P-1

Increasing incidence of type 1 diabetes mellitus in Greek Cypriot children and adolescents in 2000–2004

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Introduction: The incidence of type 1 diabetes mellitus (DM 1) has dramatically increased recently in some countries.
Aim: To ascertain the incidence of DM 1 in our population during the years 1990–2004, detect any gender differences on the age of onset and any increasing trend over the years.
Methodology: All cases of newly diagnosed DM 1 children under the age of 15 years were registered and relevant information was obtained. The population data were provided by the Ministry of Finance and statistical analysis was processed with SPSS.
Results: The mean overall annual incidence of DM 1 during this 15 yr period was: 11, 95 /100 000, with a statistically significant increase in the last five years. The incidence during the 5 year periods was as follow: (90–94): 10, 5/100 000, (95–99): 10, 8/100 000 (p: 0.55) and (00–04): 14, 8/100 000 (p: 0.0014). The female/male ratio was: 1.06/1. There is a gender influence on the age of onset as more males manifest DM 1 before the age of 6 yr and after the age of 13 yr. The mean age of onset for males is 6, 8 yr and 8, 9 yr for the females. Most cases were diagnosed during winter and autumn. This seasonal variation however was not observed in children diagnosed before the age of 5 years and interestingly during the 5 yr period 2000–2004.
Conclusion: The overall incidence of DM 1 in Cyprus is similar to most European countries. The number of newly DM 1 cases has increased during the last 5 years, which maybe a transient phenomenon probably attributed to the epidemic of Coxcakie virus gastroenteritis and meningitis seen in 2000 and 2001. The gender differences in the age of onset could be explained by the combination of genetic loading and pubertal hormonal changes.

P-2

Ethnic and regional differences in metabolic control and the rise of type 2 diabetes in New Zealand, data from STARBASE

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Introduction: STARBASE is a prospective database on children with diabetes, initially developed in Auckland 1993, expanding over the next decade to currently involve 9 regional centers around New Zealand. New Zealand has one of the higher rates of both type 1 and increasing type 2 diabetes in the world and has a unique geographic location.
Aim: Analysis of regional diabetes data.
Methodology: All centers send data electronically encoded to a central secure database (at Auckland) for analysis. From 1993 to 2004 there were >900 children registered, with information recorded from >9000 clinical assessments. Age range is from 0–17 years, but due to structure of service delivery, the majority of children is STARBASE are between 0–14 years.
Results: The GRAND overall mean HbA1c is 8.6%. The mean HbA1c/patient/year has significant variation and is significantly lower in proportion to the larger diabetes centers, however some smaller centers perform as well. HbA1c for ethnicity is significantly increased in the Maori 9.5 (1.3) and Pacific Island 9.1 (1.3)% populations, significantly higher than that for Europeans 8.4 (1.2) $P < 0.01$. The duration of diabetes as related to metabolic control, at 5 years mean 8.3 (1.2), >5 years 8.9 (1.7), >10 years 9.2 (1.3), $P < 0.01$. This mirrored the trend in higher HbA1c with increasing age. Data on insulin injection/day and HbA1c, BMI, and influence of celiac disease will also be presented.
Conclusion: STARBASE is a prospective useful tool that shows that there are Ethnic and Regional differences in metabolic control and the rise of type 2 diabetes in New Zealand.

P-3

Monitoring experiences from a nutritional diabetes prevention study

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Introduction: TRIGR is a double-blinded, randomised trial of dietary prevention of type 1 diabetes (T1D). The hypothesis is that weaning to a highly hydrolysed cow's milk based infant formula compared to standard cow's milk based formula decreases risk of developing diabetes-predictive autoantibodies and/or clinical T1D by the age of 6 years and clinical T1D by the age of 10 years in children having a first-degree relative with T1D and having increased HLA-conferred disease susceptibility. Twelve European countries, Australia, Canada and USA are participating in the study.
Aim: The recruitment target is 2032 eligible newborns. Target study compliance is above 90% with lost to follow-up less than 20% in each of the participating centers.
Methodology: Data are derived from questionnaires, blood samples and growth charts. An electronic web-based data capture system enables direct entry into the database. Regional Study Monitors communicate with and visit local centers while the single Data Management Unit (DMU) continuously evaluates and reports on study compliance to the local study centers and provides continuous assessment of national, regional and study-wide performance.
Results: The efforts for the recruitment are by now well established and accrual exceeds predictions. By May 2, 2005 1331 infants have been found HLA eligible. The average compliance with visits and completed forms is 98% and that with samples 93%. The lost to follow-up rate is presently 8.9%. About 79% of the subjects have been exposed to the study formula.
Conclusion: The experience shows that compliance monitoring and direct interactions of the co-ordinating teams facilitate and improve recruitment and compliance. Excellent compliance with study center visits and acquisition of data can be achieved with a web-based data entry system and continuous monitoring of performance through the DMU and by active monitoring in the field.

P-4

Initial recruitment experiences in Poland in a nutritional intervention study for primary prevention of type 1 diabetes

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Introduction: Our study is a prospective, randomised, double-blinded, multicenter trial, carried out in 15 countries around the world, with dietary intervention during the first 6–8 months of life and a follow-up period of 10 years.
Aim: The main objective is to answer the following question: can the risk of developing type 1 diabetes mellitus (T1D) in children with increased genetic disease predisposition be decreased by weaning to a highly hydrolysed formula?
Methodology: The potential candidates for the study are pregnant women who are affected by T1D or whose partners have T1D or whose older children have T1D. After birth HLA genotyping is performed from cord blood, and only subjects with genotypes known as predisposing to T1D are considered eligible. In Poland we now have four centers: Krakow, Katowice, Lodz and Wroclaw – the last one being the co-ordinating center.
Results: Recruitment started in June 2003. Among 127 families invited to the study 14 (11%) have refused to take part, 113 babies have been registered and 108 randomised. Sixty-seven (62%) were not eligible according to their genotype, and do not continue in the study; 41 (38%) had a genotype conferring increased risk, and they were entered into the intervention. Among those one has all three family members affected, one has both parents affected, one an affected father and older sister, three have a diabetic father, nine have a sibling with T1D and 26 an affected mother. At the age of 11 months two boys were diagnosed with T1D based on clinical symptoms and biochemical data.
Conclusion: Our results indicate that successful recruitment is possible only with excellent cooperation between at least three different specialities: obstetrics, adult endocrinology and pediatric endocrinology. Recruitment rate among mothers and children affected by T1D is good, but we still lack a good strategy to attract families with T1D men.

P-5

The EarlyBird diabetes study: challenging the paradigms

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Introduction: The rising prevalence of T2D in young people is a recent phenomenon and, by implication, a product of environmental rather than genetic change. Accordingly, it is important that theories to explain it be drawn from data on contemporary children. EarlyBird is a non-intervention cohort study documenting lifestyle, physical and metabolic development of very young children.
Aim: To identify candidate factors likely to lead to the development of insulin resistance (IR).
Methodology: Observation of 300 healthy children from 5 yr. Main outcome measures include anthropometry, adiposity and physical activity (PA). Uniquely, fasting blood samples are monitoring IR and its progressive impact on metabolic health.
Results: Several novel and unexpected findings have emerged: 1. IR correlated positively with weight at 5 yr ($r = 0.44$, $p < 0.001$), not birthweight ($r = 0.02$). Low birth weight is relatively rare in the UK and can no longer be held responsible for increasing prevalence of diabetes. Early weight gain should be the principal target in prevention. 2. IR was 35% greater in girls than boys ($p < 0.001$), the difference impacting adversely on metabolic status (triglycerides, HDL cholesterol all $p < 0.01$). This intrinsic difference may help explain the greater prevalence of T2D among female adolescents. 3. PA levels were strikingly consistent year-on-year, $r = 0.50$, $p < 0.001$. There was a four-fold variation in PA between children, but school provision (9 hr v 1.8 hr) explained <1% of the variance. A child's PA may be under biological control and not amenable to change. 4. Adiposity (% fat) rose significantly from 5–7 yr, yet IR and other metabolic risk markers unexpectedly improved. This needs to be explained. 5. Sixty percent of parents of overweight/obese children were unaware and unconcerned. Overweight is increasingly perceived as the norm.
Conclusion: Understanding the pathogenesis of IR from its earliest development is crucial to diabetes prevention. This prospective study will continue to add to that understanding.

P-6

Preliminary biochemical typing of childhood diabetes: the search for diabetes in youth study

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SEARCH for Diabetes in Youth has registered 9000+ persons with diabetes <20 years old, 3367 attended a visit and identified ethnicity. We have developed and applied a biochemical algorithm to those having a visit using GAD65 and IA-2 DM autoantibodies (DA) and fasting c-peptide (FCP ng/ml) to classify these participants as: type 1A (T1A, DA+ and FCP < 3.7 ng/ml, n = 2490); type 1 (T1, DA– and FCP < 0.8 ng/ml, n = 564); type 2 (T2, DA– and FCP ≤ 3.7 ng/ml, n = 102); and hybrid (DA+ and FCP ≤ 3.7 ng/ml, n = 47). Individuals who were DA– and had FCP ≤ 0.8 and <3.7 ng/ml remained unclassified (n = 250). SEARCH confirmed that diabetes autoimmunity occurs in youth with clinical characteristics indistinguishable from youth with type 2 diabetes (hybrid diabetes). Autoimmunity was also identified in American Indians and Asian Americans. Youth with T2 and hybrid diabetes were significantly older at diagnosis, more obese, more likely to have acanthosis nigricans and less likely to be NHW than T1A cases ($p < 0.01$ for both for all comparisons). T2 were more likely to be girls than T1A cases ($p < 0.01$). Using DA and FCP, the SEARCH biochemical algorithm identified 88% of recently diagnosed cases and 94% with longer DM duration. The longer the duration of diabetes, the higher the proportion of T1 cases. The proportion of cases that remain unclassified is greater in the older age group and in overweight and minority youth. The increase in T1 over time may be due to the study's cross-sectional nature since T1 may include originally DA+ T1A cases who are now DA– and originally T2 cases who are now insulinopenic. Limitations of this biochemical algorithm are a conservative definition of T2 diabetes and lack of race specific DA and FCP criteria. Further a laboratory determinations and follow-up may clarify how unclassified cases should be typed.

P-7

Persistence of enterovirus genom in the blood of newly-diagnosed diabetic children and in non-diabetic children after 1 year of recovery from enterovirus infection

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Aims: to reveal a persistence of enterovirus genom in the blood of newly-diagnosed diabetic children and in non-diabetic children after 1 year of recovery from enterovirus infection and detect a presence of diabetes specific auto-antibodies & HLA-haplotype in non-diabetic children with persistence of enterovirus genom.
Patients: 10 children after 1 year of recovery from enterovirus infection and 10 children with newly-diagnosed diabetes.
Methods: persistence of virus genom (RNA) in the blood (by polimerase chain reaction); diabetes-specific autoantibodies (detection of GAD65 and ICA); diabetes-specific HLA alleles (HLA

typing); detection of enterovirus IgM antibodies (by standard RIA method).

Preliminary results: At this stage of the study has sampled material from 90 newly-diagnosed children with diabetes type 1 and 50 children, 1 year recovered from enterovirus infection. Group of newly-diagnosed type 1 diabetes children : enterovirus IgM antibodies have found in 9 patients (10% of patients in this group; 5 girls, 4 boys; age from 3 to 12 years), GAD positive 5, ICA positive 2, GAD+ICA positive 2, HLA – Dw4 in 3 patients, DR3 – 4, DQB1*0302 – 2 (both girls and ICA negative).

Group of non-diabetes children, 1 year recovered from enterovirus infection: enterovirus IgM antibodies have found in 36 patients, GAD positive 2, ICA positive 1 (none of them has clinical diabetes), GAD+ICA positive 0, HLA – Dw4 in 2 patients (GAD positive – 1), DR3 – 4 (GAD positive – 1; ICA positive – 1), DQB1*0302 – 1.

Conclusions: Our preliminary results reveal presence of enterovirus IgM antibodies in 10% of newly-diagnosed type 1 diabetes children, with no dependence neither on sex nor age. 7 patients in this group (78%) are GAD positive, but 4 (44%) – ICA positive; HLA typing reveals enterovirus related haplotypes – DR3 and DQB1*0302 in 6 patients of this group (66%). In group of non-diabetes children, 1 year recovered from enterovirus infection, in turn, positive diabetes specific autoantibodies we have found just in 8% of all enterovirus IgM antibodies positive patients. Presence of diabetes related HLA haplotypes in this group is in 19% cases.

More exact conclusions (especially – if production of diabetes specific auto-antibodies after enterovirus infections probably is dependent on presence of both persistent enterovirus genom in the blood and diabetes-specific HLA alleles?) will be possible after detection of persistence of virus genom (RNA) in the blood when full number of cases (10 + 10) will be recruited.

P-8

Type 1 diabetes a man made disease: secular trends in diabetes incidence may pinpoint environmental triggers

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Introduction: Type 1 diabetes has been with us for millennia, but only recently has the incidence increased dramatically in most western countries. This trend is also appearing in emerging economies. Environmental changes which correspond in time with these increases are 'modern'.

Methodology: Suggested factors include obesity, 'excessive' hygiene, immunisation, exposure to new infectious agents, and dietary changes. Wilckens has espoused the obesity hypothesis and there are many suggestive experimental and immunological observations consistent with the 'hygiene' hypothesis. Association of diabetes with immunisation has had little supportive evidence.

Results: Occasionally exotic 'new' viruses (e.g. bank vole virus) could account for some cases. Dietary factors suggested include nitrosamines, milk proteins (or insulin) bafilomycins in root vegetables and advanced glycation end products. The latter result from the modern habit of eating precooked or ultra heat treated foods containing protein and carbohydrate. Reduced ascorbic acid resulting from heating of ascorbic acid added as an antioxidant to foods has been shown to be diabetogenic. Ascorbic acid use in the food industry has increased globally in parallel with the incidence of type 1 diabetes Glycated (or 'ascorbated') proteins yield unusual intestinal enzymatic cleavage products some of which may interfere with immune function. Beta casomorphin-7 form yielded from A1 but not A2 cow milk beta casein is quickly removed from the blood by PP1V, but not its glycated form. PP1V is CD 26 – a lymphocyte activation factor. Glycated BCM-7 may be an inhibitor of this lymphocyte activation marker.

Conclusion: Man made changes to the environment may be responsible for the epidemic of type 1 diabetes.

P-9

Prospective investigation of the environmental determinants of diabetes in the young

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Introduction: The mechanisms by which environmental factors may trigger either islet autoimmunity, type 1 diabetes (T1D), or both are not understood. Identification of such factors will lead to a better understanding of disease pathogenesis and result in new strategies to prevent, delay or reverse T1D.

Aim: The aim of the TEDDY study is to identify infectious agents, dietary factors, or other environmental agents, including psychosocial factors which may either trigger islet autoimmunity, type 1 diabetes (T1D), or may protect from the disease.

Methodology: Genetically susceptible children are identified through newborn HLA-DR/DQ screening and followed with blood draw every 3 months and monthly stool samples. Dietary, infectious, and psychosocial assessments are completed prospectively. The study has two end-points, the first is appearance of islet autoantibodies as an expression of islet autoimmunity and the second is the clinical diagnosis of diabetes Six clinical centers in the US (Washington, Colorado, Georgia/Florida), Finland, Germany and Sweden began to screen newborn babies for high risk HLA in September 2004.

Results: During the first seven months, a total of 19 403 have been screened of the 220 800 children planned over the next four years. The number infants in the general population with high-risk HLA genotypes were 846. Among 260 newborns with a mother, father or a sibling with T1D there were 52 eligible high-risk children. So far, 385 children have been enrolled in the TEDDY study out of which 361 (94%) are general population and 24 (6%) are children with first degree relatives.

Conclusion: The initial enrolment results demonstrate that this complex and demanding prospective study protocol is feasible. Over 5% of the general population and 25% of FDRs carry high-risk HLA genotypes.

P-10

Comparison between the prevalence of type 1 diabetes mellitus and nitrate/nitrite pollution of water in different areas of Satu Mare district

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Introduction: Actually is widely studied the role of nitrates/nitrites in the ethyopathogeny of type 1 diabetes mellitus, as an environmental factor. One of the ways on which these factors are actioning is the alimentary way, represented by water.

Aim: To establish some correlations between the prevalence of type 1 diabetes mellitus and the pollution of the water with nitrates/nitrites.

Methodology: The pollution level of the water was established by specific laboratory methods, from samples recolted in different areas of Satu Mare county. In the same areas, we studied the prevalence of type 1 diabetes mellitus with onset in the childhood. The data were compared with statistical methods.

Results: We found 3 groups of areas with different levels of water-pollution: normal (50 mg/l), medium-high (100–200 mg/l) and very high (more than 200 mg/l). Comparatively, the prevalence of type 1 diabetes mellitus with onset in the childhood shows normal,

medium-high and very high values. These values shows a statistically significant concordance with the nitrate/nitrite pollution levels of the same geographical area.
Conclusion: Our results seems to prove once more again the relationship between the dietary nitrate/nitrite contamination and the prevalence of type 1 diabetes mellitus in different areas of Satu Mare county.

P-11
Plasma RNAse activity in juvenile diabetes mellitus: a possible factor contributing to immune dysfunction

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Introduction: A family of receptors known as the Toll-like receptors (TLRs), are critical in mediating inflammation and immune responses in diabetes. Among the macromolecules recognized by TLRs are different RNAs and oligonucleotides. It should not be excluded that they have a preference for particular RNA motifs (poly U), but such simple motifs can be present in both, viral and nonviral RNAs. The presence of extracellular ribonucleases-RNasess destroy any transiently revealed nucleic acids and oligonucleotides in the blood stream, ensuring that little or any self/nonself RNA ever reaches antigen presenting cells.
Aim: There are no literature data about plasma RNase activities in diabetics. This study was undertaken to test the possibility that plasma RNase activity may be useful in studying the dysregulation of nucleic acid and oligonucleotide metabolism as a possible pathogenetic mechanism for development and/or in immune dysfunction aggravation in juvenile diabetics.
Methodology: Children with type 1 diabetes (n = 40, age group of 5–14 years), together with age-matched control subjects (n = 40) were enrolled into the study. Free and inhibirory-bound RNase activity was measured in heparinised plasma using rRNA as well as poly (C) and poly (U) homopolynucleotides.
Results: The diabetic patients had lower free RNase activity compared to control children, (0.82 ± 0.11 vs 2.11 ± 0.23 U/L $p < 0.001$). Site-selective scission of different homopolynucleotides decreased also; poly C (0.32 ± 0.11 vs control 0.65 ± 0.14 $p < 0.001$) and poly U (0.53 ± 0.22 vs control 0.81 ± 0.24 $p < 0.001$), together with increased level of preexisting acid soluble oligonucleotides. Human plasma RNases have been classified as 1–5, where 1–4 preffer poly (C), designated as pancreatic type and RNase 5 (presumably RNaseL) preffers poly (U) as substrate-non-pancreatic type. Obtained results can be explained in terms of decreased pancreatic or non-pancreatic origin of plasma RNases.
Conclusion: Given data may support the theory about the generation of small defective RNA fragments and oligonucleotides in plasma of diabetics, capable of stimulating dramatic Th1 response through the activation of TLR.

P-12
Lymphocyte apoptosis and oxidative stress in course of type 1 diabetes in children

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Introduction: Autoimmune process in onset of type 1 diabetes is different than in its later phase. CD3+CD4+ lymphocytes cannot to stop destruction of beta cells at beginning, however autoimmune process is loosing its target finally. An oxidative stress was suspected to influence T-lymphocyte functions in diabetes.
Aim: To evaluate CD3+ and CD3+CD4+ lymphocytes' apoptosis and oxidative stress in CD3+, CD3+CD4+, CD3+CD8+ cells at start and after longer insulin therapy.
Methodology: CD3+ and CD3+CD4+ lymphocytes were labeled with antibodies and fluorescein or ficoerithrin and by annexin V bound to apoptotic cellular membrane, what was counted by flow cytometry. The oxidative stress measure based on oxidation of dihydrorhodamin to rhodamin by free oxygen radices in lymphocytes. Children with type 1 diabetes (22 girls & 12 boys; age: 12.7 ± 3.4 yrs; disease duration: 4.0 ± 1.7 yrs) were compared (t-test) to 20 healthy coevals and evaluated inside the group (correlations).
Results: Apoptosis of CD3+CD4+ ($7.5 \pm 3.6\%$ vs. $4.6 \pm 1.1\%$; $p < 0.017$) and CD3+ ($8.9 \pm 4.2\%$ vs. $6.0 \pm 2.9\%$; $p < 0.043$) was higher in children with diabetes than in controls. Diabetes duration less than 6 mo. made higher (9.4 ± 2.5 vs. $6.5 \pm 3.8\%$) rate of apoptosis for CD3+CD4+ ($p < 0.042$) than after longer disease history. Oxidative stress was unexpectedly higher (arbitrary units of fluorescence) in healthy than in diabetic cases for: CD3+ 16.0 ± 7.6 vs. 7.5 ± 4.1 ($p < 0.0001$); CD3+CD4+ 19.9 ± 4.2 vs. 14.7 ± 8.4 ($p < 0.03$) and CD3+CD8+ 16.5 ± 9.7 vs. 4.2 ± 0.7 ($p < 0.0001$). Apoptosis of CD3+CD4+ and CD3+ revealed high correlation ($r + 0.972$; $p < 0.0001$) and both of them correlated with age of diabetic patients ($r - 0.676$; $p < 0.016$ and $r - 0.648$; $p < 0.023$ respectively).
Conclusion: Children with type 1 diabetes demonstrate enhanced apoptosis of CD3+ lymphocytes, which depends on changes in CD3+CD4+ subpopulation at diagnosis but not on oxidative stress.

