL-selectin and tumor necrosis factor alpha (TNF-alpha) levels in children with type I diabetes mellitus

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Human L-selectin is a cell surface glycoprotein which acts as an adhesion molecule of leukocytes to the endothelium. Diabetes mellitus type I (DM) is characterized by autoimmune beta-cell destruction. The purpose of this study was to investigate sL-selectin (sCD62L) and TNF-alpha levels in patients with diabetes mellitus as well as how those may be related to glucemic control (HbA1C) and illness duration. Our study group comprised 15 children (mean age11.75 $\pm$ 4.3 years) with type I diabetes mellitus of variable duration (2 months–7.8 years). Subgroups consisted of children with disease duration <3 years (group I- nine children) or more than 3 years (group II- six children) and those with adequate ($n = 5$) (HbA1C $< 7\%$) or inadequate glucemic control ($n = 10$) (HbA1C $> 7\%$). The control group involved 15 healthy children of similar age and sex. Serum sL-selectin and TNF-alpha levels were assessed with the ELISA immunoassay. Our results showed

no difference between L-selectin levels of healthy (median = 1099 ng/ml) and diabetic children (median = 1088 ng/ml, Mann–Whitney $p > 0.05$). The same result applied for TNF-alpha (healthy, median = 2.60 pg/ml – diabetic 2.23 pg/ml, $p > 0.05$). However, further analysis in diabetic children according to the duration of disease and glucemic control revealed significantly higher L-selectin levels in those with shorter duration and adequate control (group I median = 1255 ng/ml vs. 916 ng/ml in group II, $p = 0.05$ and group I 1255 ng/ml vs. 983 ng/ml in group II, respectively). No differences regarding TNF-alpha were found in diabetic children in relation to disease glucemic control and duration. Adequate glucemic control of diabetes mellitus as well as shorter duration of the disease are connected with higher L-selectin levels, perhaps because of an ongoing inflammatory process that subsequently remits. Further studies are required to substantiate this finding.