P-13
Evaluation of TNF-alpha, soluble TNF-alpha receptor and VEGF in children with IDDM

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Introduction: TNF-alfha, soluble TNF-alpha receptor and VEGF may play a great role not only in obesity and/or type 2 diabetes but also in pathogenesis and complications in type 1 diabetes.
Aim: The aim of the study was the evaluation of TNF-alpha, soluble TNF-alpha receptor and VEGF in pre-pubertal children with IDDM and estimates of the influence of different kinds of therapy.
Methodology: Sixty seven patients and 15 age-matched, healthy children were included into the study. All children were prepubertal, diagnosed with IDDM for more than two years, without any coexisting diseases. All patients were divided into groups according to the kind of therapy: 22 children were treated with conventional insulin therapy (CIT), 21 received multiple insulin injections (MII) and 24 were treated with continuous subcutaneus insulin infusion (CSII). Blood samples were obtained between 7:30 and 8:30 a.m. from children in normoglycemia (after a night without episodes of hyperglycemia or hypoglycemia). All analyses were made by enzyme-linked immunosorbent assay (ELISA) commercial kits.
Results: TNF-alpha and soluble TNF-alpha receptor levels were lower in children with IDDM than in healthy children but only TNF-alpha in a statistically significant way. VEGF levels were higher in children with IDDM: the highest in CSII, lower in both CIT and MII groups (lower even than in control groups).
Conclusion: 1. Levels of all measured parameters were different in children with IDDM than in healthy children but only TNF-alpha and VEGF in a statistically significant way. 2. The kind of therapy appears to have had an influence on TNF-alpha and VEGF levels.

3. It is necessary to estimate the influence of age, sex, height and weight, BMI, duration of ilness, guantity of insulin.
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P-14

Differences in nitric oxide metabolism in streptozotocin-treated rats and children with type 1 diabetes

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Introduction: One possible mechanism for islet destruction in diabetes is the induction of nitric oxide (NO) synthesis in pancreatic islet cells, leading to the overproduction of NO. Aim of our study was to test whether the measurement of stable NO end products and the determination of the expression of inducible nitric oxide synthase (NOS II) in white blood cells were suitable to predict the presence of early diabetes before its onset.
Methodology: The hypothesis was first tested in an animal model, using streptozotocin treated rats. Additionally children with recent onset diabetes were also studied. Urinary nitrite and nitrate content was measured by Griess reaction, using nitrate reductase. The expression of NOS II protein amount was determined by Western blotting.
Results: Both urinary nitrite and nitrate level [nitrite/creatinine (mmol/mmol) in diabetic rats: 0.19 ± 0.04, in control rats: 0.05 ± 0.01, $p < 0.05$] and the expression of NOS II protein (diabetic rats: 2.9 ± 0.04, in control rats: 0.6 ± 0.05) were increased in diabetic rats. Urinary nitrite plus nitrate level was also elevated in children with type 1 diabetes, [nitrite/creatinine (mmol/mmol) in diabetic children: 0.046 ± 0.005, in control children: 0.005 ± 0.001, $p < 0.05$], however only a small proportion of patients exhibited an increased NOS II protein expression.
Conclusion: Pathomechanism of streptozotocin-induced and spontaneous human Type 1 diabetes must be different. Measurement of urinary nitrite plus nitrate content, as well as the determination of NOS II expression of white blood cells in an early symptom-free phase of diabetes are not suitable predictors of the disease in humans.

P-15

Risk factors of diabetes type 1 in children of father with type 1 diabetes

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Introduction: The risk of diabetes type 1 in relatives from diabetic patients higher than in the population.
Aim: to ascertain the frequency of genetical and immunological diabetic risk markers in children of fathers with type 1.
Methodology: From November 1996 since February 2002 examined were 42 healthy children from fathers with type 1 diabetes. The age of the children varied between 0.9 to 26.8 years. 46 were boys and 46 girls. The children were divided in three age groups: 1) 0–6 years; 2) 7–14 years; 3) ≤15 years. The control group included 20 healthy children, without diabetes in the family. In all the children designated the immunological markers, antibodies ICA, IAA, lA2A, GAD, the genetical markers in children and their fathers. The immunological markers were repeated after 2 years and after following 3 years. The whole observation included 6 years. The genetic markers were designated in the Department of Virology, Finland by professor Jorma Ilonen and the study was an analysis of the 1) correlation between the HLA system and the presence of ICA, IAA, IA2 and GAD antibodies; 2) if there exist any correlation between the presence of antibodies, the age of the children, sex body mass at birth, time of breast feeding, age of the fathers at the moment of the child birth; 3) observed was the eventually dynamic of the immunological risk factors. In all the results performed was a statistical analysis in the statistical program.
Results: in 76% children was not diabetes type 1 in the family, in 15% diabetes type 1 in the family of the father, in 9% diabetes type 1 in the family of the mother, in 55% without diabetes type 2 in the family, in 40% type 2 diabetes in the family of the mother. The allele DQB1*0302 were present in 41.7% and DQA1*03 in 20.8% of the children from diabetic fathers. In the control group these alleles were not observed.
Conclusion: 1) the risk of type 1 diabetes in children from diabetic fathers is higher than in the control group; 2) positive antibodies ICA, IAA, GAD, IA2A were observed more frequently in children with HLA DQB1*0302; 3) ascertained was a high correlation between the alleles DQAf05 and DQB*0302 and the alleles DQA1*0203 and DQB1*02 in children of fathers with type 1 diabetes; 4) in children of fathers with type 1 diabetes the allele DQB1*0302 were observed more frequently in comparison with the control group; 5) in fathers with type 1 diabetes ascertained was a more frequent presence of the allele DQB1*0302, DQA1*05 and DQA1*03 in comparison with the control group; 6) in children of diabetic fathers the presence of ICA was more frequent; 7) in the families of fathers with type 1 diabetes observed was type 1 and type 2 diabetes in a high percentage; 8) during the 6 years observation there was not ascertained and increase, but fluctuation of the antibodies.

P-16

Diabetes risk HLA genotypes affect birth weight in the general population

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Introduction: A high birth weight (BW) has previously been reported to increase the risk of type 1 diabetes. However, it is not established whether this relationship is a result of genetic factors associated with both increased risk for type 1 diabetes and high BW. HLA-DR13 was recently reported to be associated with BW in the general population. The aim was to test the hypothesis that diabetes risk HLA-genotypes, cord blood autoantibodies or both are associated with increased BW.
Methodology: HLA-genotypes were determined in dried blood spots of cord blood from a total of 16 709 children born to healthy mothers in the Diabetes Prediction in Skåne (DiPiS) study, a population-based observational clinical investigation in newborn children. Children born to mothers with diabetes or gestational diabetes were excluded. Autoantibodies to glutamic acid decarboxylase (GAD65Ab) and insulinoma-associated protein 2 (IA-2Ab) were determined in standard radioligand binding assays. BW was adjusted for gestational age and divided into quartiles. Upper quartile was defined as high relative birth weight (HrBW) and lower quartile as low relative birth weight (LrBW).
Results: Type 1 diabetes risk genotypes were strongly associated with relative birth weight (rBW) ($p = 0.01$). The high risk HLA-DQ2/8, DQ8/0604 and DQ8/X genotypes were associated with HrBW (OR (95%CI) = 1.20 (1.08–1.33), $p = 0.0006$). The type 1 diabetes negatively associated HLA-DQB1*0603 allele was also associated with HrBW ($p = 0.025$), confirming the previous report on DQB1*0603-linked HLA-DR13. GAD65Ab were negatively associated with HrBW [OR (95%CI) = 0.72 (0.56–0.93), $p = 0.01$].

Regression analysis showed that the HLA associated increase in rBW was independent of confounding factors.
Conclusion: HLA-genotypes may be associated with intrauterine growth independent of type 1 diabetes risk. The epidemiological observation that high BW is a risk factor for type 1 diabetes could possibly be a result of diabetes high risk HLA moderating intrauterine growth.

P-17

Type 1 diabetes prediction at birth – is it possible?

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Introduction: Identification of pre- and/or perinatal predisposing factors for the development of T1D will be a prerequisite for future diabetes prevention. Ongoing prospective studies are able to include only a limited number of new cases. Thus, studies with high power and high predictive value are needed which can be performed within short time.
Aim: To define and to evaluate prediction criteria for the development of T1D on the basis of a unique case-control collection.
Methodology: The samples are Dried Blood Spot Samples (DBSS) of ~2500 Danish T1D cases from the birth cohort 1981–2001, and 2 matching controls per case. All samples will be analyzed for genetic and immune factors: a) candidate genes (HLA DQB1, INS, CTLA4) b) cytokines c) mannan-binding lectin (MBL), C-reactive protein (CrP), d) auto-antibodies (GAD65, IA-2). a) Following WGA from DBSS, specific DNA-sequences are amplified by standard PCR. HLA DQB1 genotyping is performed by Time-resolved-fluorometry, CTLA4/codon 17 and INS/Msp1 by Restriction Fragment Length Polymerization and /CT60 by ABI Prism Detector 7900. b), c) analyzed by antibody-based multiplex analysis (Luminex). d) analyzed by Radio-binding assay.
Results: 2715 validated T1D cases were identified by combining several Danish registries. Sample collection is ongoing. By now, CTLA4 and INS genotyping has been performed on approximately two thirds of cases and controls.
Conclusion: The predictive value of risk factors at birth will be tested by combining stored samples from Danish newborns from to decades, and registry information on T1D, with >95% ascertainment and advanced technology. The described project is characterized by great statistical power, it is fast and highly cost-effective.

P-18

Type 1 diabetes DNA repository for confirmatory genetic case-control studies

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Introduction: The etiology of type 1 diabetes (T1D) is unknown, but it is recognized that both genetic and environmental determinants are important in defining disease risk. A large number of studies have sought to identify genetic susceptibility factors by testing for association and linkage in T1D, and more than 20 loci have been implicated in T1D risk. However, both linkage and association studies are plagued by the impression that they are not consistently reproducible. This inconsistency may mainly be due to underpowered studies.
Aim: To save and to make available a large ethnically homogeneous, population-based case-control collection for the study of T1D genetics, which will enable research groups to perform sufficiently powered confirmatory studies of T1D candidate genes.
Methodology: DNA from Dried Blood Spot Samples (DBSS) of ~2500 Danish T1D cases from the birth cohort 1981 through 2001, and 2 matched controls per case, will be amplified by Whole genome Amplification (WGA) and stored in a repository. Method of choice for WGA is Multiple Displacement Amplification.
Results: Status: We are currently collecting the DBSS from the registry. So far, WGA has been performed on 5000 DBSS. Success rate of WGA appears to be close to 100%.
Conclusion: This will be the first large, homogeneous, population-based T1D case-control material for genetic confirmatory studies with great statistical power. Results of the studies, performed on the repository's material, will be collected in a central database. As data will be made available for following studies, 'double-typing' will be avoided and the repository can be used in a cost-effective way. This resource will make possible numerous T1D studies contribute to throw light upon the disease's genetic etiology.

P-19

Transmission disequilibrium of parental susceptibility genes to children with or without childhood-onset type 1 diabetes mellitus (T1DM)

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Introduction: Both genetic and environmental factors are needed for the development of T1DM. In Japanese, HLA haplotypes that influence the risk of adult-onset T1DM have been identified. In a French study, maternal (DR3) and paternal (DR4) transmission disequilibrium were identified.
Aim: To identify susceptibility genes for childhood-onset T1DM and to investigate the transmission disequilibrium of the disease susceptibility genes from parents to type 1 diabetic children and their unaffected siblings.
Methodology: In thirty Japanese childhood-onset type 1 diabetic patients (m/f 16/14, mean age at onset 6.53 ± 3.68 y/o), their parents, their 19 unaffected siblings and 97 healthy controls, the penetration rates and the transmission disequilibrium of the disease susceptibility genes were analyzed by case-control study. HLA-*DRB1*, -*DQA1*, -*DQB1* alleles were determined by the PCR-sequencing-based typing method. A parent-of-origin effects on the transmission of these genes were analyzed by the transmission disequilibrium test.
Results: The penetration rate of the *DQB1*0901-DQA1*0301-DQB1*0303* haplotype in type 1 diabetic patients was higher than that of control subjects (53.3 vs 23.7%, $Pc = 0.0378$). Paternally transmitted susceptibility haplotype *DRB1*0901-DQA1*0301-DQB1*0303* in patients and their unaffected siblings showed higher transmission disequilibrium than that of maternally transmitted same haplotype.
Conclusion: Susceptibility genes for T1DM are detected, and our results suggest that a paternally transmitted haplotype is disease sensitive in childhood-onset T1DM.

P-20

First description of mutation in the liver glucokinase isoform causing transient neonatal diabetes mellitus (TNDM)

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Introduction: Neonatal diabetes mellitus (NDM) is insulin-requiring hyperglycemia occurring in the first month of life, its incidence is 1 : 400 000 newborns; it can be either transient (TNDM) or permanent (PNDM). Homozygous mutations of glucokinase (GCK) gene leading to complete protein deficiency cause PNDM, while heterozygous mutations cause maturity-onset diabetes of the

young (MODY2) and less frequently TNDM. GCK is mainly expressed in pancreas and liver where is synthesized in two distinct isoforms. More than 200 mutations have been described in GCK gene, all belonging to its pancreatic transcript.
Aim: To describe a new mutation of the liver GCK isoform, A10V (C29T), causing TNDM.
Methodology: A female proband was diagnosed as TNDM at age of 11 days. No insulin treatment was given, except to infusion of physiological solution for few hours. The patient had a remission period but hyperglycemia recurred after 6 months following an infectious disease; the same treatment was given with remission of the hyperglycemia The entire GCK gene was amplified by PCR and strands were sequenced in forward and reverse. For detection of low-level mosaicism associated with the C29T mutation, exon 1b of the GCK gene was amplified and PCR products of proband and her mother were digested with Ava II enzyme and then electrophoresed.
Results: These data are consistent to the clinical history of other TNDM carrying mutation in the GCK gene. Interestingly PCR restriction fragment length polymorphism analysis showed that the mother was a low-level mosaic of normal and mutant GCK, suggesting a recurrence caused by germiline mosaicism.
Conclusion: This is the first description of TNDM caused by a mutation of the liver GCK protein. We underline the importance of screening the complete transcript coding region of GCK and the role of liver GCK in glucose homeostasis, supporting that its deficiency contribute to the development of diabetes.

P-21

Transient neonatal diabetes mellitus due to UPD-6. Spontaneous recurrent hypoglycemia following diabetes remission

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Transient neonatal diabetes mellitus (TNDM) due to paternal chromosome 6 uniparental disomy (UPD-6) is rare and characterised by remission of diabetes and independence from insulin therapy during infancy. Recurrence of diabetes in childhood is recognised and permanent beta cell dysfunction suspected. We report an infant [F; 29 wks gestation; BW 1.13 kg (–0.5 SDS)] with TNDM due to UPD-6 with evidence of ongoing beta cell dysfunction in the diabetes remission phase. Presenting with poor weight gain [1.38 kg at 30 days (–1.9 SDS)] and hyperglycemia [mean blood glucose (BG) 14.3 mmol/l (range 3.1–23.3)] from birth, continuous subcutaneous insulin infusion (CSII) therapy (mean insulin infusion 0.18 u/kg/d) and continuous blood glucose monitoring (*Medtronic Minimed* CGMS) were initiated. Normoglycaemia [BG 7.7 mmol/l (2.5–13.1)] and catch-up growth [2.15 kg on day 57 (–1.4 SDS)] were achieved. Remission from insulin therapy occurred on day 57 and euglycaemia maintained until day 68 [BG 5.3 mmol/l (2.4–8.1)] following which recurrent postprandial hypoglycemia unresponsive to increased feed frequency and calories was observed. Hypoglycemia (BG 1.5 mmol/L) was associated with inappropriate insulin secretion (pro-insulin 7.0 pmol/L (NR 0–7); insulin 6.0 pmol/L (NR 0–60); pro-insulin : insulin ratio 1.16 (normal 0.16). Other causes of hypoglycemia were excluded and oral Diazoxide (10 mg tds) therapy commenced (age 86 days). On therapy, normoglycaemia [BG 4.7 (2.2–15.4 mmol/l)] and reduced insulin precursor production (pro-ins : insulin ratio 0.4) have been observed. In conclusion, in infants with TNDM due to UPD-6 spontaneous recurrent hypoglycaemia occurring during the diabetes remission phase has not been previously reported. Evidence of inappropriate insulin secretion and responses to Diazoxide suggest ongoing beta cell dysfunction with abnormal glucose sensing and insulin processing, possibly mediated via the glucokinase / AKT pathway.

P-22

Permanent neonatal diabetes associated with a sulfonylurea receptor gene mutation

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Introduction: The KATP-channel of pancreatic beta-cells is central in regulating insulin release. In beta-cells the channel is formed by two subunits, the Kir6.2, important for control of K+ selectivity, and the SUR1, a receptor with high affinity for sulfonylureas. Mutations in both genes have been linked to congenital hyperinsulinism. Permanent neonatal diabetes mellitus (PNDM) may also be caused by heterozygous activating mutations in the Kir6.2 gene or homozygous inactivating mutations in the glucokinase gene.
Clinical: We report here a child with PNDM where a mutation in the gene coding for the SUR 1 subunit was found. The patient, a girl, was born at term with birth weight 2540 g, birth length 49 cm of unrelated caucasian parents. She was brought to hospital at 5 weeks of age in a state of prechock with convulsions. B-Glucos at admission was 60 mmol/L, pH 7.07 and P-Sodium 158 mmol/L. The dehydration was severe and by MR intracranial thromboses and hemorrhage was found. She was brought to the ICU, put on ventilator, rehydrated with correction of electrolytes and pH and treated with heparine, phenobarbiturate and insulin with good response. At six months of age her general condition was good and B-Glucose was well controlled on an insulin dose of 0.4 U/kg/day administered by subcutaneus insulin pump. The mother is bearing the same mutation and is under clinical investigation. She has no history of diabetes. At OGTT (WHO) she shows a sharp increase of B-Glucose up to 10.0 mmol/L at 60 min after the glucose load with a corresponding relatively low S-Insulin of 16 mIU/L. The glucose curve otherwise shows no classical diabetes pattern. Mother is also testing positive for GAD-antibodies.
Methodology: Mutation analyses by DHPLC screening and sequencing of rare DNA variants were all performed at Odense University Hospital, Department of Clinical Genetics.
Results: No mutations were found in the glucokinase gene or in the Kir6.2 gene. In the SUR1 gene, however, a novel mutation in exon 28, 3533A>G was found leading to the amino acid change Q1178R. Also the mother has this mutation in a preliminary test. The affected codon 1178 is situated at the border between the SUR1 transmembrane spanning region 16. This area is a binding site for glibenclamid, which inhibits KATP-channel opening and facilitates insulin secretion.
Conclusion: The mutation may, unlike glibenclamid, result in increased KATP-channel activity and suppression of glucose-induced insulin secretion. Further investigations are however necessary to explain its functional role and the difference between the PNDM manifestation of the child and the mothers weakly subnormal glucose response on the loading test.

P-23

Clinical picture versus DNA diagnostics in MODY 3 and MODY2

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Introduction: Frequency and nature of mutations in genes responsible for MODY3 and MODY2 have been intensively investigated across Europe. Nonetheless, the information on frequency of MODY3 and MODY2 mutations in Slovak population is missing. Clinical suspicion for MODY can be postulated upon the following criteria: 2 generations with diabetes, it's manifestation until the 25th year of life, no or very low insulin requirements and detectable C-peptide. True verification offers, however, the DNA analysis only.
The aim of this study was to compare the frequency of MODY3 and MODY2 as confirmed by DNA analysis in families which either meet or not the clinical criteria.
Methodology: in response to a nation wide call among pediatric diabetologists, DNA samples from 31 families with clinical suspicion for MODY, including their 80 family members, were analyzed. Promoter and coding regions were bidirectionally sequenced, using the BigDye Terminator 3.1. Cycle Sequencing kit with ABI Prism 310 sequencer.
Results: 17 families met clinical criteria and in eight of them (47%) mutations in MODY genes were identified. In particular, in the MODY3 gene 5 mutations (R131Q, Y163N, R200Q, R229P, R263C), and in the MODY2 gene 3 mutations (R36W, V244G, G318R) (see Table 1 and Table 2) were found.

In 14 families, which did not follow the criteria, only one mutation R131Q in the MODY3 gene was identified.
Conclusion: Frequency of MODY3 and MODY2 is much higher (47%) among families with true clinical suspicion, than in families which did not completely meet the clinical criteria (7%). Thus, our results confirm the necessity of consistant determination of clinical criteria for Maturity Onset Diabetes of the Young.
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P-24

Diabetes in children and adolescents with wolfram-(DIDMOAD)-syndrome – a German nationwide case-finding study (DPV-WISS)

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Introduction: Wolfram syndrome is a rare autosomal recessive syndrome associated with loss-of function mutations of the wolframin gene (*WFS1*). Wolframin is considered to be involved in membrane trafficking, protein processing or regulation of calcium homeostasis and its deficiency is presumed to be the cause of juvenile onset pancreatic beta cell atrophy and progressive neurodegeneration. The acronym DIDMOAD refers to the most prominent clinical signs, i.e. diabetes mellitus and bilateral progressive optic atrophy variably associated with diabetes insipidus, deafness or other symptoms.
Aim: To focus on clinical data concerning diabetes of children and adolescents with Wolfram syndrome and to analyze possible phenotype-genotype correlations.
Methodology: The medical records of 15 confirmed cases of Wolfram syndrome registered in Germany through the nationwide survey of pediatric diabetes clinics (DPV) in 2004 were reviewed.
Results: Diabetes was diagnosed at 1–17 years of age (mean: 7.5 years). It was the first manifestation of Wolfram-Syndrome in most of the patients, preceded by optic atrophy in 2 patients and hearing loss in 1 patient. Diabetes presented with hyperglycemia in all and ketonuria in one patient, but ketoacidosis (PH less than 7.3) was not observed. Initial glycated haemoglobins ranged from 7.5% to 20.2%. All patients but one were treated with insulin from the time, their diabetes was diagnosed. Autoantibodies against pancreatic beta-cells were detected in only one of the patients. Diabetic ketoacidosis was not reported in any of the patients after the beginning of insulin substitution. Mean insulin requirements (in 2004) were 0.8 IE/kg/day with a standard deviation of 0.49 IE/kg/day. Mean DCCT-standardized HbA_{1C} was 8.7% (range: 5.1–13.3%). None of the patients had persistent microalbinuria or diabetic retinopathy.
Conclusion: Insulin dependent non autoimmune diabetes is one of the first manifestations of Wolfram-syndrome in childhood, rarely preceded by other symptoms such as optic atrophy or hearing loss. Insulin requirements and stability of glycemia seem to be comparable to type 1 diabetes, nevertheless the risk for ketoacidosis or diabetic complications appears to be lower.

P-25

The Pro12Ala polymorphism of the PPAR-γ gene (PPARG) is associated with reduced insulin requirements in children and adolescents with newly diagnosed type 1 diabetes

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Introduction: The peroxisome proliferator activated receptor gamma (PPAR-γ) is a nuclear receptor with regulating properties on fat cell differentiation and glucose homeostasis. Activation of the receptor by thiazolidinediones increases sensitivity to insulin, thereby acting as an anti-diabetic drug. The Pro12Ala polymorphism of PPAR-γ is associated with a 1) reduced risk for developing type 2 diabetes, 2) with increased insulin sensitivity, and 3) possibly with type 1 diabetes.
Aim: The aim of this study was to investigate the impact of the Pro12Ala variant on residual beta-cell function, glycaemic control, and daily insulin dose in 273 children and adolescents with newly diagnosed type 1 diabetes.
Methods: A Boost-test (mixed meal) was carried out in each patient at 1, 6, and 12 months after diagnosis to analyze the change in the residual β-cell function. In addition HbA1c % was measured and the daily insulin dose (U/kg/24 h) recorded.
Results: Genotyping for the Pro12Ala variant of the PPAR-γ showed, that carriers of the variant received a significantly lower insulin dose ($p = 0.04$; adjusted for age and gender) compared with wild type carriers during the first 12 months, while there was no difference in HbA1c % or rate of residual beta-cell function.
Conclusion: Despite similar beta-cell function and glycaemic control (HbA1c %) Pro12Ala carriers required less insulin during the first twelve months after disease diagnosis. This finding suggests that the Pro12Ala variant associates with higher insulin sensitivity among patients with type 1 diabetes, as found in glucose tolerant populations.

P-26

Hepatomegaly and malnutrition in three newly diagnosed patients with type 1 diabetes mellitus

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Background: Type 1 DM results from chronic autoimmune destruction of beta cells that usually starts many months or even years before the disease becomes evident. However, the clinical onset of type 1 DM is usually abrupt, rapidly leading to DKA if untreated. We describe 3 children with newly diagnosed type 1 DM who reported symptoms of hyperglycemia of 6–24 months duration before presenting with DKA. None had a family history of DM. All 3 had severe malnutrition and liver enlargement at the time of diagnosis.

Clinical cases: Selected characteristics of the patients at diagnosis are shown in the table. Extensive evaluation revealed no evidence of malabsorption, including negative evaluation for celiac disease. All had liver enlargement by physical exam. Hepatomegaly and diffuse increased echogenicity of the liver were found on ultrasound. With insulin therapy and proper caloric intake all 3 patients experienced growth, weight gain, gradual decrease in liver size, and normalization of serum albumin and prealbumin.

Gender	Age at Dx (Yrs)	Height (cm)/ %	Weight (kg)/ %	BMI/ BMI %	HgbA1c (%)	Reported Duration of Symptoms	Albumin (g/dL)/ Prealbumin (mg/dL)	SGOT (U/L)/ SGPT (U/L)	Hepatomegaly
F	11.9	149.3 50%	30.0 30%	13.5 15%	>14.0	1 Yr	2.5 –	40 48	+
M	9.3	120.5 <5%	19.1 <5%	13.2 <5%	11.9	>6 Mo	2.6 12.7	70 161	+
M	11.3	130.6 <5%	23.7 <5%	13.9 5%	>14.0	2 Yrs	2.3 8.0	29 24	+

Conclusions: In some children with newly diagnosed type 1 DM symptoms of hyperglycemia are long lasting, and the onset of DKA delayed. This leads to severe caloric losses, malnutrition, and liver enlargement. The reasons for this unusual presentation have not been determined. Insulin therapy and proper caloric intake can result in reversal of the nutritional and liver abnormalities.

P-27

Home care of the 'well' child presenting with type 1 diabetes (T1D)

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Introduction: DiabNet is a Managed Clinical Network for T1D in the young, working across 3 Health Board areas in Scotland. Out-patient care of the 'well' child at presentation of type 1 diabetes is an established management strategy. DiabNet agreed to aim for out-patient management whenever possible.

Aims: To study trends, over 5 years, in admission of the 'well' new patient and investigate factors influencing out-patient management strategy.

Methodology: Retrospective review of patient registration forms, collecting data on age, gender, family history of T1D, year, month and day of diagnosis, and length of hospital stay.

Results: From 1/5/99–30/04/04 there were 281 new patients with T1D. Of those 46 (17%) presented in diabetic ketoacidosis (DKA). Of the remaining 235, 138 (59%) were treated as out-patients, and 96 (31%) as in-patients. Age, gender and month of diagnosis did not affect management choice. A higher proportion of those with a family history of diabetes were managed at home. Most new cases (20%) presented on a Monday (1st working day of week), and this day also had the highest proportion of DKA. Fewer children presented on weekend days (8% each Saturday and Sunday), although there was a trend for admission of the 'well' child presenting on Sunday. Areas 1 and 2 admitted 17% and 29% respectively of 'well' children, area 3 admitted 84%. Total number of days in hospital decreased significantly in area 3.

Conclusion: Despite working to agreed management strategies, significant differences in the 3 areas to provide out-patient care are apparent. Significant reduction in length of stay in area 3 has been achieved over time. These data suggest that day of presentation may be important in determining mode of presentation and chosen management strategy. This information may be of value in planning services and when considering interventions to reduce DKA at presentation.

P-28

Severe hyperlipidemia and edema complicating the presentation of type 1 diabetes in a child

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An 8 yr old girl presented with 6 months of general malaise and one week of polyuria, polydipsia and perineal candidiasis. On examination she was tachycardic and tachypnoeic with Kussmaul respirations, but fully conscious. Capillary refill time was 4 seconds. Blood glucose was 34.9 mmol/l with gross ketonuria and glycosuria, venous pH 7.0, PCO2 4.57 kPa, BE –23.4 mmol/l, HCO_3 6.8 mmol/l. HbA1c was 19.5%. Her venous blood appeared grossly lipaemic and this impaired the analysis of plasma electrolytes. Total cholesterol was 18.9 mmol/l (ref <5) and triglycerides 122.63 mmol/l (ref <2.3). She was treated according to the standard UK protocol for diabetic ketoacidosis. Accurate monitoring of electrolytes was not possible in the first 48 hours of treatment due to the hyperlipidaemia, so fluid management was based on clinical evaluation and blood gases only. After 48 hours blood gases had returned to normal and subcutaneous insulin was commenced. She was discharged after 5 days. The patient was noted to develop peripheral edema on day 7 after diagnosis, and hepatomegaly was noted on day 21. Further investigations did not find a cause for the edema. A liver ultrasound on day 36 was normal. Lipid levels returned to normal after 14 days. The peripheral edema resolved spontaneously by 28 days. The finding of severe hyperlipidemia complicating diabetic ketoacidosis is a very rare finding in children. Peripheral edema occurring several days after institution of insulin is also a rare finding in children and if other causes of edema are ruled out this is termed insulin edema. To our knowledge this is the first reported case of severe hyperlipidemia and edema occurring together in a child. This may suggest a common etiology. Further genetic investigations regarding lipid metabolism are proposed.

P-29

Incidence and severity of ketoacidosis at onset of type 1 diabetes mellitus in Montenegrin children

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Introduction: Incidence of type 1 diabetes mellitus (DM) in children is progressively increasing. Many risk factors are associated with the development of diabetic ketoacidosis (DKA) at the onset of type 1 diabetes mellitus (DM). Presentation of newly diagnosed DM is changing.
Aim: Prospective evaluation of metabolic acidosis in Montenegrin children at diagnosis of diabetes.
Methodology: The data from period 1995–2004 were obtained from The National Pediatric Diabetes Registry and 216 diabetic children with onset of type 1 diabetes mellitus before the age of 18 were taken in account. The registry is estimated to include >96% (n = 216) of all new pediatric cases in Montenegro during these years.
Results: The incidence of type 1 DM (<14 years) is in rising from 6.5 in period 1985–1994 to 11.8 in 1995–2004. A group of the youngest children (0–4 years) had the most intensive increase in incidence ratio from 3.5 (1985–1994) to 7.7 (1995–2004). At the onset diabetes, any degree of DKA (Ph < 7.3) was present in 34% children and adolescents. During the period 1995–2004, the percentage of patients presented with DKA was not stabile. From 1995 to 1999, which was a period right after the civil war and destruction of former Yugoslavia this percentage was 48.2%. During last five years the percentage of patients with DKA was 20.4%. The 5–9 year old children suffered more frequently ($p < 0.001$) from DKA (45%), compared to the 10–14 years old (33.7%), 0–4 years old (33.3%), and >14 years old (15.6%). Severe form of ketoacidosis (Ph < 7.1) was found in 32.5% children. Severe form of DKA was three times rarer in last five years. The incidence of severe ketoacidosis was similar in all age groups and sexes. The length of initial hospitalisation from 1995–1999 was 16 ± 4 days, and in last five years 11.5 ± 3.7 days ($p < 0.001$). Mean HbA1c at diagnosis of DMT1/DKA was 11.3 ± 1.8%, range 5.4–17.2%. No differences in mean HbAlc between various age groups were noticed. All children recovered completely and no deaths were recorded.
Conclusion: The proportion of DKA in children with newly diagnosed diabetes mellitus is significant (34%). In last five years, diagnosing of type 1 DM in children has been improved. We speculate that new social factors and increased public awareness might have contributed to this increase in patients presenting without DKA at the diagnosis.

P-30
Misdiagnoses of diabetic ketoacidosis in childhood

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Introduction: Diabetic ketoacidosis (DKA) is a severe state of insulin deficiency where patients present acutely ill with vomiting, abdominal pain, dehydration, acidotic breathing, drowsiness or coma. It is a medical emergency and potentially fatal. Often precipitated by a febrile illness, it could be misdiagnosed as severe acute gastroenteritis (AGE), pneumonia and meningitis in countries where these childhood infections are frequent reasons for hospital admissions.
Aim: Misdiagnoses of diabetes and ketoacidosis in childhood.
Methodology: Diabetis Type 1 managed by the author between 1984–2004 were identified from the diabetic clinic database. Their case notes were reviewed to determine their 1) demograhic features 2) clinical presentation 3) initial diagnosis and 4) presence of diabetic ketoacidosis (DKA: dehydration, BG > 11.1 mmol/L pH < 7.3 and/HCO3, <15 mmol/L, and heavy glycosuria > 55 mmol/L).
Results: Out of 61 children, 55 were evaluated, 6 excluded because diabetes was secondary to other disorders. There were 24 Chinese (43.6%), 18 Malays (32.7%) 12 Indians (21.8%) 1 (1.8%) Caucasion. Male to female ratio 1.1 : 1. The mean age at presentation was 6.1 years (range 2 weeks to 12.7 years). Almost all (98%) had classical symptoms of diabetes with 42 (75.3%) presenting with DKA. Misdiagnoses was significant in young patients, mean age 2.8 ± 2.6 years affecting seven patients (12.7%): as AGE in 3 (5.5%), meningitis in 2 (3.6%), pneumonia in 1 (1.8%), and acute appendicitis in 1 (1.8%).
Conclusion: Frequency of DKA was high. There was 12.5% misdiagnoses, significantly affecting patients younger than 5 years old. Health care professionals must have a high index of suspicion for diabetes and DKA. Routine blood glucose check is mandatory in any ill child to avoid misdiagnosis.

P-31
Clinical presentation and frequency of diabetic ketoacidosis at first diagnosis of diabetes

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Introduction: Diabetic ketoacidosis (DKA) is life-threatening and is a medical emergency. It is present in 15% to 67% of diabetic children at first diagnosis in developed countries. Reports from tropical countries are few.
Aim: To determine the frequency of DKA and clinical characteristics of children at first diagnosis of diabetes in a tropical developing country.
Methodology: Retrospective analysis of case notes of children with type 1 diabetes managed by one of us over a 20-year period from 1984 to 2004 to determine symptoms of diabetes (polyuria, polydipsia weight loss) and DKA (defined as heavy glycosuria, ketonuria, hyperglycemia (BG > 11 mmo/L), acidosis (pH < 7.3 and/or bicarbonate <15 mmol/L), dehydration (>5% body weight). Their biochemical results were recorded and analyzed.
Results: Fifty five diabetic patients were identified and evaluated. DKA was present in 42/55 (75.3%), mean age was 5.3 years (range 0.1 to 12.7). Duration of classical symptoms was 4.6 weeks (range 1.6–5.5), DKA symptoms 1.7 days (range 0.4–3.5). The HbA1c was 13.7% (range 12.8 to 18.4%), corrected serum sodium was 140.8 mmol/l (range 134–155), serum osmolarity 309.2 mOSm/kg (range 294–328). Seven (12.7%) needed intensive care, 5 (9%) had pH < 7.0, 2 (3.6%) ventilation. Age at presentation, gender or serum osmolarity made no difference but duration of classical symptoms, serum sodium and HbA1c were significantly higher in those with DKA. There were no deaths.
Conclusion: DKA was present in 75.3% patients, higher frequency was due to delay in diagnosis. The community and health care givers should be made aware of disease symptoms especially when polydipsia and polyuria are mistakenly attributed to hot weather in tropical countries.

P-32
Frequency of diabetic ketoacidosis in children diagnosed with type 1 diabetes in northern Finland between 1982 and 2001

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Introduction: Diabetic ketoacidosis (DKA) is a serious consequence of insufficient insulin secretion and the leading cause of morbidity and mortality in children with newly diagnosed type 1 diabetes (T1D).
Aim: To study the possible change in the frequency of DKA during a 20-year time period among children with newly diagnosed T1D.

Methodology: The clinical characteristics at disease onset were studied retrospectively by collecting data from the patients' case records. The study population comprised 601 patients (264 girls, 43.9%), diagnosed with T1D under the age of 16 years between January 1, 1982 and December 31, 2001 in Oulu University Hospital taking care of all new T1D cases from the area of Northern Ostrobothnia. The first 10-year period (1982–1991) was compared with the later 10-year period (1992–2001). Two definitions for DKA were used: pH < 7.30 (A) or pH < 7.30 and/or bicarbonate <15 (B). Chi-square statistics, Student's two-tailed t-test and Mann-Whitney U-test were used in the analyses.
Results: In the first 10-year period children more often had DKA at diagnosis (A: 22.3% vs 15.6%, p = 0.038 and B: 29.9% vs 19.2%; p = 0.003). The proportion of children under the age of 4 years at diagnosis increased over time especially when comparing the first and last 5-year periods (16.4% in 1982–1986 and 23.6% in 1997–2001, p = 0.041). DKA was more common in children diagnosed under 4 years of age (A: 28.6% vs 16.5%, p = 0.004 and B: 33.7% vs 21.8%, p = 0.011).
Conclusion: The frequency of DKA in children with newly diagnosed T1D is decreasing in Northern Finland, although the proportion of children diagnosed under the age of 4 years is increasing.

P-33

Comparison of two different treatment protocols in diabetic ketoacidosis

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Introduction: There are still different protocols in the treatment of DKA especially with respect to Na content of the IV fluid therapy. The aim of this study was to compare retrospectively two protocols with different Na and glucose contents in treatment of DKA.
Methods: The two protocols used in this study with different Na and glucose contents are shown in Table 1. Protocol 1 had lower Na, higher glucose and Protocol 2 higher Na and lower glucose content. All patients had proven DKA and received IV insulin perfusion. Serum electrolytes, glucose and blood gases were measured at 2–4 hourly intervals in the first 12 hours and at 6 hourly intervals thereafter.
Results: The descriptive and laboratory parameters of the patients and comparison between the two protocols are seen in Table 2. Protocol 1 patients had significantly more severe dehydration and deeper acidosis at initial presentation than Protocol 2. During treatment serum osmolality showed a more rapid decrease in protocol 1 at 2nd hour (p: 0.05) whereas serum glucose level showed a rapid decrease in Protocol 2 between 6–12 hrs. Although serum osmolality normalized at 12th hour in both protocols, it reincreased in Protocol 2 at 24th hour (p: 0.035). Suspicious clinical findings of cerebral edema which required mannitol treatment were present in 5.3% in Protocol 1 and 10.8% in Protocol 2 (p < 0.05). All other clinical and laboratory parameters improved in Protocol 1 and 2 without significant differences. There was no mortality in either of the groups.
Conclusion: These findings support the use of high Na (100 mEq/L) during the first 6 hours and low Na (75 mEq/L), after 6–12 hours in the fluid and electrolyte treatment of DKA.

Table 1. Treatment protocols

	Na content (mEq/L)			Glucose content (%)		
	1–12 hrs	12–24 hrs	24–36 hrs	1–12 hrs	12–24 hrs	24–36 hrs
Protocol 1	75	50	35	2.5	3.3	3.75
Protocol 2	100	75	50	1.7	2.5	3.3

Table 2. Some clinical and laboratory findings at presentation

	Protocol 1 (n: 37 18M/19F) mean (SD)	Protocol 2 (n: 46, 25M/21F) mean (SD)
Age (year)	8.6 (3.9)	9.2 (4.0)
Dehydration degree (%)		
Modest	18.4	43.5
Severe	81.6	56.5
Serum glucose (mg/dl)	456.5 (121.5)	452.8 (113.4)
pH	7.03 (0.17)	7.16 (0.13)
Corrected Na mEq/L	141.1 (5.7)	142.1 (5.7)

P-34

Frequency of cerebral edema (CE) complicated with diabetic ketoacidosis (DKA) in Japan

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Introduction: The frequency of DKA have been reported to be 25–40% of patients with new onset diabetes and about 5%/year of those with established diabetes. CE has been reported to be 1–3% of those cases of DKA. Morbidity and mortality due to CE have been described as 21–35% and 20–25% respectively.
Aim: We tried to clarify the frequency of CE-DKA in Japanese diabetic children. This study is the first report concerning about the children's CE-DKA in Japan.
Methodology: Surveillance of CE-DKA in Japanese diabetic patients with the age less than 16 yr was carried out (from 04/2000 to 03/2003, in 60 hospitals). We aimed to determine incidence, outcomes and risk clinical courses of child CE-DKA, defined as sudden or unexpected deterioration in level of consciousness associated with pH < 7.35 and with diabetes/ketonuria. To increase the numbers for risk factor analysis, cases of CE-DKA occurring from 1993–2003 were identified by medical record searches.
Results: The incidence of CE in DKA by surveilalance was less than 1% (0.86%: 2 cases of 233 patients with DKA). By medical records, we found another two cases of CE-DKA. They were 2 boys and 2 girls and their ages were 2 mo (two cases), 7 yr, and 13 years. 3 cases were new onset diabetes mellitus. 2 cases had mild to moderate neurological sequelae and another 2 were reported as normal. One patients died (mortality rate was 25%). Laboratory data on admission were as follows: Mean BG were 746 mg/dl, pH 7.07. They were treated by continuous intravenous insulin infusion. Physiologic saline was used for 3 of them.
Conclusion: These data indicate that primary prevention of DKA is the critical step to avoid CE-DKA and its sequelae.

P-35

In spite of significantly increased use of insulin pumps in Norwegian children with type 1 diabetes, the incidence of diabetic ketoacidosis (DKA) and hypoglycemia is unchanged

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Introduction: Increasing numbers of children with type 1 diabetes are using insulin pumps. However, diabetic ketoacidosis and severe hypoglycemia are possible complications of the pump.
Aim: To describe incidence of DKA and severe hypoglycemia as the use of insulin pumps rises.
Methodology: Children and adolescents with type 1 diabetes in Norway are treated by pediatricians in 25 different hospitals. These hospitals have been benchmarked since 2001. Data concerning treatment, complications and risk factors for the development of complications are collected yearly with standardized methods. HbA1c is measured at a central DCCT approved laboratory.

Results: In 2004, 23 hospitals were benchmarked, covering 75% of the potential patients. The benchmarking was based on 919 patients in 2002, 1129 patients in 2003, 1417 patients in 2004. In 2004, mean HbA1c for the total group was 8.1%. In 2003, mean HbA1c was 8.4% and in 2002, 8.3%. In 2004, mean age was 13 years. The age span for the insulin pump users was the 2.4 years to 21 years, with a mean of 13.6 years. 28% of the patients used insulin pumps in 2004 vs. 21% in 2003 and 15% in 2002. In 2004, 4% of the patients had DKA compared to 5% in 2003 and 4% in 2002. Incidence of severe hypoglycemia was in 2004, 10%, 11% in 2003 and 12% in 2002.
Conclusion: A prospective nation wide benchmarking study of diabetes treatment in Norway shows that the incidence of DKA and severe hypoglycemia is not rising even though the number of patients using insulin pumps is growing very quickly.

P-36
Insulin pump treatment in children from the onset of type-1 diabetes

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Introduction: Continuous subcutaneous insulin infusion (CSII) has become increasingly popular in children with type-1 diabetes. CSII is the most physiologic method of insulin administration. Still there remains little consensus about who is an appropriate candidate for this therapy.
Aim: We investigated whether CSII is feasible in treating all children from the onset of type 1 diabetes regardless of age in a routine clinical setting.
Methodology: In all children with diagnosed type-1 diabetes in our department in 2003–2004, CSII-treatment was routinely started within 1–2 days after admission. The children were hospitalised for 10 to 14 days and then followed every second month in the outpatient clinic. To evaluate the length of the remission phase, Sustacal stimulated C-peptide-test was performed at 6 and 12 months after diagnosis. The patients and their parents were informed that they at any time could change the mode of treatment to e.g. multi-injection (MI).
Results: 30 patients (15 girls), mean age 9.1 yrs (range 1.2–15.6) were admitted in the study-period. One boy (age 8 yrs) changed treatment to MI after one week. None of the remaining 29 children have stopped using CSII. Eight of the children were originally of African/Asian origin. In the children who have been followed for more than 6 months, the mean HbA1c after 6 months was 7.1% (6.5–7.6, n = 24), after 9 months 7.4% (6.7–8.0, n = 18) and after 12 months 7.7% (6.9–8.5%, n = 16). The median stimulated c-peptide after 6 months was 412 pmol/l (n = 17) and after 12 months 226 pmol/l (n = 16).
Conclusion: This study shows that CSII is feasible, well tolerated and managed by all children from the onset of type-1 diabetes. The metabolic control is acceptable, and the children and their parents do not want to replace the CSII with other treatment.

P-37
Continuous insulin infusion therapy in children

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Objective: To assess the efficacy and tolerance of continuous insulin infusion in children and the degree of patient and parent satisfaction with this treatment.
Patients and methods: We present 10 type 1 diabetic children, 6 women, 6 pubertal, age at start of infusion 1.7–13.6 years [mean 9.3 (4.7)], diabetes duration 0.2–10.7 years [mean 4.2 (3.9)]. Indications for infusion were optimization of metabolic control, improvement of quality of life and hypoglycemia unawareness. The following variables were compared before and after pump period: glycated hemoglobin, daily insulin dose, number of hypoglycemic Pediatric Endocrinology Unit. Torrecárdenas Hospital. Almería, Spain and ketotic events, body mass index standard deviation score (SDS) and patient and parent satisfaction with diabetes treatment, assessed by the scale of Boot. Wilconson test, signification when $p < 0.05$.
Results: Patients were treated with insulin infusion for periods ranging from 9.0 to 24.0 months (mean 16.2). The degree of treatment satisfaction increased after infusion period [+81.4 (19.5) points vs. – 47.8 (37.2)] ($p < 0.001$). Glycated hemoglobin level [7.29% (0.69) vs. 7.59% (0.56)], insulin dose (0.85 (0.14) U/kg/day vs. 0.94 (0.22)], incidence of hypoglycemia [3.55 (4.62) episodes per month vs. 5.10 (7.14)] and body mass index SDS [+0.51 (0.98) vs. +0.69 (0.98)] did not change significantly. All the children tolerated the infusion. There were two episodes of ketosis and no severe hypoglycemia.
Conclusion: In selected children insulin infusion is well tolerated, provides good glycemic control with a low incidence of hypoglycemia, and substantially increases the degree of patient and parent satisfaction with diabetes treatment.

P-38
A 2-year population study of pediatric ketoacidosis in Sweden: predisposing conditions and insulin pump use

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Introduction: Pump users are at risk for diabetic ketoacidosis (DKA) if there is an interruption in insulin supply.
Aim: To investigate DKA triggering causes and pump usage.
Methodology: Data from 1999 and 2000 was collected retrospectively from the whole of Sweden.
Results: 142 DKA episodes (pH < 7.30) were identified in 115 children (60 girls, 52.2%) with established diabetes. HbA1c was 10.0 ± 2.1% (girls 10.0%, boys 9.8%, p = n.s.), mean age 14.6 ± 3.1 years (range 1.5–19.9) and diabetes duration 6.6 ± 3.5 years (0.4–17.7). The DKA incidence was 1.5/100 patient years (py) 1999 and 1.7/100 py 2000. Reported causes were missed insulin doses (48.6%), gastroenteritis (14.1%), pump problems (12.7%), infection (13.4%), social problems (1.4%) and unknown (5.6%). Alcohol was involved in 8 episodes and drugs in one. 30/115 patients (19 girls) used insulin pumps and none of these had relapsing DKA. 14/85 persons (7 girls) on insulin injections had >1 DKA episode (8 persons had 2, 3 had 3, 2 had 4 and 1 had 8). For pump users, the DKA incidence was 2.5/100 py 1999 and 3.5/100 py 2000. pH among pump users was significantly higher than with injections (7.15 vs. 7.12, p = 0.013). There was no difference in HbA1c or age. The median duration of pump use at the DKA episode was only 7.2 months.
Conclusion: Pump users had approximately twice the DKA incidence. Most episodes occur within a short time after pump initiation, reflecting that patients had not yet learned avoiding the risks of pump therapy. The high number of episodes reported to be caused by gastroenteritis is alarming, since it may well reflect a misinterpretation of DKA symptoms. Increased teaching and awareness programs are vital to prevent DKA in children and adolescents.

P-39
Continuous subcutaneous insulin infusion (CSII) in young patients with type 1 diabetes mellitus (T1DM): a follow-up study

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Introduction: CSII to improve the treatment of T1DM in pediatric patients is increased rapidly in many countries, and the assessment of intensive insulin therapy under real life is therefore possible.
Aim: To evaluate the effect of CSII in young patients during a 18 month follow-up.
Methodology: We started CSII in 15 patients (5 males, 10 females), aged 15–29 years, with disease duration raging from 5.2 to 25.2 years. Their HbA1c mean levels were 9.3 ± 1.36% (range 7.4–12.7%), mean insulin requirement (IR) was 0.91 ± 1.2 U/kg/day (range 0.6–1.2 U/kg/day) and mean BMI (kg/m^2) Mwas 22.9 ± 2.3 (range 1.2–28.1). CSII was proposed to highly motivated patients because of brittle diabetes (8 cases), hypoglycemia unawareness (1 case), pregnancy (4 cases), or need of more flexible lifestyle habits (job, physical activity etc) (2 cases). All of them underwent a training period about CSII management, either in normal conditions or during physical activity or intercurrent illnesses; a strict self-monitoring of diabetes was mandatory. CSII was started with an insulin dosage about 75–80% than previously, 50% as basal and the remaining 50% divided in boluses. No drop-out was observed.
Results: During a 18 month follow-up a reduction of HbA1c levels ($p = 0.014$, Friedman test) and an increase of BMI ($p = 0.02$, Friedman test) were found (Table) with no difference between males and females. Insulin requirement initially decreased, then gained, but not significantly ($p = 0.049$, Friedman test); no difference between males and females was found. Time (months) 0 + 6 + 12 + 18 Median (min–max) Med (min–max) Med (min–max) Med (min–max) HbA1c (%) 9.8 (8.6–12.7) 8.6 (6.9–10.9) 8.5 (6.1–10.7) 8.6 (6.6–11.2) BMI (kg/m^2) 22.8 (18.2–28.1) 23.6 (18.9–26.6) 23.4 (19–27.5) 23.5 (19–28.3) IR (U/kg/day) 0.92 (0.6–1.2) 0.74 (0.41–1.3) 0.83 (0.53–1.5) 0.90 (0.65–1.4).
Conclusion: In young T1DM patients CSII has been shown to ameliorate the degree of metabolic control, but the risk of weight gain should be carefully considered.

P-40

Sustained decrease of GlyHbA$_{1c}$ in T1D patients using CSII

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Background: CSII is a routine method of treatment for children, adolescents and young adults with T1D in our center since 1999 (Table). Poor metabolic control, dawn phenomenon, hypoglycemia unawareness, and brittle diabetes are among the most common indications.
Method: 340 patients (162 male and 178 female) were using CSII at the time of analysis. Mean age was 14.3 years (range 1.3–33.3) at the start of the CSII, with an average duration of T1D of 6.5 years (range 0.2–28.7) before starting CSII. GlyHbA$_{1c}$ levels were analyzed (DCA 2000+, Bayer) at 3 months intervals on CSII treatment. The change of GlyHbA1c in the first 6 months was calculated for each patient. Events of severe hypoglycemia (i.v. glucose or i.m. glucagon) and ketoacidosis (i.v. fluids) were recorded. 24-hours phone and e-mail contact with diabetologist was available to all patients. A group of 42 patients with emotional problems and/or eating disorders was among patients using CSII.
Results: All patients preferred CSII therapy to multiple daily injections with mechanic injectors. A mean drop in GlyHbA$_{1c}$ of 0.8% (SEM 0.1) was recorded in the first 6 months after the start of CSII. GlyHbA1c remained below 8% (DCCT standard) for up to 36 months. The rate of severe hypoglycemia was 0.023 per patient-year and ketoacidosis 0.021 per patient-year.
Conclusion: Sustained decrease of GlyHbA$_{1c}$ below 8% was achieved at a very low rate of severe hypoglycemia and ketoacidosis.

No./age groups (years)	Below 6	6–14.9	15–18.9	Over 19
All patients	33	247	138	132
Patients using CSII	26	127	52	50
%	78	79	38	38

Table: Number of patients using CSII according to age

P-41

Long-term treatment with continuous subcutaneous insulin infusion (CSII): improvements in hemoglobin A1c persist

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Introduction: Variable responses in hemoglobin A1c (A1c) have been reported during treatment with continuous subcutaneous insulin infusion (CSII) in pediatric patients.
Aim: To evaluate change in A1c and safety during long-term treatment with CSII in pediatric pts (<21 years) with type 1 diabetes (T1D).
Methodology: 102 consecutive pts on CSII were reviewed. 73 were on CSII for >6 months, had documented pre-CSII A1c levels and were further analyzed for: A1c prior to and during CSII, occurrence of DKA, severe hypoglycemia (SH), and discontinuation of therapy. Statistical analyses consisted of paired t-tests and multivariate analysis using logistic regression.
Results: Mean age at CSII initiation (AI) was 12.4 yrs and mean duration of CSII was 2.3 yrs. Mean A1c at 6, 12, 24, and 36 months during CSII (7.69%, 7.79%, 7.65% and 7.79%, respectively) were significantly lower than mean pre-CSII A1c (8.19%). At 48 months, the lower A1c trend continued. A1c at most recent visit was lower than pre-CSII in 75% of patients (mean decrease 0.85%). In 169 pt-yrs, rate of DKA = 1.8/100 pt-yrs and SH = 2.4/100 pt-yrs. Six pts (8%) discontinued CSII. Pre-CSII A1c, AI and sex were not predictive of A1c during treatment; there was a trend toward better outcomes in patients <8 yrs old.
Conclusion: CSII resulted in statistically significant sustained improvement in A1c for 3 yrs. The rates of DKA, SH and discontinuation were similar to or less than those previously reported. Our data suggest that CSII is an effective, safe and acceptable long-term treatment option for pediatric patients with T1D.

P-42

Persistence of efficacy of Continuous Subcutaneous Insulin Infusion on metabolic control: 4 years follow-up in children and adolescents with type 1 diabetes

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The CSII was demonstrated effective in improving short and medium-term metabolic control in children and adolescents with type 1 diabetes, but there is a few date about the long-term efficacy of this treatment. The aim of this longitudinal study was to evaluate the long-term efficacy of insulin pump therapy on metabolic control of pediatric patients with type 1 diabetes.
Methods: In 42 children with type 1 diabetes (18 girls and 24 males) aged 4.5–17 years (mean age 12.2 ± 3.4) and mean duration of the disease 5.1+/3.0 years the following parameters assessed in the year before starting CSII and during the 4 years of treatment with insulin pump were compared: annual mean level of HbA1c (mea-

sured every 3 months); annual mean level of Body Mass Index z score (measured every 3 months); insulin requirements (U/kg/day); severe hypoglycemic episodes (events/patients/year) and DKA episodes (events/patients/year). In the year before starting the CSII all patients had undergone insulin therapy with 4 injections per day. The insulin used in pumps was lispro (22 patients) and aspart (20 patients).

Results: During the 4 years of follow-up the annual mean values of HbA1c was reduced and respected the year before starting the CSII treatment. There was not significant difference regarding hypoglycemic events, the annual mean values of BMI z-score and DKA episodes between the year before the CSII treatment and the 4 years of insulin pump treatment. The insulin requirements decreased during the CSII treatment respected MDI treatment.

Conclusion: CSII is a durable and effective means to improve long-term metabolic control in children and adolescents with type 1 diabetes.

	Year pre-CSII (baseline)	1 year of CSII	2 year of CSII	3 year of CSII	4 year of CSII
Annual mean HbA1c (%)	9.01 ± 1.50	8.29 ± 0.90	8.66 ± 1.01	8.61 ± 0.89	8.40 ± 0.92
p vs baseline		**0.001**	**0.11**	**0.04**	**0.01**
Severe hypoglycemic events (events/patient/year)	0.02 ± 0.001	0.02 ± 0.001	0.02 ± 0.001	0.02 ± 0.001	0.00
DKA events (events/patient/year)	0.03 ± 0.001	0.03 ± 0.001	0.03 ± 0.001	0.03 ± 0.001	0.03 ± 0.001
Annual mean BMI	20.35 ± 3.40	20.85 ± 3.23	21.38 ± 3.31	21.52 ± 2.96	21.95 ± 2.78
p vs baseline		**0.0007**	**0.0002**	**0.0001**	**0.0002**
Insulin requirements (U/kg/day)	1.03 ± 0.31	0.76 ± 0.18	0.78 ± 0.16	0.81 ± 0.23	0.83 ± 0.19

P-43

Advantages of continuous subcutaneous insulin infusion (CSII) in young children and adolescents with type 1 diabetes (T1D)

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Aim: To compare the efficacy of treatment with CSII and multiple daily injections (MDI) in patients with T1D over one year using matched-pair analysis.

Methods: Clinical data of 52 patients starting on CSII (21 male) were compared with those of 52 matched controls treated with MDI. Matching criteria were: gender, age (±1 year), T1D duration (±1 year), and HbA1c (±0.3%) at study begin. Total daily insulin dose, percentage of basal rate, BMI-SDS, and HbA1c at study begin and at 12 months (mo) were evaluated. Matched pairs were analyzed separately according to age (group A: <12 years, n = 23; group B: ≤12 years, n = 29).

Results: Comparing patients with CSII and MDI at study begin, age (mean ± SD, 11.5 ± 3.3 years vs. 11.6 ± 3.4 years, p = 0.823), T1D duration (4.9 ± 3.0 years vs. 4.8 ± 2.9 years, p = 0.398) and HbA1c (8.2 ± 1.0% vs. 8.2 ± 1.0%, p = 0.498) were similar. At 12 mo, HbA1c was significantly lower in CSII group A (8.0 ± 0.8%) than in MDI group A (8.3 ± 0.9%, p = 0.033). In age group B, HbA1c increased not significantly at 12 mo in patients with CSII from 8.3 ± 1.1% to 8.5 ± 1.1% and in patients with MDI from 8.3 ± 1.1% to 8.7 ± 1.4%. Total insulin requirements were comparable between the groups throughout the study, while basal rate decreased significantly in CSII patients (group A: from 51.1 ± 12.8% to 33.3 ± 9.3%, p < 0.001; group B: from 50.9 ± 13.2% to 43.1 ± 10.2%, p = 0.011). At 12 mo, basal rate was significantly lower in CSII than in MDI patients of both age groups (group A: p < 0.001, group B: p = 0.017). BMI-SDS increased significantly from 0.38 ± 0.97 to 0.56 ± 0.89 in patients ≤12 years with MDI (p = 0.012), but not in CSII group B or in patients <12 years.

Conclusion: Compared with MDI, CSII had a favorable effect on glycemic control in young children, but not in adolescents. However, in all patients, CSII led to more physiological insulin delivery due to reduced basal rates.

P-44

Nutritional management of children on insulin pumps – a report of Australian practice

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Introduction: In the past 7 years the use of insulin pumps has grown markedly in Australia as a mode of therapy for children with Type 1 Diabetes. Diet is acknowledged as one of the cornerstones of management. However there is a lack of consensus internationally regarding the best method of dietary intervention to achieve optimal blood glucose control in children on insulin pump therapy (IPT).

Aims: The aim of this national cross-sectional survey of Australian Pediatric Diabetes Centres was to review nutrition interventions used for children on IPT. The study aimed to identify areas of consensus and discord in the dietetic management of children on IPT in Australia. These were compared with existing international evidence for best practice.

Methodology: A 4 page piloted questionnaire was sent to Dieticians at tertiary Australian Pediatric Diabetes Centres. The questionnaire gathered data on clinic demographics, HbA1c, BMI, staffing ratios and time spent in education. Details of nutrition educational strategies were identified. Dietitians were asked to report outcomes from their interventions.

Results: A 100 percent response rate was achieved (n = 12). A number of nutrition management strategies exist for children on IPT. These include carbohydrate counting, glycemic index, carbohydrate exchanges and glycemic load. At most centers nutrition education included teaching children to adjust preprandial insulin doses based on the carbohydrate content of the meal with estimations to a minimum of 5 grams. Glycemic index was taught to help reduce post-prandial blood glucose excursions.

Children on pumps had an average decrease in HbA1c of 1% (p < 0.01) at 12 months post-pump commencement. BMI Z scores did not alter significantly pre and post pump commencement.

Conclusion: The nutritional management of children on insulin pump therapy in Australia involves education regarding preprandial insulin adjustments based on carbohydrate quantity and changes in bolus administration based on glycemic index. There is a lack of evidence to support the degree of accuracy required in carbohydrate counting and the use of glycemic index in IPT.

P-45

Changes of insulin therapy after the introduction of insulin analogues in children and adolescents with diabetes mellitus type 1 in Germany and Austria

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Introduction: The introduction of rapid acting insulin-analogues in 1996 and long-acting insulin analogues in 2000 marked a new episode of therapeutic options in patients with diabetes mellitus type 1 (DMT1).
Aim: The aim of our observational study was to analyze the changes in insulin therapy over the last decade (1995–2004) in the pediatric population.
Methodology: The DPV-Science-Database is a multicenter documentation initiative as a basis for quality management in routing care (166 centers in Germany and Austria). Data are recorded locally by a dedicated computer software, anomynized and transferred for central analysis. This report is based on patients (age < 20 years) with DMT1. Data sets from 23.775 patients were available for analysis (mean age at onset: 8.2 years, mean chronological age: 13.5 years, 52.3% male).
Results: In the year 1995 100% of the patients were on regular insulin, while in the year 2004 36.3 ± 4.8% were using short acting insulin analogues, with the highest prevalence in the age group 15–20 years (50.2 ± 0.9%). A different change was observed with long-acting insulin: the use of NPH-insulin decreased (1995: 91. ± 2.7%, 2004: 55% ± 0.6%), while the use of zinc-insulin increased (1995: 9.8 ± 2.9%, 2004: 21.4 ± 4.1%) as well as the long-acting analogues: (1995: 0%, 2004: 24.8 ± 4.3%). The number of patients with intensified insulin therapy (≥4 injections/d) has increased over the period (1995: 34.9 ± 4.8; 2004: 71.3 ± 4.5%), also the injections/day (1995: 2.9 ± 8.8; 2004: 3.7 ± 5.7). CSII-treatment increased from 0.9 ± 1.0% (1995) to 10.0 ± 3.0% (2004). In 1995 only regular insulin was used for CSII-treatment, while in 2004 84.4 ± 3.5% used short-acting insulin-analogues.
Conclusion: Our study demonstrates an increased use of insulin analogues, along with intensified therapy and CSII in children and adolescents over the last decade in Germany and Austria.

P-46

Postprandial insulin aspart – a preferred alternative to preprandial administration of human insulin in preschool children with type 1 diabetes

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Introduction: Preprandial insulin injection in preschool children is complicated by irregular eating habits. Postprandial injection offers the convenience of adjusting insulin dose to match food consumed. The rapid absorption and short duration of action of insulin aspart (IAsp) makes it a suitable candidate for postprandial injection.
Aim: Evaluate safety and efficacy – including quality of life (QOL) – of two basal bolus regimens (IAsp plus NPH versus regular human insulin plus NPH in preschool children with type 1 diabetes. The two regimens will be referred to as IAsp and HI, respectively.
Methodology: A randomized, 12-week cross-over trial comparing IAsp and HI in 26 children (17 male, 9 female; age: 2.4–6.9 yrs). HI was injected 30 min before and IAsp shortly after the meals. QOL was assessed by an adapted version of the WHO DTSQ modified to measure parents' perception of their child's treatment.
Results: The incidence and estimated risk of hypoglycemia was similar for the two regimens (143 episodes/yr with IAsp and 142 with HI; relative risk (IAsp/HI) 1.06; 95% CI [0.96; 1.17]; p = 0.225). Postprandial plasma glucose increment (diff. between post- and pre-meal levels) did not differ between regimens (IAsp: 2.02 mM; HI: 1.63 mM; mean diff. (IAsp-HI): 0.518 mM; 95% CI [–1.17; 2.25]; p = 0.518). Mean HbA1c (7.7%) and mean insulin dose (0.7 U/kg) remained constant through the trial with both treatments. The ratio between basal and bolus insulin remained close to 1. QOL was generally more positive with the IAsp than HI regimen. Parents preferred to continue with the IAsp regimen (p = 0.045).
Conclusion: In a basal/bolus treatment scheme in preschool children postprandial IAsp used as bolus insulin was preferred over preprandial HI administration.

P-47

Insulin glargine in cystic fibrosis (CF) patients with diabetes (CFRD) or impaired glucose tolerance (IGT)

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Introduction: CFRD is linked with increased morbidity and mortality in CF. The aim was to investigate the efficacy and safety of Glargine in CF pts with diabetes or IGT.
Aim: The aim was to investigate the efficacy and safety of IG in CF pts with diabetes or IGT.
Methodology: We studied 6 CFRD pts (Group A: 5 females, mean age 26 yrs), 6 CF pts without fasting hyperglycemia but diabetes after OGTT (Group B: 4 females, mean age 23 yrs) and 4 CF pts with IGT (Group C: 2 female, mean age 28 yrs). A single daily dose of Glargine was performed (mean dose Group A: 0.3 U/Kg; Group B: 0.2 U/Kg, Group C: 0.15 U/Kg). In Group A Glargine took the place of insulin intermediate; Group B and Group C had never been treated before. Data about HbA1c, BMI, hypoglycemia episodes, compliance to the therapy were collected at the start and after 9 months.
Results: No significant difference was found in HbA1c (Group A: 9.6% versus 8.6%; Group B: 7% versus 7.4%; Group C: 6.76% versus 6.74%) and BMI (Group A: 21 versus 21.7; Group B: 16.68 versus 17.3; Group C: 18.17 versus 19). Hypoglycemia frequency didn't change in Group A and no hypoglycemia was observed in other Groups. Compliance improved in Group A and was good in Group B and C.
Conclusion: Even if Glargine didn't improve metabolic control, it appeared safe and had a good impact on nutritional status. Indeed the lack of significance in BMI increment might depend on the low number of pts and short follow up. We are performing an Italian multicenter study in IGT patients to investigate if Glargine can improve CF prognosis.

P-48

Diabetes control with Insulin Glargine

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Introduction: Insulin Glargine (Lantus) is a recently approved, long-acting insulin analog, which is gaining in acceptance in diabetic children. Despite its clinical acceptance, there are few papers in the literature comparing its effectiveness to previous insulin preparations. This study gives a random sample of our experience with the use of Glargine in children with type 1 diabetes.
Aim: To report our clinical picture of Glargine (Lantus) in a sample of children recently treated with Glargine.
Methodology: There are 793 children 12–18 years old followed at the Diabetes Clinic at Children's Medical Center of Dallas. This group was retrospectively randomized. Thirty percent were using Insulin (with Insulin LysPro). Criteria for inclusion were: (1) IDDM for at least 2 years before the start of therapy with Glargine + LysPro. (2) At least 1 year of the new regimen. (3) Hgb A1c at least 3×/year. (3) 12–18 years at the time of change-over.
Results: Control was evaluated with comparing the mean A1c's during the two treatment period. Results were evaluated by the matched-pairs t-test. A sample of 43 patients with the criteria above

was studied. 1) Before Glargine 8.57 ± 1.23 [mean ± sd(mean)] 2) On Glargine 8.47 ± 1.56 [mean ± sd(mean)].
Conclusion: In a sample of the size chosen, there is clearly no objective evidence of improved control with the insulin Glargine-lyspro regimen. Clearly, prospective studies of larger size could prove or refute this conclusion.

P-49

Effect of long-acting insulin analogue glargine in basal-bolus therapy in japanese children with type 1 diabetes

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Introduction: Some papers have demonstrated the efficacy of long-acting insulin analogue glargine (G) in basal-bolus insulin therapy for pediatric patients in Caucasian populations. However, there has been no published report of its clinical use in Japanese children with type 1 diabetes.
Aim: To evaluate the efficacy of the use of G switching from NPH in basal-bolus therapy for Japanese children with type 1 diabetes.
Methodology: The study subjects consisted of 30 Japanese children and adolescents, 11 males and 19 females aged 13.3 years, with type 1 diabetes. Fasting blood glucose levels, HbA1c values and the frequencies of severe hypoglycemia were evaluated before and 3, 6 and 12 months after the use of G. We used regular insulin and rapid-acting insulin analogue as bolus insulin and switched the treatment from NPH to G at bedtime or in the morning.
Results: The mean fasting blood glucose level was significantly lowed (baseline: 142.5 mg/dl vs. 3, 6, 12 months: 127.1 mg/dl, 129.0 mg/dl, 121.1 mg/dl, $p < 0.01$, respectively) and the mean HbA1c value significantly decreased after switching to G (baseline: 7.8% vs. 3, 6, 12 months: 7.6%, 7.5%, 7.3%, $p < 0.01$, respectively). Severe hypoglycemia rarely occurred before and after using G (before: twice/year, after: no episode).
Conclusion: Basal-bolus therapy using G resulted in improved overall glycemic control with a low risk of severe hypoglycemia. G appears to be a more suitable basal insulin preparation than NPH in Japanese children and adolescents with type 1 diabetes.

P-50

Evaluation of metabolic control and quality of life children and adolescent patient treated with insulin Lantus

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Introduction: Improving glicemic control can reduce the risks of long-term microvascular complications. However hypoglicemic episodes could be a barrier to achieving better HbA1c values, the nev genetically engineered insulin analogues have resulted in improved glicemic control with reduced hypoglicemic episodes.
Aim: The aim of this study is to evaluate the metabolic control and quality of life children and adolescent patient treated with insulin Lantus, remaining under care of Diabetes Outpatient Clinic in Kielce.
Methodology: The 44 patients aged from 6 to 22 and 4/12 with type 1 diabetes maintaining 6 and 5/12 was investigated. An average levels of HbA1c was compared before (about 4 indication per annum) and after introduction of treatment with Lantus, the daily insulin dose, incident of hypoglicemic events, events of 'dawn phenomenon'.
Results: Averages HbA1c after introduced a Lantus therapy was decreased to 0.94%, total daily insulin was decreased to 0.1 U/kg. The 24-hour profile of glycemia is more stable when using the long acting analog (Lantus) – we can reduce events of dawn phenomenon (22 children resigned from taking dose insulin a 3 a.m.).
Conclusion: The therapy with Lantus is allowed to achieve the better metabolic control. The patients confirmed significant improvement of quality of life.

P-51

Body composition in young females with type 1 diabetes mellitus

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Introduction: Overweight is common during late puberty in females with Type 1 diabetes.
Aim: To examine if overweight during puberty in females with Type 1 diabetes persists in young adulthood.
Methodology: Eighteen females with type 1 diabetes and 18 healthy controls were recruited in a case-control study at the age of 16–19 year. Six years later 16 of the diabetic females and 16 of the controls were re-examined. Body composition was assessed with BMI and dual energy x-ray absorptiometry. HbA1c (upper reference limit 5.3%) was 8.0 (1.1)% at baseline and 7.6 (1.1)% at follow-up. Daily dosage of insulin was 1.1 (0.3) and 0.8 (0.2) U/kg, respectively. The groups were compared using ANOVA after log transformation of body composition variables.
Results: BMI and percentage body fat (BF%) were significantly higher at baseline in females with type 1 diabetes compared to the controls [26.3 (2.6) kg/m^2 vs. 23.6 (3.8) kg/m^2, $p < 0.05$ and 37.1 (5.5)% vs. 32.1 (7.7)%, $p < 0.05$]. At follow-up there was a tendency for higher BMI [27.8 (4.8) vs. 24.9 (5.8); $p = 0.10$] and BF% [40.4 (10.3) vs. 34.4 (11.8); $p = 0.11$] in the diabetic group. There were no significant difference in change of BMI or BF% between the to groups. There was a strong correlation between BMI at baseline and at follow-up in both diabetic females ($r = 0.61$; $p < 0.05$) and controls ($r = 0.83$; $P < 0.01$).
Conclusion: The previously observed overweight in pubertal girls with type 1 diabetes seems to persist in young adulthood. This study emphasizes the need for strategies to prevent overweight during puberty.

P-52

The evaluation of metabolic control in children with type 1 diabetes mellitus

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Introduction: It is well known that good metabolic control of diabetes decreases the risk of acute and chronic complications and assures proper physical and psychical development.
Aim: The aim of this study was to evaluate metabolic control in children with type 1 diabetes mellitus during puberty.
Methodology: 100 patients (47 girls and 53 boys) at the age of 12.3 ± 1.5 year were included in the study. Duration of diabetes was 3.82 ± 2.66 years. Children were divided in three groups – 1st group (44 children) treated with MDI, 2nd group (27) treated with functional insulin therapy, 3rd group (29) received CSII. The metabolic control was ascertained by the level of HbA1c, total cholesterol (CT), HDL, LDL, TG. TSH and anti tTG antibodies level was measured in all cases. During each examination child's height, mass, BP and BMI were recorded.
Results: The mean level of HbA1c for 1st, 2nd and 3rd group was 8.82%, 8.61% and 8.64% respectively. 30% of diagnosed children had elevated CT level and LDL. 3 patients had elevated TSH level.

6 children were positive for anti tTG, no one had IgA deficiency. One hypertension case was discovered. 5 children with Hashimoto disease were in the group (2 of them were diagnosed during this study) 3 with celiac disease and one girl with anorexia.
Conclusion: There is no significant difference in metabolic control between the groups. Abnormal lipide profile might be a result of inadequate metabolic control or dietary intake during puberty. Diabetic children should be screened for other autoimmune diseases regularly.

P-53

Treatment of type 1 Diabetes Mellitus revealed below 6 years of age in the Silesian Center, Poland

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Introduction: Type 1 diabetes Mellitus is more and more often diagnosed in preschool children.
Aim: The aim was to assess metabolic control and insulin therapy methods in children diagnosed with diabetes in the years 1998–2003, aged up to 6 yrs.
Methodology: Charts of all 57 children, treated in our center were analyzed up to 2005. The mean age at the time of diagnosis was 4.0 ± 1.6, mean HbA1c was 10.1 ± 1.9% and for the time of the study 7.0 ± 0.8%. Metabolic control (mean HbA1c), mean daily insulin requirement (DIR), base insulin, weight were estimated every 2 yrs. Additionally methods of insulin therapy were assessed.
Results: HbA1c showed no statistic significance in the analyzed periods. DIR and base significantly raised in the first 2 intervals [0–2 ($p < 0.01$ for both) and 2–4 yrs after diagnosis (respectively $p < 006$; $p = 0.049$)], but didn't in the last one (4–6 year of observation). Mean contain of basal insulin in DIR wasn't significantly reduced in observed intervals (respectively: 55.7 ± 22.1; 51.2 ± 13.4; 44.1 ± 7.0%). No difference in weight (percentile) was found. At diagnosis there were 57 children out of which 37 (64.9%) used premixed insulin in 2 shots (MIX), 16 (28.1%) multiple daily injections (MDI) and 4 (7.0%) pumps. The 44 children, who suffered from diabetes for 2 yrs, were treated with MIX – 19 (43.2%), MDI – 11 (25.0%) and pump – 14 (31.8%). Respectively, the group treated for 4 yrs (23 children) used MIX – 4 (17.4%), MDI – 7 (30.4%) and pump – 12 (52.2%) and for 6 yrs (12 children) used only MDI 3 (25%) and pump 9 (75%). The HbA1c results showed no significant change after switching from MIX to either MDI or pump.
Conclusion: During the observed intervals metabolic control was good and can be maintained in small children for a longer period.

P-54

Children with type 1 DM with younger age at onset show worse metabolic control after 1 year of disease but not after 3 and 5 years

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Introduction: Age at onset of type 1 DM influences some features of the disease. Furthermore, therapy and metabolic control are believed to be more difficult in younger children.
Aim: Age at onset and metabolic control in DM.
Methodology: We analyzed the characteristics at onset and during the first 5 years of disease in 80 children, who developed type 1 diabetes between 1994 and 2002, subdivided in two groups: Group 1 (n. 41) with onset before the age of 5 yrs (n.21 < 3 yrs) and Group 2 (n.39) with onset after the age of 10 years. N.79 have completed a 3 year and n.57 a 5 year follow-up.
Results: At onset, Group 1 showed lower HbA1c values ($p = 0.0001$), C-peptide ($p = 0.04$), duration of symptoms before diagnosis (0.0001), than Group 2. The duration of symptoms significantly correlated with C-peptide at 1 and 3 yrs of disease and with the duration of detectability of C-peptide. The latter, on the contrary, did not correlate with C-peptide levels at onset. At 1 and 3 years of disease, mean C-peptide values were significantly lower in Group 1 than in Group 2, while at 5 years of disease most patients had undetectable C-peptide levels. HbA1c mean annual levels were significantly higher in Group 1 than in Group 2 only at 1 year of disease. At 5 years of disease 20% of the younger and 26% of the older patients showed a good metabolic control, i.e. HbA1c levels <7%.
Conclusion: C-peptide levels at onset are not predictive of duration of its detectabilility. Group 2 show a slower process of beta-cell destruction, as proved by high levels of HbA1c and C-peptide at onset and longer duration of symptoms. It is not confirmed the clinical impression of a worse metabolic control in younger children.

P-55

Evaluating 'Sweet Talk' using the RE-AIM framework for behavioral interventions in diabetes care

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Introduction: A meta-analysis of behavioral interventions in young people with diabetes showed that few become incorporated into routine clinical practice. The RE-AIM framework assesses Reach and Efficacy of such interventions, and the extent to which they can be Adopted, Implemented and Maintained in other clinic settings.
Aim: The challenge is to develop innovative behavioral support interventions, which are feasible within existing health resources, engage young people and fulfil the 'RE-AIM' criteria.
Methodology: 'Sweet Talk' delivers a recognised behavioral intervention by text-messaging. This text messaging support system is web-based, and developed with 'user-centred' design methodology to automatically deliver daily text-messages based on patients' individual profiles and diabetes self-management goals. The 'Sweet Talk' system has been evaluated in a 3-group RCT (Group 1 – control, Group 2 – conventional insulin therapy and 'Sweet Talk', Group 3 – intensive insulin therapy (IIT) and 'Sweet Talk').
Results: The Sweet Talk intervention had high 'reach', with 73% of the eligible population participating in the study, creating close to a 'normal' clinic population. Furthermore the majority of patients felt that it had helped their diabetes management, and wanted to continue with the intervention at the end of the study. Efficacy has been demonstrated in the patients randomised to IIT with an overall reduction in HbA1c of 1.1% after one year. The user-centered design methodology resulted in a software package that is robust and easy to use – it is therefore easily 'Adopted', 'Implemented' and 'Maintained' in other clinic settings. In addition, content of text-messages could readily be modified to reflect individual clinics protocols, philosophy and approach.
Conclusion: Scheduled tailored text-messaging offers an innovative, inexpensive and effective means of offering support to adolescents with diabetes. Attention to the 'RE-AIM' framework means that the 'Sweet Talk' system could easily be adapted for use in other diabetes clinic settings.

P-56

Insulin regimen and metabolic control: what is the optimal injection regimen?

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Introduction: Previous cross sectional international studies of the Hvidore Group have shown a deterioration in metabolic control in a large adolescent cohort over a three year period despite modifications in insulin regimens. Good metabolic control is not only reducing the risk for late complications, but is also related to a better quality of life.
Aim: To perform a prospective non-intervention study to evaluate metabolic control and possible contributing factors.
Methodology: Eighteen centers in 15 countries, offering multidisciplinary diabetes care, included over a period of 12 months the newly diagnosed children with type 1 diabetes. Centralised HbA1c values were measured 1, 3, 6, 9, 12, 18, 24, 36 months after diagnosis. Insulin type, injection frequency, severe hypoglycemia (unconsciousness or seizures) and DKA (standard bicarbonate <15 mmol/l) were documented.
Results: 275 children (M: 131, F: 144; age range: 0.2–16.8 yrs, median: 9.6 yrs) were included, whereas 60 declined participation. After three years of diabetes, HbA1c ≥ 8% was observed in only 31.5%, with 39% of them on 4 injections per day or more (27% on 2 and 33% on 3 injections). Mean HbA1c levels in the 4 or more injection group was significantly lower ($p < 0.05$) than in the twice or three daily group (resp 8.3% ± 1.3, 9.1% ± 1.4 and 9.2% ± 1.8) Different insulin types were used in various combinations without significant change in outcome. Fair glycaemic control was achieved without increase in severe hypoglycemia (0.1 episode per patient trial year). DKA after diagnosis was seen in 5% of the children (no difference between injection frequency).
Conclusion: Despite multidisciplinary approach, 68.5% of children have 3 yrs after onset unsatisfactorily high HbA1c levels. However, Intensifying insulin regimen does improve metabolic outcome.

P-57

Etiology and metabolic control of childhood and adolescent diabetes mellitus: an experience in Siriraj Hospital, Bangkok, Thailand

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Introduction: Few data on metabolic control in children and adolescents with diabetes mellitus (DM) in developing countries revealed suboptimal glycemic control. At Siriraj Hospital, children with DM have been provided care by the multidisciplinary care team.
Aim: To obtain the information on etiology of childhood onset DM in Thai children and the outcome of therapy.
Methodology: We retrospectively reviewed case records of children and adolescents with DM seen at Siriraj Hospital between January 2003 and December 2004. Age, duration of diabetes, height, body weight, insulin regimen, and HbA_{1c} at the most recent visit were recorded.
Results: There were total of 157 patients. Type 1 DM comprised 84.7% (n = 133) and type 2 DM 15.3% (n = 24). Age at onset and body mass index were significantly higher in patients with type 2 DM. The mean age of patients with type 1 and type 2 DM were 12.14 ± 4.72 years and 14.55 ± 2.38 years (p 0.015), respectively. Mean HbA_{1c} was 8.83 ± 2.09% in patients with type 1 DM and 6.79 ± 2.34% in type 2 DM (p 0.002). Among patients with type 1 DM, 72% of children (n = 96) had two injections daily, while 28% (n = 37) were on three or four daily injections. No difference in glycemic control was found among patients treated with two, three or four daily injections. Only 38% of children (n = 49) had HbA_{1c} of < 8%. Adolescents had poorer glycemic control compared to the prepubertal group.
Conclusion: Despite the multidisciplinary team approach, most of our patients with type 1 DM had suboptimal glycemic control.

P-58

Worsening of glycaemic control on a basal bolus regime

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Introduction: Since September 2002 children in Wigan have been encouraged to consider changing to a basal bolus regime from the traditional twice daily (BD) injections. The benefits suggested were a more flexible lifestyle and improved glcyaemic control. This approach is supported by the National institute of Clinical excellence. New cases were offered basal bolus as being the best regime.
Aim: To study the effect on glycosylated hemoglobin (HBA1C) of switching children to a basal bolus regime.
Methodology: Notes were retrospectively analyzed. The average HBA1C for the last six months and for the six months before and after a change to basal bolus was recorded.
Results: 98 children aged under 16 (m/f; 52/46) attend the clinic. Five were excluded due to being within 4 months of diagnosis or unavailability of recent records. HBA1C values within four months of diagnosis were not used. The overall average HBA1C was 8.84. Thirty children switched to basal bolus with an average HBA1C of 8.6 beforehand, an average of 8.65 six months later and a most recent average of 9.23. Children (16) commenced on basal bolus had an average HBA1 of 8.36, children on BD (35) 8.62 and children on pumps (10) 9.013. However 8 children have managed a sustained improvement in HBA1C following a change to basal bolus.
Conclusion: Basal bolus is widely advocated as being a good regime to improve glycaemic control. However our experience is that control has worsened. Several children have admitted that they found four daily injections burdensome and that they have sometimes omitted injections. Some are opting to return to a BD regime. Careful patient selection and assessment of family motivation is necessary prior to changing to a basal bolus regime.

P-59

Assessment of the metabolic control of diabetes mellitus type 1 in children and adolescents based on the continuous glucose monitoring system

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Introduction: According to the current recommendations, treatment of diabetic patients should result in achieving tight glycemic control – nearnormoglycemia. It is particularly difficult in pediatric patients with type 1 diabetes in spite of frequent self-monitoring of blood glucose. CGMS is a new tool available for continuous measuring of glycemia.
Aim: The main objective was to determine the frequency of hypoglycemic (≥60 mg%) and hyperglycemic episodes (≤180 mg%), lasting for at least 15 minutes, in children and adolescents with type 1 diabetes based on the CGMS.
Methodology: 57 patients (28 girls and 29 boys) aged from 5 to 18 years (mean 12.5), treated with insulin for 1 to 13 years (mean 5.5) entered into the study. At the time of CGMS use 15 patients were treated with conventional and 42 with intensive insulin therapy (18 patients on the CSII). Mean HbA1c value in the studied group was 7.6% (5.7–10.6%).
Results: In total 235 days (99 hours per patient) of glucose monitoring were registered by CGMS. 279 hypoglycemic events were

present in 53 subjects. They lasted for up to 8 hours and composed up to 27% of patient's CGMS time. In 43 patients (75%) 90 episodes of nocturnal hypoglycemia lasting for up to 7 hours were registered. 29 incidences of post-exercise hypoglycemia were seen in 19 children. Asymptomatic hypoglycemias, present in 49 patients (86%), constituted 94% of nocturnal and 79% of post-exercise hypoglycemic events. Overall 755 hyperglycemias were seen (4–47 per patient), lasting for up to 20 hours. They composed 5 to 72% of the patient's CGMS time. 513 (68%) of them were postprandial ones. In 21 patients 33 episodes of rebound hyperglycemia were seen and 16 patients proved to suffer from the dawn phenomenon. 162 hypoglycemias (58%) and 257 hyperglycemias (34%) were missed by self-monitoring (SMBG) and were detected only by CGMS.
Conclusion: The majority of patients experienced asymptomatic, nocturnal hypoglycemias. Postprandial hyperglycemias, present in all patients, were the most frequent cause for high blood glucose. CGMS was well tolerated by all patients and proved to be effective in detecting asymptomatic hypoglycemias and hyperglycemias missed by SMBG.

P-60

The experience of CGMS usage in patients with diabetes mellitus type 1

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Introduction: Continuous glucose monitoring system (CGMS), measuring blood glucose level every 5 minutes, entered diabetologists' practice worldwide during the last years. The data from CGMS are more detailed, than traditional glycemic self-control with test strips.
Aim: To determine: a) dependence of asymptomatic hypoglycemia frequency upon HbA1c and time period. b) frequency of inadequate hypoglycemic counterregulation syndrome in patients with Diabetes Mellitus Type 1.
Methodology: 61 patients (23M/38 F) with Diabetes Type 1 aged 2.7–37 yrs (11.8 ± 6.2) with duration of disease 0.1–24 yrs (4.49 ± 5.2) and HbA1c 4.9–18.8% (11.8 ± 2.6%). CGMS (Medtronic MiniMed, Sylmar, CA) was used during 3 days. The patients were divided in 2 groups: with HbA1c upper and lower of 9%. The criterion of hypoglycemia was glucose level less than 3.2 mmol/l. The criterion for inadequate hypoglycemic counterregulation was the presence of hyperglycemic peak after the episodes of evident or latent hypoglycemia.
Results: 29.5% patients presented with asymptomatic hypoglycemia, 18.0% – with noctural and 24.6% with daytime hypoglycemia. Inadequate hypoglycemic counterregulation syndrome was evident in 27.9% patients. Hypoglycemia was much more frequently detected in patients with better control of HbA1c (see table). HbA1c > 9% HbA1c < 9% n = 43 n = 18 Asymptomatic hypoglycemia, % of patients 23.3 44.4 Noctural hypoglycemia, % 14.0 27.8 Daytime hypoglycemia, % 18.6 38.9 Inadequate hypoglycemic Counterregulation syndrome % 23.3 33.3.
Conclusion: Better self control can not prevent from hypoglycemia. The patients with optimal and suboptimal HbA1c level are at risk of both evident and asymptomatic hypoglycemia 24 hours a day.

P-61

The appreciation of the degree of the thmetabolic control in children with type 1 diabetes treated with a personal insulin pump and continuing glucose monitoring system (CGMS)

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Introduction: With the intensive insulin-therapy connected is the necessity of frequent measurements of blood glucose levels and to adapt the insulin dose several times a day to the glucose levels, meal and the intensity of physical activity.
Aim: was an around the clock monitoring of the blood glucose levels in children with type 1 diabetes treated with a personal insulin pump, with the CGMS / glucometer.
Methodology: The examinations were performed in 20 patients, aged 8–18 years. Each patient received the CGMS system in 3 cycles. On the support of the results of the examinations with CGMS and the glucometer performed was also a correlation of the glucose levels through the calculation of the linear regress function $y = a*x + b$, which parameters estimated was with the method of the least squares. Designated was correlation coefficient r for the examined variables.
Results: During the study duration of 237 days recorded were 45 318 measurements with the CGMS system and 1192 with the glucometer. Unaware nocturnal hypoglycemia was observed in 17 patients only with the CGMS system. In 19 patients observed was postprandial hyperglycemia in 80% only with the CGMS. With the CGMS ascertained were also unaware decrease of the glucose level to 50 mg/dl immediately after physical activity, also during the night. The appreciation of the correlation of glucose levels performed with a glucometer and CGMS showed the highest correlation in the second and third cycle (r = 0.95). The correlation coefficient for all results was 0.93; what indicates an almost absolute correlation between the examined variables.
Conclusion: 1) the results of a CGMS permit a better adjustment of the insulin dose to the actual glycemia, the amount of consumed carbohydrates and physical activity. 2) the CGMS enables the detection of by hypoglycemia during the night.

P-62

Use of CGMS during scuba dive

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Introduction: In Sweden the standard clinical advice is against persons with type 1 diabetes participating in scuba diving. In certain cases it is, however, allowed but then under certain circumstances and with some restrictions. The major concern is the threat of a hypoglycemic episode while diving since this could be fatal for both the diver and the diving partner.
Aim: To identify if CGMS can be used when scuba diving in a dry suit.
Methodology: Two adolescents, 17 and 20 years, with onset of type 1 diabetes at 6 and 10 years, volunteered to use CGMS during an Advanced Open Water Diver Coarse. Both fulfilled the criteria of diving with type 1 diabetes in Sweden and had a PADI-certificate. The CGMS was used over a period of three days where five scuba dives where carried out during day two and three. SMBG were compared alongside those registered by the CGMS. Episodes with hypo-, hyperglacaemia and ketosis were recorded.
Results: Five dives were accomplished to the maximum depth of 29 meters. No interruption of recording was noticed during the two days of diving. The correlation between SMBG and CGMS was 0.61 and 1 respectively 0.62 and 0.82 during diving days. During day 2/3 we noticed 16% respectively 5% duration below 4 mmol/L and 30/56% duration above 10 mmol/L. During day 3/3 we noticed 0/0% duration below 4 mmol/L for both, whereas 67/91% duration was noticed above 10 mmol/L. During the five dives we noticed no hypoglycemia. No ketosis was recorded.
Conclusion: The CGMS could be used during scuba diving in a dry suit in order to increase the safety for individuals with type 1 dia-

betes. A CGMS with an alarm signal would furthermore increase the safety since hypoglycemia prior to and during a scuba dive then would be able to detect.

P-63

Clinical evaluation of continuous glucose monitoring system in type 1 diabetics

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Introduction: Continuous Glucose Monitoring System (CGMS) is a holter type of device for measuring the glycemia in every 5 minutes for a period of 72 hours.
Aim: To evaluate the clinical performance of CGMS in type 1 diabetic patient.
Methodology: Thirty-two type 1 diabetics (male 14, female 18, mean age: 23.4 ± 3.9 years) were included in the study in period January–December 2004. Mean HbA1c was 8.8 ± 1.4%. All patients were treated with intensive insulin therapy (3 or 4 daily injections). CGMS (Minimed CGMS gold) was performed for 72 hours.
Results: A mean of 1.1 ± 1.4 asymptomatic nocturnal hypoglycemic events per patient was registered with CGMS during the night and early morning. Reactive hyperglycemia over 22.2 mmol/L were registered in 12 patients. Prolonged period of hyperglycemia was recorded in 15 patients. Seven patients were found to have the Dawn phenomenon. Modification for glycemic food was made in 22 patients. HbA1c showed significant lowering of 0.9%, two months after (8.8 ± 1.4% vs 7.9 ± 1.3%, $p < 0.05$).
Conclusion: A 3-Day Glucose profile obtained by CGMS is representative of the whole metabolic control of the patient. There was an improvement of HbA1c in our study after 2 months.

P-64

High prevalence of celiac disease in Swedish children with type 1 diabetes

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Introduction: Celiac disease (CD) has a well known co-morbidity with type 1 diabetes and screening for antibodies against IgA-gliadin, IgA-endomycium and/or IgA-transglutaminase is a routine procedure in many centers.
Aim: To investigate the prevalence of celiac disease in a large group of children with type 1 diabetes (T1DM).
Methodology: All children with T1DM, screened for CD, at Astrid Lindgren Children's Hospital from 1995 to 2004 (n = 847) were retrospectively studied through three patient file systems (BMS, Diabase and paper charts). Patients were screened with different combinations of antibody tests over this period. Children with CD before T1DM diagnosis or CD diagnosed only with small intestinal biopsy were also included.
Results: 123 out of 847 children had at least one positive antibody test. The prevalence of biopsy-confirmed celiac disease among the diabetic children was 8.8% (75/847). 89% (67/75) were diagnosed after T1DM onset. Three were diagnosed with CD only with biopsy. Eight children had CD verified by biopsy before diagnosis of T1DM. The majority of children with CD (58%) had no symptoms. 33% were diagnosed at the first screening close to diagnosis of T1DM, 57% within the first 2 years and 87% within 4 years of T1DM. 39% (48/123) of the T1DM patients with a positive antibody test had not been referred for a biopsy.
Conclusion: The prevalence of CD in T1DM children of 8.8% is among the highest reported. A large group was not further investigated with a small bowel biopsy, maybe due to the lack of overt symptoms of CD. Using the positive predictive value for each of the three antibodies in the biopsied group to calculate the expected frequency of silent CD in the non-biopsy group could eventually result in a prevalence of 14%.

P-65

Risk factors for celiac disease in children with type 1 diabetes mellitus

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Introduction: Type 1 diabetes and celiac disease are frequently associated and recognize a common genetic background.
Aim: The aim of the study was to evaluate genetic predisposition in class II HLA for developing celiac disease (CD) in children with type 1 diabetes mellitus (DM) and to determine a relationship between CD and diabetes specific antibodies.
Methodology: Antibodies to tissue transglutaminase (tTG) were assayed by ELISA during yearly screening examination of children with type 1 DM, aged 1–18 years in the Department of Pediatric Endocrinology and Diabetes in Katowice. A group of 22 children was selected (12 girls and 10 boys) with a level of tTG above the norm and with no clinical symptoms characteristic for CD. In the examined group (n = 22) biopsy of the small intestine was performed and the material was assessed according to the Marsh scale. Class II HLA was identified in the locus DR and DQ. Antibodies to insulin (IAA), tyrosine phosphatase (IA2A) and glutamic acid decarboxylase (GADA) were assayed using radioimmunological method and their level at the onset of DM was analyzed.
Results: The mean age at the onset of DM in the examined group was 6.07 ± 3.39 years (ranging from 2–11.5 years). Celiac disease occurred after 2.23 ± 2.39 years after the onset of DM and in 1 child CD was diagnosed before the onset of DM. In 5 children (22.7%) tTG antibodies appeared at the onset of DM and in 16 (72.7%) within 4 years after the onset of DM. On the grounds of biopsy silent celiac disease was diagnosed in 15 (68.2%) cases. In 7 (31.8%) children a latent form was found (additionally endomysium antibodies were positive in all these children). Positive GADA was noted in 18 patients (81.8%), whereas IA2A were present in 17 (77.3%) and IAA in 15 (68.2%) cases. Twelve (80%) out of 15 children with silent CD had positive GADA which correlated with positive result of biopsy. Elevated titers of all three types of antibodies (GADA, IAA, IA2) were found in 6 (40%) children with silent CD. So far 15 assays of HLA have been performed and in 11 (73.3%) cases haplotype DRB1*03 DQB1*0201 was found, which is the most common haplotype in CD. The incidence of the other common haplotype – DRB1*04 DQB1*0302 – being found in 12 (80%) patients. Only one subject was homozygous in the haplotype DRB1*03 DQB1*0201. All children examined so far had at least one of characteristic haplotypes.
Conclusion: According to our data, the incidence of CD in children with type 1 DM can be expected in the following cases: young age at the onset of DM and within first years of duration of DM presence of antibodies GADA, presence of haplotypes DRB1*03 DQB1*0201, DRB1*04 DQB1*0302.

P-66

Screening for celiac disease in Egyptian diabetic children and adolescents using anti-endomysium antibody

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Background: Celiac disease (CD) and type 1 diabetes mellitus can frequently coexist, presumably due to a common genetic predisposition.
Objective: The present study was designed to evaluate the frequency and clinical presentation of celiac disease among Egyptian diabetic children and adolescents and to evaluate whether CD affects insulin dose, growth, and glycemic control.
Subjects and methods: A total of 270 consecutive type 1 diabetics (126 males; age range 6.0–19.0 years, and diabetes duration ranging between 1 & 17 years) were screened for CD by determination of IgA-endomysium antibodies (EMA). Those children with positive results were offered small bowel biopsy.
Results: Of 270 patients, 19 were positive for EMA accounting for 7% of cases. Seventeen of 18 EMA positive diabetics who accepted to undergo biopsy had morphological changes consistent with CD. Only one child from the latter group had normal small intestinal biopsy. In another group of 19 IgA-EMA negative control diabetics with gastrointestinal symptoms, biopsies were normal. So, calculated sensitivity and specificity of EMA were 100% and 94.5% respectively. There was nonsignificant difference in the frequency of gastrointestinal symptoms in diabetics with CD versus those without. Forty-two percent of celiac patients presented with diarrhea, while 47.4% were completely symptom-free. The prevalence of CD seems to be significantly related to the duration of diabetes. Compared to matched type 1 diabetic controls, those with CD had higher mean insulin dose. Growth parameters were markedly affected in diabetics with CD reflected by significant decrease in weight and height standard deviation scores. Presence of CD in diabetics was associated with poor glycemic control.
Conclusion: The present study confirms that CD is prevalent in Egyptian pediatric type 1 diabetic population and emphasizes the benefit of screening programs on populations at risk.

P-67
Autoimmune thyroiditis and celiac disease in children and adolescents with IDDM

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Introduction: Patients with IDDM frequently suffer from numerous, co-existing autoimmune diseases. The most common among children are autoimmune thyroiditis, mainly Hashimoto disease, and celiac disease (CD). The aim of this study was to evaluate how often autoimmune thyroiditis and celiac disease co-exist with IDDM among children and adolescents.
Methodology: The study included 139 children and adolescents with new-onset IDDM in the years 2001–2004. The study group comprised 69 girls (50%) and 70 boys (50%) aged 1–18 (mean 9.7). All the patients had the concentration of TPO-Ab and EutTG IgA determined.

In case when TPO-Ab titers were elevated (over 60 UI/ml), autoimmune thyroiditis was diagnosed. Concentration of TSH and FT4 were evaluated and thyroid gland ultrasound examination was performed. Higher level of EuTG IgA antibodies imposed the execution of small bowel biopsy.
Results: Higher concentration of TPO-Ab (80.0–4440.4 IU/ml) was observed in 20/139 patients – 14.4%. Among them we had 12/69 girls – 17.4% and 8/70 boys – 11.4%. One girl suffered from hypothyroidism following autoimmune thyroiditis diagnosed a year before IDDM. The rest of children were euthyreoid. Ultrasound examination showed hypoechogenic and heteroeroechogenic changes in 8/20 cases –40%. CD was diagnosed in 4/139 cases (2.9%), children aged 2, 8, 9 and 13. Their EuTG IgA–Ab levels ranged from 56.6 to over 100. Small bowel biopsies revealed in case of two of these children CD type of atrophy. None of these 4 youths displayed clinical features of CD.
Conclusion: Autoimmune thyroiditis was diagnosed in 14.4% and CD in 2.9% of children with new-onset IDDM. Thyroiditis is more often observed among girls. We suggest those patients should be brought under screening test for thyroiditis and CD, as no clinical features were visible at the onset of IDDM.

P-68
Asymptomatic thyroid and celiac autoimmunity in Polish children with type 1 diabetes

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Introduction: Type 1 diabetes mellitus is characterized by increased prevalence of autoimmune disorders in digestive tract and thyroid gland but diagnosis is delayed when children are asymptomatic.
Aim: To assess the prevalence of thyroid peroxidase (anti-TPO), thyroglobulin (anti-TG) and antigliadin (AGA) autoantibodies in pediatric patients with type 1 diabetes without symptoms of additional disease.
Methodology: The study group included 90 children with type 1 diabetes at age of 12.5 ± 3.9. Thyroiditis or celiac disease were determined, when anti-TPO, anti-TG and AGA antibodies titers exceeded an upper limit of normal range, even without symptoms. A questionnaire was used to interview patients and their relatives to determine any autoimmune manifestations in family members.
Results: HbA1c was 7.7 ± 1.6%; diabetes duration: 4.5 ± 3.4 years and age at the diabetes onset was 7.9 ± 3.8 years in the investigated group. The prevalence of autoimmune thyroiditis determined by high TPO and/or TG titers was 31%. The prevalence of positive celiac antigliadin autoantibodies was 33.3%. Girls were more predisposed than boys to have diabetes and positive AGAs (60% vs. 40%) or thyroid autoantibodies (75% vs. 25%) concomitantly. AGA positive patients in this group were characterized by earlier onset of diabetes (6.5 ± 4.5 yrs) and higher HbA1c (8.4 ± 3.3%) values than AGA negative individuals. The family history of children with diabetes has revealed information about autoimmune diseases in similar frequency when investigated autoantibodies were positive or negative (55.6%). Diabetes was diagnosed first usually.
Conclusion: Screening for celiac and thyroid disease in type 1 diabetes is recommended even when symptoms are absent. Delayed diagnosis of other autoimmune diseases can effect in worse metabolic control in patients with type 1 diabetes mellitus.

P-69
A simple method of screening for hypothyroidism in children with type 1 diabetes using finger prick blood samples

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Introduction: Children with diabetes are at increased risk of developing hypothyroidism. Hypothyroidism is clinically difficult to diagnose in the early stages and can affect diabetes control. Screening for hypothyroidism is currently available nationally in the UK for all infants, but not routinely available in at-risk patient groups. We propose that this method is suitable for screening in children with type 1 diabetes.
Aim: To determine whether finger prick blood spot sampling onto filter paper is an accurate method of screening and detecting hypothyroidism in this population of children.
Methodology: Capillary blood spot evaluation of TSH according to the methods used in Guthrie screening for congenital hypothyroidism. This will involve taking a small finger prick blood spot sample onto filter paper. TSH is measured by radioimmunoassay. Children screened had type 1 diabetes for at least one year.

Results: In total, 62 patients were tested. Mean age was 10.75 years (range 3.9–14.5 years). Mean duration of diabetes 4.3 years (range 1.2–10.8 years). None of the patients had an elevated TSH result. Mean TSH 0.7 mU/L (range 0.1–2.0 mU/L). All children were clinically euthyroid.
Conclusion: Finger prick sampling of blood for TSH using the method of filter paper sampling is an effective and reliable method of screening for hypothyroidism in children with type 1 diabetes. We recommend this method is used as a tool for screening for hypothyroidism in all children with type 1 diabetes.

P-70

Autoimmune thyroiditis (AT) in T1DM: role of TPO and TG AB as predictor of thyroid failure

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Background: Autoimmune thyroiditis is more frequent in type 1 diabetes than in general population however there is disagreement on how and when to screen for thyroiditis. Objective 1) To investigate the frequency of AT in type 1 diabetic children; 2) To establish the predicting value of TPO and TG antibodies titer in progression of thyroiditis.
Patients and methods: Annual screening for thyroid disease (TPO and TG Ab titer, TSH, fT3, fT4) was performed in 86 type 1 diabetic patients (31 girls and 55 boys) during a period of 17 years. A cut-off of 600 U/ml, correspondent to ten times the minimal positive value, was used to define lower and higher titer. AT was diagnosed by positive TPO and/or TG antibodies and ultrasonography. Criteria for starting therapy was a persistent TSH > 7 µU/ml.
Results: Twenty-nine out of eighty-six patients were followed up for more than 3 yrs. At onset of T1DM eight patients were TPOAb positive (6 low and 2 high titer), one patient was TGAb low titer positive and four patients were positive to both TPO and TG antibodies. During the first 3 years of follow-up TPO and TG Ab switched from negative to positive low titer respectively in seven and four patients and TPO Ab high titer in one patient. During the long-term follow-up (>3 years) TPO and TG Ab switched from negative to positive low titer respectively in two and nine patients and TPO Ab high titer in six patients. Moreover two patients with low titer TPO at onset switched to negative. Three patients TPO negative at onset started treatment with L-thyroxine after 3 or more years of disease duration. Two patients developed hyperthyroidism.

Outcome	TPO/TGAb at onset		
	Neg	Low	High
Euthyroids	48/30	0/0	0/0
Ab +	22/24	6/4	4/0
L-Thyroxine Tx	3/2	0/0	1/1
Hyperthyroidism	1/2	0/0	1/0
Odd ratio	0.06/0.07	0.00/0.00	0.5/1.0

Conclusions: According to our results both TPO and TG Ab high titer are good predictors of thyroiditis progression, however negative TPO and/or TG titer at onset does not exclude AT during the following 3 or more years.

P-71

Association of autoimmune polyendocrine syndrome and pigmental retinae degeneration in a 13 year old girl

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Introduction: Autoimmune mediated diseases are rare in pediatric practice, but more often diagnosed in children with type 1 diabetes than in the general population. T1DM is one of the most frequent components of autoimmune polyendocrine syndrome and it often precedes the others.
Aim: Clinical case report.
Methodology: Clinical case of polyendocrinopathy and dystrophy retinae.
Results: A girl aged 6 years born small for gestational age (2470 g, 40 weeks), presented with symptoms of severe diabetic ketoacidosis, short stature (–3.6 SD). Her diabetes control was constantly poor, with a few hypoglycemic seizures and severe ketoacidosis, low insulin requirements (0.6 U/kg/24 h). At the age of 9 years hypoparathyreosis was defined and treatment by Calcitriol was administered. Clinical assessment revealed chronic urinary tract infections, persistent vulvovaginitis, hypogonadism, epicanthus, ptosis, multiple pigmentary changes in retinae, muscular hypotonia, intensional tremor, disorder of coordination, mental retardation. Growth hormone stimulation test with clonidine showed a poor STH response with a plasma growth hormone levels of 0.26, 0.37, 5.5, 0.85 ng/ml at 0′, 30′, 60′, 90′ (normal response > 10 ng/ml) and normal STH response with levodopa – 7.1, 8.1, 11, 8.4 ng/ml at 0, 30, 60, 90 min. Aged 13 years she presented with increased weakness, lethargy, hypotension, mild hiperpigmentation. She was prepubertal (stage B1P1; LH < 0.2 IU/L, FSH < 0.2 IU/L, E2 = 120 pmol/l), height – 118 cm (–6.3 SD), growth velocity – 3 cm/yr, weight – 19 kg. A short Synacthen stimulation test showed a normal cortisol response with plasma cortisol levels of 397 nmol/l, 684 nmol/l, 776 nmol/l at 0′, 30′, 60′. Baseline ACTH was 1.73 pmol/l, and electrolytes were normal.
Conclusion: T1DM, hypoparathyreosis, persistent vulvovaginitis, hypogonadotropic hypogonadism, short stature can be associated with autoimmune polyendocrine syndrome type 2. Also this rare combination of polyendocrinopathia with retinal degeneration, neurological symptoms would not object to Kearns-Sayer syndrome. Definitive diagnosis of this syndrome requires genetic examination.

P-72

Turner syndrome coexisting with insulin-dependent diabetes mellitus and autoimmune thyroiditis – the case report

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In Turner Syndrome (TS) higher risk of carbohydrate metabolic disturbances development and increased incidence of diabetes mellitus (DM) type 1 and 2 are observed. It is suggested that the primary defect is the resistance for insulin action. The impaired secretion of insulin in TS is also reported.
The aim: Presentation of a girl aged 11.5 with TS and DM type 1. The perinatal history is unknown (adopted child). In the age of 11 years due to phenotype features, short stature and karyotype 45,X[43]/46,X,i(X)(q10)[7] the TS was diagnosed. The treatment with L-thyroxine was started (elevated TSH level). The glycosuria with no other coexisting symptoms was noticed. The DM was recognized due to increased glucose concentrations: fasting (127–157 mg%), OGTT (max. 296 mg%). The insulin concentration was 8.3 uIU/ml. The conventional therapy with insulin was started. The insulin requirement was 0.5 U/kg/24 h. The additional tests revealed the left ureterostenosis. The present physical examination showed: height 123.5 cm (due to Lyon, Preece chart 25–50 cent., comparing to normal population –4.4SD), the height velocity 2.8 cm/year, predicted adult height 140 cm, BMI 20, prepubertal. In laboratory tests: normal TSH and fT4, increased thyroid antibodies (ATPO 2835 IU/ml, ATG 19 IU/ml), LH 18 mIU/ml, FSH 66.2 mIU/ml, estradiol 21 pg/ml, HbA1c 6.1%, insulin antibodies 7.0%, IGF-1 697 ng/ml. In other examinations: ECG and ECHO were normal,

abdominal ultrasonography – the right ovary absent, ultrasonography of thyroid gland – the picture typical for inflammation, bone age 10 years, audiometry – left ear hearing loss, laryngologic examination – adenoid. Actually the growth hormone treatment is planned. Because of growth hormone therapy the metabolic control of DM will require a particular monitoring.

P-73
Cystic Fibrosis Related Diabetes – the Dublin experience!

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Cystic Fibrosis Related Diabetes (CFRD) is an ever-increasing diagnosis with improved survival in children with Cystic Fibrosis (CF). CFRD has been reported to be the second most prevalent form of diabetes in children and Danish studies report an incidence of 50% by 30 years of age. It is a clinically unique illness requiring a different approach from type 1 and type 2 diabetes. Ireland has no definitive management protocols for CFRD and little is known about the prediabetic or Impaired Glucose Tolerance (IGT) group in CF children at all. The morbidity and mortality increases by six fold once diagnosed with CFRD; studies show early intervention with insulin can reduce this. It has been hypothesized that the prevalence of CFRD or IGT at present is underestimated in our pediatric population. Screening protocols should be set up both for the identification and efficient management of these children with CFRD.

Aims: 1. Define the prevalence of diabetes and non-diabetes in the Dublin Pediatric CF population. 2. Establish the current demographics on CFRD & non-diabetes CF children. 3. With dietary and exercise advise alone, can we prevent progression to CFRD. 4. Assess the Continuous Glucose Monitoring System (CGMS) as a monitoring tool for CFRD to aid the diagnosis confirmed on OGTT.

Methods: A retrospective review of all CF charts was undertaken. All OGTT, fasting glucose and random glucose results were sought, including HbA1c. Steroid dependence and Aspergillus titers were also collected.

Results: Cystic Fibrosis children aged 10–19 years screened with OGTT, fasting blood glucose & random glucose according to WHO Diagnostic Criteria (1998): (Centers: [1,2+3] see title)

Total population n = 360	Total 10–19 yrs	NCF non-diabetic	IGT	CFRD CF diabetes	TOTALS
NCH[1] n = 125	70	52 (74%)	9 (13%)	9 (13%)	70
OLHSC[3] n = 38	38	25 (66%)	5 (13%)	8 (21%)	38
TSCUH[2] n = 80	21	16 (76%)	0	5 (24%)	21
Totals in 3 centers:	**129**	**93 (72%)**	**14 (11%)**	**22 (17%)**	**129**

We reviewed all current data available by October 1st 2004. Total number aged 10–19 years is 157 (45%), of which 129 are completely screened to date. 93 (73%) CF children have no diabetes, 14 (11%) have IGT and 22 (17%) are diagnosed with CFRD. One year ago 27 IGT children previously screened are now normoglycaemic with dietary and exercise advice alone. Thus only 9 children in the NCH group remain prediabetic and this accounts for a reduction of 43%. In total, one CFRD child has died and 5 new CFRD were diagnosed over a one year period. 4 CF children have been transferred on to Adult Care with CFRD. Finally the data from Temple Street is different to the other children's hospitals, namely no CF child has IGT, and all children are non-diabetic (76%) or CFRD (24%). The percentage of CFRD children in Temple street on steroids was 5%, 55% in the NCH. Thus steroids remain important in CF children for treatment of ABPA and may trigger CFRD. To date the CGMS has been used as an adjunct to the OGTT when screening for CFRD. We present the first few CF children in Ireland screened for CFRD and show surprising trends. The CGMS trends show a large fluctuations in blood sugars which is mirrored by the changing glucose tolerance state ranging from normal to impaired to Diabetes in the CF children on an almost monthly basis. Some CF children with non-diabetes show a lag phase in insulin release and then hypoglycemia, when the endogenous insulin peaks. We will show these CGMS trends in non-diabetes and CFRD.

Conclusion: This study provides the prevalence of normal CF, prediabetic-CF and CFRD children in Dublin based on current data in March 2005. Dietary advice alone has converted 43% of the prediabetic CF children to normoglycaemia and may have stopped the progression to CFRD. We provide basic demographics on an ever changing, poorly compliant group of CF children according to their glucose status. CGMS monitoring confirms these fluctuations and may be an important diagnostic tool in the future in CFRD. We aim to provide best practice guidelines for CFRD in Ireland with the help of a prospective trial in all 8–20 year old CF children commencing in July 2005.

P-74
Diabetic retinopathy, nephropathy and cardiovascular disease in a patient with GH-N gene deletion

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Introduction: Longstanding oversecretion of growth hormone (GH) causes glucose intolerance and Type 2 diabetes mellitus (T2DM) and its vascular complications. There are only two publications on the development of diabetic retinopathy (one transient) in patients with acquired multiple pituitary hormone deficiencies. We have encountered two patients with Laron syndrome (GH resistance) who developed T2DM and its vascular complications.

Aim: Forthwith the first report of a patient with untreated IGHD who developed T2DM and its complications.

Methodology: At age 19 a Jewish Yemenite male was referred because of dwarfism. He was diagnosed to have GH-N gene deletion. As his epiphyses were closed due to prior androgen therapy he was not eligible for GH therapy. At age 30 he was diagnosed to have T2DM and high cholesterol (479 mg/dl). At age 40 metformin was added to dietary treatment. The patient returned at age 50 when due to difficulties in vision he was found to have severe diabetic retinopathy necessitating laser therapy.

Results: Fig. 1. Red free photo of the left eye shows soft exudates in the posterior pole and flame-shaped hemorrhages combined with

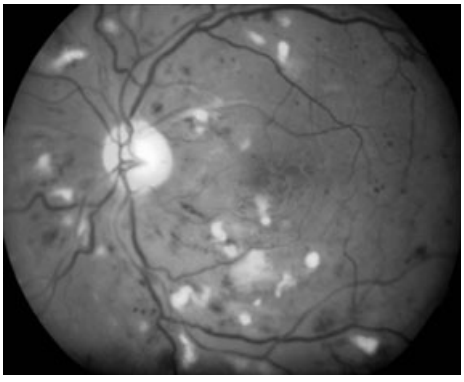

Figure 1.

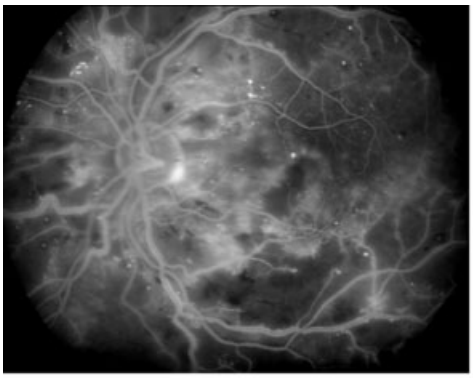

Figure 2.

microaneurysms around the disc. Fig. 2. Fluorescein angiography in the late stage reveals areas of non perfusion and leakage from the blood vessels wall. He also had nephropathy and impotence. Soon thereafter he developed an acute myocardial infarction.
Conclusion: It is evident that diabetic vascular complications can develop also during (or by) longterm GH/IGF-I deficiency, denoting also that VEGF can induce neovascularization in the absence of IGF-I. Practical implications may be that GH receptor antagonists should be used with caution.

P-75

Tumor Necrosis Factor alpha is a risk factor of retinopathy in poor controlled type 1 diabetes mellitus children

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Introduction: The etiopathogenesis of the diabetic retinopathy (DR) remains unclear, though it is generally acknowledged that poor metabolic control is the most important factor accelerating its progression. It has been suggested that hyperglycemia may lead to the activation of proinflammatory cytokines that are crucial for micro- and macroangiopathy development.
Aim: The analysis of the serum levels of pro- and anti-inflammatory cytokines in relation to the metabolic control in type 1 diabetes mellitus (DM) children with and without retinopathy and in a group of healthy children.
Methodology: Fifty six children with type 1 DM were recruited from Outpatient Diabetic Department of the Medical University of Gdansk. On the basis of the ophthalmologic examination the children were categorized into those with and without diabetic retinopathy. Basic laboratory data were obtained for all the patients. Moreover we were measured levels of Tumor Necrosis Factor alpha (TNFα), Interleukin 6 (IL6), Interleukin 12 (IL12) and Interleukin 10 (IL10) in serum.
Results: Children with DR had significantly longer duration of the disease, higher HbA1c, C reactive protein (CRP), triglyceride, total cholesterol and LDL-cholesterol levels. No significant differences in albumin excretion rate, creatinine in serum, fasting glucose and HDL-cholesterol levels there were. The level of HbA_1c was the most powerful independent retinopathy predictor [(OR 2.07; 95%CI 1.14–3.75) p = 0.01]. In the unadjusted logistic regression, the risk of retinopathy was dependent equally on TNF [(OR 2.52; 95% CI 1.4–4.5) p = 0.0003] and CRP [(OR 2.51; 95%CI 1.2–4.8) p = 0.004] levels. However there were no significant differences the levels of IL6, IL12 and IL10 between diabetic groups.
Conclusion: An inflammatory process manifested by the elevated serum levels of TNF-alpha, induced by a poor glycaemic control, may be a mechanism responsible for retinopathy in type 1 DM children.

P-76

Low retinopathy rate in 367 pediatric patients by screening with a non-mydriatic ultra-widefield laserophthalmoscope

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Introduction: Annual retinal screening is recommended for pediatric diabetes patients with the onset of puberty. Using sensitive methods like fluorescein angiography previous studies have shown mild to moderate retinopathy in several adolescents. In recent years only few eye changes were detected through routine eye checks by ophthalmologists in private practice and the compliance with these checks was only 60%. We investigated therefore the feasibility of a screening with a non-invasive non-mydriatic ultra-widefield laser ophthalmoscope directly in the outpatient clinic with later evaluation of the image by an ophthalmologist.
Methodology: We performed a cross-sectional study using the Optomap Panoramic 200® laser-ophthalmoscope including 96% of the eligible patients in the diabetes center (202 boys, 165 girls, mean age: 14 ± 3 y; diabetes duration 6 ± 4 y). A total of 1468 digital images in an angle of 200° where evaluated independently by two ophthalmologists blinded to the patients' data. HbA1c-Levels have been calculated by using data since diabetes manifestation or of the last ten years (median 7.55%, mean 7.7 ± 1.1%) (Bayer DCA 2000, DCCT-standard).
Results: Evaluable digital retinal photographs were available in 99% of the patients (two patients blinked constantly, one had a cataract). Early retinal changes (microaneurysms) were found in 17 patients (5%) Recent inconspicuous mydriatic eye exams by ophthalmologists in private practice were available in 256 patients, 14 of these had microaneurysms. The screening procedure was well accepted by children and adolescents and produced low anxiety levels.
Conclusion: The ultra-widefield laser ophthalmoscope proves to be a feasible method of retinal screening for pediatric patients which is more sensitive than routine mydriatic examination by an opthalmologist. The prevalence of retinopathy remains relatively low in comparison to previous studies possibly due to an improvement in the average level of glycaemic control.

P-77

Effect of some calcium channels blockers in experimentally induced diabetic nephropathy in rats

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Introduction: Introduction & Aim: Diabetic nephropathy (DNP) is considered a CRD (Chronic Renal Disease); it is a major cause of illness and premature death in people with DM. Furthermore, it is considered the single most important cause of end stage renal disease in the western world and accounts for more than a quarter of all end stage renal diseases.
Aim: The present study was designed to illustrate the role of CCBs (amlodipine and diltiazem) in prevention and treatment of DNP in rats.
Methodology: Eighty male albino rats weighing (130–180 mg) were used in this study. These animals were subdivided into five equal

groups. Insulinopenic diabetes was induced by STZ, two weeks later, 30 minutes of complete ischemia was induced in the left kidney to induce diabetic nephropathy then treatment was started for 12 weeks. At the end of experiment urine samples and blood samples were taken for biochemical analysis and kidneys were taken after scarification for histopathological evaluation.
Results: Combination of renal ischemia with DM produced a significant increase in rat weight, rat kidney weight, BUN (Blood Urea Nitrogen) level, K/B (Kidney/Body weight) ratio, random blood glucose, 24 hrs urine proteins, and 24 hrs urine volumes and creatinine clearance. Treatment with diltiazem or amlodipine significantly lowered elevated SBP and elevated 24 hrs urine volumes. Furthermore, treatment with captopril produced a highly significant lowering of elevated SBP and elevated serum creatinine; and a significant reduction in elevated K/B ratio and proteinuria. Light microscopic examination of diabetic kidneys revealed glomerulopathy characterized by thickening of the glomerular basement membrane, mesangial matrix expansion, arteriolar hyalinosis and large proteinaceous deposits occluding some capillary loops and hyaline droplets within the glomeruli. Moreover, examination of kidneys of ischemic animals by light microscope revealed focal tubular necrosis at multiple points along the nephron, interstitial edema and accumulation of leucocytes within dilated vasa recta.
Conclusion: It can be concluded that, renal ischemia hasten the progression of DNP, diltiazem and amlodipine have a tendency to reverse of changed parameters toward normal values except biochemical parameters, generally speaking, diltiazem is better than amlodipine in reversing biochemical and histopathological changes produced by DNP, and captopril reversed most of changed parameters except histopathological changes.

P-78

Arterial hypertension and diabetes mellitus type 1

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Introduction: The arterial hypertension is one of the complications of a diabetes mellitus.
Aim: The purpose of the present work was revealing an arterial hypertension at patients with type 1 diabetes.
Methodology: Data Basic Information Sheet of 181 patients with type 1 diabetes living in city Baku have been used.
Results: An average age of patients has made 30.2 year, the duration of disease 9.4 year. According to arterial hypertension classification (WHO, 1999) optimal hypertension has been revealed at 70.7%, normal hypertension at 7.8%, a hypertension of 1st degree at 4.4%, 2nd degree at 4.4%, 3rd degree at 2.2%, isolated systolic hypertension at 9.4%, boundary hypertension at 1.1%. Thus, with the help of Basic Information Sheet the raised arterial hypertension has been revealed at 21.5% patients with type 1 diabetes. Between arterial hypertension and age of patients ($r = +0.61$), arterial hypertension and duration of disease ($r = +0.42$) the positive correlation has been revealed. It is interesting that there has not been revealed correlations between an isolated systolic hypertension and age of the patients ($r = +0.09$), an isolated systolic hypertension and duration of disease ($r = +0.13$).
Conclusion: Thus, the frequency of occurrence of different degrees of arterial hypertension was investigated among the patients with type 1 diabetes.

P-79

The influence of poor metabolic control and hypoglycemic episodes on the function of peripheral nerves in children with type 1 diabetes

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Introduction: Poor metabolic control is a well-known risk factor of diabetic polyneuropathy. However, the influence of coexistent hypoglycemic episodes in history and poor metabolic control on diabetic polyneuropathy is not detected.
Aim: The aim of the study was to establish the influence of coexistence of chronic, poor metabolic control and hypoglycemic episodes in history on function of peripheral nerves in children with type 1 diabetes.
Methodology: 97 children with type 1 diabetes (55 girls, 42 boys, mean age 15.4 ± 2.16 years, mean duration of diabetes 8.11 ± 2.9 years, mean age in onset 7.16 ± 2.96 years, mean HbA1c 8.58 ± 1.06%) at least 10 years old and with at least 3 years duration of diabetes, were included to study. Children were divided into four groups: Group A-HbA1c < 9% (the mean value from the whole duration of diabetes), without history of hypoglycemic episodes ($n = 38$); Group B-HbA1c > 9% but without history of hypoglycemic episodes ($n = 15$); Group C-HbA1c < 9%, with history of hypoglycemic episodes ($n = 28$), and Group D-HbA1c > 9% and history of hypoglycemic episodes. Nerve conduction studies of the median, ulnar, tibial and peroneal motor nerves, and median, ulnar and sural sensory nerves were performed with standard surface stimulating and recording techniques. The sensory and motor amplitude, velocity and latency were detected. Univariate ANOVA or Kruskall-Wallis tests of significance were used, depends on normal distribution and homogenicity of variance of dates.
Results: Group D had significantly lower conduction velocity of peroneal ($p < 0.01$) and sural nerves ($p < 0.001$) in comparison to the other groups. Group D had significantly longer sural sensory latency ($p < 0.005$) and amplitude ($p < 0.005$) than the remaining groups, too. Group A had the best results in all the tests done. In the remaining electrophysiological parameters we didn't detect any differences, between the groups, maybe because of small differences detected in nerves conduction tests.
Conclusion: The study revealed the significant, poor influence of coexistence of the poor metabolic control and history of hypoglycemic episodes on all electrophysiological parameters of sural nerve and in conduction velocity of peroneal nerve.

P-80

Decrease of visual evoked potentials amplitude in children with type 1 diabetes

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Introduction: Glucose is an essential nutrient for the brain, therefore the perturbation in glycoregulation in diabetes mellitus can cause cerebral functional or even structural impairment. Measurements of electrically evoked potentials provide an opportunity to evaluate the functional integrity of the neural pathways of the central nervous system.
Aim: The aim of the study was to evaluate the electrophysiological abnormalities in the central nervous system by visual evoked potentials (VEP).
Methodology: 97 children with type 1 diabetes (55 girls, 42 boys, mean age 15.4 ± 2.16 years, mean duration of diabetes 8.11 ± 2.9 years, mean age in onset 7.16 ± 2.96 years, mean HbA1c 8.58 ± 1.06%) at least 10 years old and with at least 3 years duration of diabetes, were included to study.
Results: The study revealed a significant correlation between decrease of VEP amplitude and long duration of diabetes ($p < 0.05$) and poor metabolic control ($p < 0.01$). There were no significant

correlations between VEP P100 latencies and duration of diabetes, mean HbA1c, age at onset, but a significant negative correlation between the age and P100 latencies ($p < 0.005$) exists. In studied population we detected significant correlation between decrease of VEP amplitude and mean ($p < 0.0005$) and actual BMI ($p < 0.00001$).

Conclusion: The study revealed decrease in amplitude of P100 potential, which depends on metabolic control and diabetes duration. Increase in latency P100 is not related to this factors.

P-81

Effects of the omega-3 polyunsaturated fatty acids in the treatment of cardiovascular autonomic neuropathy in type 1 diabetes mellitus patients

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Introduction: Dietary supplementation with fish oil, a source of highly long- chain marine polyunsaturated fatty acids (PUFA), such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) has been proposed as an antithrombotic and antiatherosclerotic therapy.

Aim: The aim of study was to assess the effects of EPA and DHA on the activities of Na^+, K^+-ATPase, Ca^{2+}, Mg^{2+}-ATPase, levels of fatty acids in the RBC's membranes; the ^{125}I-6-ketoprostaglandin $F_{1\alpha}$ (6-keto$PGF_{1\alpha}$), ^{125}I-thromboxane B_2 (TXB_2) levels in the blood plasma in Type 1 diabetic patients (Type 1 DM) with cardiovascular autonomic neuropathy (CAN).

Methodology: 36 patients (27 ± 6 years) were allocated into two treatment groups. The 1st group (n = 16) was receiving capsules of fish oil every day (1.75 g EPA, 1.75 g DHA and 0.1% α-tocopherol acetate); the 2nd group – placebo capsules of olive oil. All patients were on the same diet.

Results: After 2 months of treatment there was a decrease in TXB_2 level (151.4 + 15.4 pg/ml, $p < 0.001$) with increases in EPA level, EPA/arachidonic acid (AA) ratio (from 0.3 to 0.6), Na^+, K^+-ATPase (from 0.05 ± 0.003 to 0.08 ± 0.003 mMol PI/mg protein per 1 hour, $p < 0.001$), Ca^{2+}, Mg^{2+}-ATPase and the concentration of 6-keto$PGF_{1\alpha}$ in the first group. Increases in the level of EPA and EPA/AA ratio, activities of membrane-bound enzymes lead to an increase in their deformability, decrease in the ability to aggregate.

Conclusion: In conclusion, EPA and DHA at moderate doses may exert antithrombic effects and may be used for prophylaxis and treatment of CAN.

P-82

The assessment of selected lipid parameters in children suffering from diabetes mellitus type 1

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Introduction: One of the most important factor progressing the development of vascular complications and increasing the heart-vascular risk in the course of diabetes mellitus type 1 (DM.t.1) is abnormal lipids metabolism. Maintaining the normal lipid concentration in the serum of diabetic children, is essential for proper and effective treatment, delaying the development late complications of the disease.

Aim: assessment of selected lipid parameters in the patients suffering from DM.t.1 depending on metabolic control, duration of the disease, method of treatment and the value of BMI.

Methodology: Total group of 147 patients, 84 (57%) girls and 63 (43%) boys, aged from 5.25 to 22.33 years old (X = 14.83 ± 3.11), suffering from DM.t.1. DM.t.1 mean duration time 5.35 ± 3.57 years. Lipid parameters, HbA1c, BMI were assessed. Subgroups of good, satisfactory and badly controlled and below 5, 5–10, over 10 years disease duration were created. 58 (39.5%) – treated with conventional therapy, 89 (60.5%) – intensively.

Results: Strong positive correlation was found between the level of HbA1c and the concentration of the lipids. Patients with longest duration of the disease had statistically significant higher level of triglycerides. Significant positive correlation was found between the level of HbA1c and the concentration of cholesterol, triglycerides, LDL, HDL in the group of the patients suffering from DM.t.1 longer than 5 years. No correlation was found between the method of treatment and the concentration of cholesterol, triglycerides, HDL or LDL. Strong correlation was found between the level of BMI and the method of treatment.

Conclusion: 1. The lipids concentration depend on duration of the disease as well as on metabolic control. 2. Increased level of LDL is a very sensitive indicator of bad metabolic control in the course of DM.t.1.

P-83

Soluble thrombomodulin (sTM) – a molecular marker of endothelial cell injury in children and adolescents with type 1 diabetes

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Introduction: Endothelial damage is an early step in the pathogenesis of atherosclerosis which begins in early childhood after exposure to atherogenic risk factors such as diabetes mellitus. Its progression may lead to very severe cardiovascular complications. TM-a specific marker of endothelial cell damage, is a transmembranous glycoprotein with anti-coagulant properties. It has a large, extracellular region comprising a thrombin binding site. TM-thrombin complex becomes an activator of protein C which inactivates Va and VIIIa and thereby inhibits the blood coagulation cascade.

Aim: The aim of the present study was to investigate if plasma concentration of sTM is higher in children and adolescents with type 1 diabetes.

Methodology: We studied 35 diabetic children, 19 girls and 16 boys, (age range 9.9–20.7 years), with good metabolic control, without chronic diabetic complications and 17 normal weight healthy controls, (age range 12–17.9 years) without family history of cardiovascular diseases. The concentration of sTM was measured by the methods of ELISA. The concentration of total cholesterol, HDL, triglicerydes were assessed using routine laboratory kits. The concentration of LDL was calculated by means of Friedewald's formula. We also calculated body mass index (BMI) and measured average blood pressure using ABPM (Arterial Blood Pressure Monitoring). As sTM is excreted by the kidney we also measured plasma level of creatynine and its clearance.

Results: Plasma concentration of sTM in the group with type 1 diabetes mellitus was significantly higher than that in the control group (4.06 ± 0.92 vs. 3.43 ± 0.4 $p < 0.05$). Compared with non-diabetic patients, diabetic children had higher plasma concentration of total cholesterol and significantly lower level of HDL-c. In addition statistically significant correlation between sTM and total cholesterol and LDL was observed in diabetic group. We did not notice differences in blood pressure, BMI and parameters of renal function in studied groups. There were no significant associations between sTM and age or sex.

Conclusions: 1. The increased level of sTM was reported in children with type 1 diabetes. 2. Higher level of sTM in children with diabetes makes us sure that endothelium cells may be damaged in this group. These results constitute an additional signal that a lot of

effort should be put into the endeavors to eliminate atherogenes risk factors in children population in order to prevent cardiovascular events.

P-84

Prevalence of dyslipidaemia in children and adolescents with type 1 diabetes

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Introduction: Cardiovascular diseases (CVD) are important causes of morbidity and mortality in type 1 DM. We should pay more attention to diagnostic and correction of dyslipidaemia from early stage of diabetes.
Aim: To investigate prevalence of dyslipidaemia in children and adolescents with type 1 DM and to analyze impact of glycemic control, microalbuminuria and thyroid function on lipids level.
Methodology: This study involved 94 children and adolescents with type 1 diabetes at routine clinic attendance, M/F 48/46. There was no statistical difference between males and females in mean age M/F 14.1 ± 0.28/13.9 ± 0.32 yrs (range 10.1–17.4 yrs), mean diabetes duration M/F 5.9 ± 0.36/5.2 ± 0.35 yrs and insulin dose 0.89 ± 0.037 U/kg/day, but females had higher BMI M/F 18.8 ± 0.29/20.2 ± 0.41 kg/m^2 ($p < 0.05$). Fasting lipids: total cholestrol (TC), triglycerides (TG), β-lipoproteins (βLP), TSH and microalbuminuria (MA) in 24 h-urine samples were measured. Metabolic control was estimated by fructosamine (FA).
Results: Metabolic control was significantly better in females with type 1 DM: FA in M/F 424.6 ± 5.5/410.1 ± 4.6 mmol/l ($p < 0.05$). The lipids level was significantly higher in females: mean TC level M/F 4.2 ± 0.08/4.8 ± 0.1 mmol/l ($p < 0.01$), mean TG level M/F 0.8 ± 0.05/1.29 ± 0.14 mmol/l ($p < 0.01$), mean βLP level 43.1 ± 1.5/48.8 ± 2.1 g/l ($p < 0.05$). 23.9% girls and 4.2% boys had TC above 5.2 mmol/l. Only 1 girl had elevated TG level above 1.7 mmol/l (2.2%). High βLP level (above 55 g/l) was found in 17.4% girls and 8.3% boys. In 2 girls hypercholesterolemia was associated with hypothyroidism. MA was presented in 22.5% of participants (more frequent in males 25% vs 19.5% in females) and was related to poorer metabolic control in males and to diabetes duration in females. In our study we did not find the correlation between metabolic control (FA), BMI, MA and lipids level. The level of blood lipids did not correlate with age and duration of diabetes.
Conclusion: Dysipidaemia is common condition in type 1 DM especially in girls. The data showed that early intervention for prevention of CVD should be started from pre-pubertal age in young people with type 1 DM. Screening for thyroid function is recommended in all females with type 1 DM and hypercholesterolemia.

P-85

Lipid-lowering effect of simvastatin and behavioral modification in patients with type 2 diabetes mellitus

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Introduction: Dyslipidemia is an important factor in causation of macrovascular disease in type 2 diabetes.
Aim: This study compared the effect of simvastatin together with behavioral modification and behavioral modification alone, in age, sex and body mass index harmonized patients with type 2 diabetes with dyslipidemia, in lowering the levels of various lipids.
Methodology: An open-label, prospective study was conducted on 64 patients with type 2 diabetes. The patients in the test group were advised behavioral modification and given simvastatin. The patients in the control group (30) were treated with only behavioral modifications like decreased fat intake and daily walking for 30 minutes, and no lipid-lowering agent was given. The lipid profile was re-evaluated after 8 and 16 weeks. The starting dose was 10 mg at bed time. After 8 weeks of simvastatin therapy, a lipid profile was done and if the goal of total cholesterol was not achieved, the dose of simvastatin was increased to 20 mg at bed time for another 8 weeks.
Results: In the test group, there was a significant decreased in lipid profile without change in glycemic control and liver function. In the control group, there were a favorable alteration in lipid levels but none was statistically significant.
Conclusion: In our study behavioral modification alone did not showed significant decrease in lipid profile in diabetic dyslipidemia. The therapy with simvastatin was safe and efficacious in lipid-lowering in patients with type 2 diabetes.

P-86

The relation between nitric oxide, oxidative stress and circulating immune complexes with metabolic control in juvenile diabetics

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Introduction: The relation between diabetes and premature vascular disease was well established. Endothelial dysfunction accompanies poor glucose control with oxidative/nitrosative stress and circulating immune complexes (CIC) deposition.
Aim: The aim of the present study was to investigate the level of stable end products of nitric oxide- plasma nitrate and nitrite (NOx) carbonyl group (PCO), nitrotyrosine (NTY) and CIC level in juvenile diabetic patients.
Methodology: Twenty-six diabetic patients and 20 age-matched control healthy children were included in the study. Glycated hemoglobin (HbA_{1c}) is used to monitor metabolic regulation in patients
Results: Plasma nitrate/nitrite (NOx) concentration significantly increased in juvenile diabetics (33.2 ± 4.2 micromol/L vs control 7.8 ± 0.81 $p < 0.001$), as well as NTY (25.23 ± 3.86 micromol/gprot vs control 19.51 ± 1.24 $p < 0.05$) and PCO (10.9 ± 1.2 micromol/gprot vs control 7.5 ± 1.28 $p < 0.05$) while the CIC was about ten times lower (1.28 ± 0.0% vs control (12.5 ± 2.3 $p < 0.001$).
Conclusion: Results of the current study suggest that negative correlation that was documented between the level of CIC and plasma NOx, NTY and PCO concentration may point out early endothelial dysfunction, CIC deposition, which could proceed to the development of mycroangiopathy. Our explanations are supported by the results that development of experimental autoimmune vasculitis by immune complexes infusion into cells requires the presence of a functional NOS2 gene and NOS2-generated NO. In this way, the hyperglycemia and poor metabolic control can be causally linked to abnormality of peroxynitrite production and metabolism producing the nitration and oxidation of aromatic rings of proteins. The decrease in the level of CIC was presumably due to tissue deposition when active immune disease was fully developed.

P-87

Clinical investigation of Silybum marianum seed extract (silymarin) treatment in type 2 diabetic patients

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Introduction: The free radical production and consequently metabolic oxidative stress disorder is hallmark of chronic disease

particularly in uncontrolled hyperinsulinemic type 2 diabetic patients. Inhibition of free radical production, its neutralization or correction of oxidative metabolic abnormality in diabetic patients following antioxidant therapy may influence the glycemic control.

Aim: The present study was designed to investigate the efficacy of silymarin treatment with known antioxidant property on glycemic control in type 2 diabetic patients.

Methodology: A 12 month randomized double blind clinical trial was conducted in 80 non-insulin dependent diabetic patients in two well – matched groups. One group (n = 48) received 200 mg silymarin tablet 3 times a day plus standard therapy, while the control group (n = 32) received placebo plus standard therapy. The patients were visited every two month and glycosylated hemoglobin (HbA1c), fasting blood glucose, total cholesterol, LDL and HDL, triglyceride, SGOT and SGPT levels were determined at the beginning, after four month and at the end of the study.

Results: There were significant decrease in HbA1c, fasting blood glucose, total cholesterol, LDL, SGOT and SGPT levels in silymarin treated patients as compared to placebo group.

Conclusion: In present study the silymarin treatment to hyperglycemic type 2 diabetic patients for 12 months improved glycemic as well as lipid profile.

P-88

Evaluation of DCA 2000+ for rapid in-clinic measurement of HbA1c on capillary blood in young type 1 diabetic children and adolescents

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Introduction: The glycation of hemoglobin, estimated as HbA1c, is described as the 'gold standard' by which to judge the effectiveness of glycemic control in clinical practice. However, consistency of HbA1c results is worse when compared across different laboratories. The DCA 2000+ instrument (Bayer Inc.), based on an immunological technique, has been proposed for the rapid (6 minutes) and simple in-clinic measurement of HbA1c, even using capillary blood.

Aim: Therefore, it is necessary to compare the HbA1c levels obtained with the DCA 2000+ with those of an excellent reference method.

Methods: We evaluated 230 type 1 diabetic children and adolescents with different degrees of metabolic control. The DCA 2000+ model, used by a nurse in the diabetology clinic, was compared with the HPLC system (Menarini 8160), with DCCT standardization.

Results: The within laboratory imprecision (CV) was 1.6%; the deviation from the DCCT was < 0.1% across the clinical range; the linearity was excellent (r = 0.996) (2004 independent audit by the National Scientific Institute of Public Health). The correlation between the 2 different systems was good (y = 1.101× –0.67; r = 0.949). The percentiles of the differences between values obtained with the HPLC system and the DCA 2000 were: P10 = –0.3%; P25 = –0.1%; P50 = 0.1%; P75 = 0.1%; P75 = 0.3%; P90 = 0.75%. The 95% confidence interval for the mean difference between the 2 methods was 0.075. The DCA 2000+ was linear till an HbA1c level of 12%, the upper detection limit being 14%.

Conclusion: In the clinical field of interest, the DCA 2000+ gives HbA1c results very closed to those of an excellent reference method DCCT-aligned, the median deviation being only 0.1%. It can be sited in a clinic environment and produces results in 6 minutes, i.e. during the consultation, in order to give patient direct medical advices.

P-89

Changes of insulin regimens and glycemic control during the past 5 years in Japanese children with type 1 diabetes

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Introduction: Intensified insulin therapy has widely permeated in pediatric patients with type 1 diabetes. Various reports have demonstrated that a basal-bolus insulin regimen including insulin analogs provides better glycemic control without increasing hypoglycemic episodes.

Aim: To investigate the relationship between insulin regimens and glycemic control during the past 5 years in Japanese children with type 1 diabetes.

Methodology: Changes of insulin regimen and HbA1c values from 2000 to 2004 were evaluated in Japanese children with type 1 diabetes under 15 years of age. The subjects yearly enrolled in JSGIT during the study period were 785, 729, 686, 602 and 482, respectively.

Results: The frequency of two daily injections significantly decreased (26.3, 20.6, 16.5, 13.5, 9.8%, $p < 0.01$), whereas that of three or more daily injections significantly increased (73.6, 77.5, 80.7, 81.4, 83.6%, $p < 0.05$) during the past 5 years. In 2004, 56.2% of the subjects used a rapid-acting insulin analog as bolus insulin and 28.4% used a long-acting insulin analog as basal insulin. The regimen of multiple daily injections using the analogs varied greatly and could be adapted to fit individual needs. CSII was introduced in about 5% of the subjects each year. There were no statistical changes of HbA1c values (8.1, 8.2, 8.1, 8.2, 8.0%) and the frequency of severe hypoglycemic episodes did not change (0.12, 0.12, 0.11, 0.09, 0.08/person/year) throughout the study period.

Conclusion: The use of a basal-bolus regimen including insulin analogs widely increased during the past 5 years among Japanese children with type 1 diabetes. These changes of the insulin regimen did not contribute to significantly improve glycemic control. However, it was ascertained that in Japanese children with type 1 diabetes, the average HbA1c value was similar to that observed in Caucasian populations and the occurrence of severe hypoglycemic episodes was rare in recent years.

P-90

Childhood diabetes in Iceland; evaluation of quality of treatment

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Introduction: The importance of adequate metabolic control has been repeatedly demonstrated in recent years. The care of diabetic children and adolescents in Iceland is centralized to one unit. The aim of the study was to analyze the quality of treatment and clinical outcome of Icelandic children with Type-1 diabetes.

Methodology: A cross-sectional survey was performed for the period 15.3–14.7.2004, and the results for the patients last visit to the diabetes clinic were recorded. HbA1c levels (DCA 2000), number of severe hypoglycemic episodes, were evaluated.

Results: The total number of diabetic children < 18 years was 104. The number of visits to the clinic during the 4 month interval were 83 (43 boys), the mean age was 13.26 ± 3.78 years. Mean value of HbA1c in the cross-sectional survey was 8.18 ± 1.31%. The proportion of patients with HbA1c < 8.0 in different age groups were 0–4 years (no patients), 5–9 years: 48%, 10–14 years: 39%, 15–18

years: 26%. Adolescent girls (12–18 years) had higher HbA1c levels than boys (8.80 ± 1.27% vs. 7.95 ± 1.42%). Ten children (12%) experienced severe hypoglycemic episodes during the follow up period.
Conclusion: The metabolic control in children and adolescents with IDDM in Iceland is relatively good compared to other countries. However, it is important to focus attention on children and specially adolescents with inadequate metabolic control.

P-91

Diabetes camps for teenagers with type 1 diabetes

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Introduction: Diabetes camp is one model of educational programs for teenagers. Clinical experience shows that many young people benefit from attending camp, but also that many teenagers do not want to attend camp. In a review Gage et al. concluded that most educational programs, including camps, for adolescents with diabetes have some favorable impact. We found no previous studies focused on camp attendance and the differences between campers and non-campers.
Aim: To evaluate whether teenagers attending diabetes camps differ from non-attenders in attitudes and self-care, and to evaluate the impact of educational camps for youths with diabetes.
Methodology: 90 campers in six camp groups and 90 non-campers, aged 14–18 years, with type 1 diabetes were included. A questionnaire and an attitude form measuring attitudes towards diabetes and self-care were sent to both groups. Attendees of four of the six camps also completed the attitude form before and six months after camp. Medical data were collected from the medical records before, 6 and 12 months after camp.
Results: The campers reported more positive attitudes towards diabetes and self-care and more frequent contacts with others with diabetes. They monitored blood glucose more often and felt less disturbed by diabetes. Camp had a positive impact on attitudes towards diabetes. There was no significant change in HbA1c in either campers or non-campers but the use of insulin pumps was initiated at camp.
Conclusion: Camp attracts teenagers who have positive attitudes towards diabetes, who are used to camps and who have more frequent contacts with others with diabetes. Camp may help young people with diabetes become more positive towards the disease, and may inspire them to try new treatments, but does not affect metabolic control.

P-92

Risk factors for poor control of diabetes mellitus in minority Singaporean children

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Introduction: We had previously studied HbA1c data in Singaporean children. In the 2001 Diabcare Asia – Singapore study, the mean HbA1c for type 1 patients was 8.5% ± 1.5% and 72% had HbA1c level of >7.5%, while mean HbA1c of type 2 patients was 7.6% ± 2.2%, of whom 29% had HbA1c levels >75%. In 2004, our mean clinic HbA1c of 211 patients was 8.53%, while the HbA1c of our 166 type 1 patients was 8.77% and that for type 2 patients was 7.76%. However is a multiracial nation with 77% Chinese, 14% Malay, 7% Indian and 2% people of other races. Malays and Indian residents are particularly at risk for type 2 diabetes. We had also noted the relatively poorer clinical outcomes of our young Malay patients with diabetes mellitus, including poorer HbA1c and repeated readmissions, and we decided to study how to improve their outcomes.
Methodology: Data was collected from the KKH Children's Diabetes Registry which has been functioning since 1997 as an epidemiological and clinical care case management and audit system. HbA1c was done using the automatic HPLC using Bio-Rad VARIANT™ Glycoslyated Hb Analyser System at KKH.
Results: There were 33 ethnic Malay children with evaluable data (14 type 1 and 19 type 2 DM), representing 8% of our type 1 DM cohort and 44% of our total clinic cohort of type 2 DM patients. For the first time since we have collected data (1992), there are more pediatric type 2 than type 1 patients in the clinic cohort in any ethnic group. The mean HbA1c of our 33 Malay patients as a whole was 9.2 ± SD 2.4%. The mean HbA1c of our 14 Malay type 1 patients (7 males and 7 females, aged 7–19, mean age 14.1 ± SD 4.0 yrs) was 10.7 ± SD 2.45%, while 93% had HbA1c over 7.5%. The mean HbA1c of our 19 Malay type 2 patients (10 males and 9 females, age range 9–21 yrs, mean age 15.7 ± 2.7 yrs) was 8.11 ± 2.4%, with 44% having HbA1c over 7.5% Review of clinical charts revealed risk factors including: pattern of failing to attend clinic appointments, poor socio-economic status and financial difficulties, single parent households or family discord, resource limitations especially for home blood glucose monitoring, lack of family and parental support, lack of acceptance of diabetes as a serious problem, and issues arising from a strong family history of diabetes with parents and grandparents affected.
Conclusion: 1. While the risk factors are not unique to this community, we will need to focus our attention on resource limitations in the home, improving diabetes education and acceptance. 2. We will need to address the accessibility to basic resources such as glucose testing strips, as well as accessibility to analogue insulin products and newer technologies such as continuous glucose monitoring systems and insulin pumps, and access to learning programs such as diabetes camps. 3. We need to look out for individuals at risk and offer appropriate help where needed.

P-93

Is central HbA1c registration associated with improved metabolic control – the Danish experience from 1996–2004?

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Introduction: In 1996 The Danish Childhood Diabetes Register was founded. It is a nation-wide register collecting data from all Danish pediatric diabetes centers treating type-1-diabetic patients aged 0–15 years. All newly diagnosed type-1-diabetic patients < 15 years have been enrolled since 1996 and in 1997 the majority of patients < 15 years with diabetes onset prior to 1996/1997 were included. A broad spectrum of diabetes-related data has been collected. Here we report the HbA1c level over the years 1996–2004.
Methods: Central HbA1c determination from all participants has been established. Linear regression analysis was applied and the following explanatory variables were tested: diabetes center, age, diabetes duration, ethnicity, gender, and year-of-onset.
Results: A total of 7549 recordings from 2497 persons were included in the analysis. Data completeness of the HbA1c recordings have increased from 39% in 1998 to 86% in 2004 of all participants in the register, today covering > 99% of known type-1-diabetic patients with onset before 15 years of age. The mean HbA1c value – adjusted for diabetes center, age/year-of-onset, diabetes duration, ethnicity and gender – has decreased by 0.09 (0.08–0.11) p.a. from 1998 to a mean HbA1c of 8.56% in 2004 ($p < 0.0001$).
Conclusion: It has been possible to establish a nation-wide diabetes registration in Denmark founded in 1996 including all Danish pediatric diabetes centers treating type-1-diabetic patients. Despite increasing data completeness the HbA1c have decreased by 0.09 p.a.

The HbA1c varies significantly between center, this difference still exists after adjustment for age, year-of-onset, diabetes duration and ethnicity, whereas there was no effect of gender or puberty.

P-94

Quality care in young people with type 1 diabetes: behavioral and cultural

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Introduction: The Centre of treatment of T1D appears to have a significant and independent effect on the glycaemic control of young people, probably by encouraging concordance with therapy.
Aim: To explore the social and cultural factors that influence the interactions between health professionals and young people in the management of T1D.
Methodology: We performed a combined qualitative and quantitative observational study (participant observation, in-depth interviews, questionnaire surveys and video consultation interaction) in three Regions in Scotland: 84 interviews (n = 65 young people aged 13–25 yr.), n = 19 health professionals – physicians, diabetes nurse specialists and dietitians).
Results: Young people wanted to be seen through a broad context rather than through the filter of their diabetes or status as adolescence. Notions of adolescence as an innate age-based condition drew attention away from a range of personal challenges. They valued continuity with health professionals who applied their knowledge skills to the specific needs of young people. Health professionals were divided about the focus on diabetes out-come measures: some believed it altered their relationships with adolescents, and the delicate system of support, between Centers in Scotland; others, believed assessment promoted the evolution of diabetes care. Both camps believed participation on standards committees promoted a sense of ownership and time out for the 'war weary'. However, production of management systems created greater complexity drawing attention away from reflection and dynamic creativity to develop patient-centered approaches.
Conclusion: Our study provides insights into the material and symbolic basis on which adolescents and health professionals build reciprocal relationships. Assumptions that relationships are driven by adult knowledge and priorities have not been revealed in this study. This supports the idea that young people are receptive to supportive relationships during adolescence and are major agents in thinking about these relationships and how their meanings and practices are shaped.

P-95

Opportunity to enhance blood glucose (BG) monitoring and improve glycemic control with an electronic logbook in youth with type 1 diabetes (T1DM)

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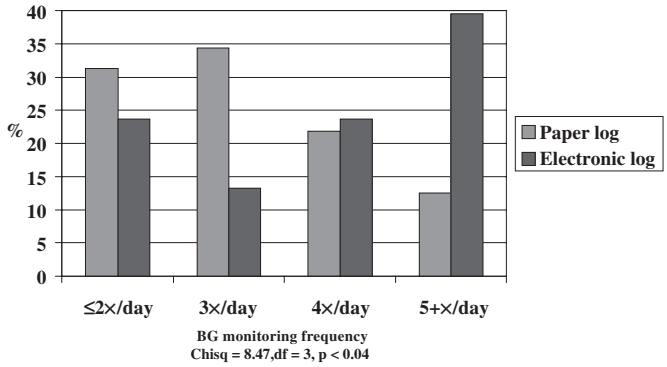
Introduction: The DCCT and EDIC studies support implementation of intensive management early in the course of diabetes. Thus, youth with T1DM will benefit from novel BG monitoring technologies that encourage monitoring and help optimize glycemic control.
Methodology: We compared a new meter equipped with an electronic logbook, One-Touch™ UltraSmart System™, (Electronic Group) to standard BG meters with paper logbooks (Paper Group). A 5-center trial included 70 T1DM youth (58.6% female), ages 4–20 years (X ± SD, 13.5 ± 3.7), 21.4% using pump Rx, with diabetes duration 6.1 ± 3.8 years, using 7 different BG meters at entry. After a 4-week run-in when participants used their usual BG meter with paper log, youth with baseline A1c ≤8% were randomized to Electronic or Paper Groups and followed monthly for 16 additional weeks. There was monthly review of BG data only by electronic log in the Electronic Group and only by paper log in the Paper Group. A1c was measured monthly at a central lab with blinded results following randomization until study's end.



Results: At entry, youth were checking BG 4.3 ± 1.4×/day and had mean A1c of 9.24 ± 1.07% (NS between Groups). During follow-up, the Electronic Group checked BG 4.7 ± 1.7×/day compared with 3.8 ± 1.4×/day ($p < 0.03$) in the Paper Group (see figure). A1c decreased significantly in the Electronic Group (ΔA1c –0.33 ± 0.87%, $p < 0.03$) while it did not in the Paper Group (ΔA1c –0.08 ± 0.92%, NS). At study's end, among Electronic Group participants, 83% of parents noted a preference for the One-Touch UltraSmart System over conventional paper logs.
Conclusion: This short-term study revealed enhanced adherence to BG monitoring and improved A1c with the use of a meter with integrated electronic log. Since checking BG is necessary for successful intensive therapy, new technologies that simplify and promote BG monitoring may support efforts to optimize glycemic control in youth with T1DM.

P-96

Use of Insuflon in young people with diabetes

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Introduction: Traditionally when a patient with diabetes has problems with injections or needles, apart from counseling, distraction therapy and altering insulin regimes there are limited options to overcome this. Needle phobia can often lead to increased emotional stress, anxiety and often insulin omission, thus effecting overall diabetes control and management. However, at the Children's Hospital Westmead we want to overcome this with the introduction of Insuflon, a subcutaneous indwelling catheter that stays in situ for up to four days. Insulin is administered through this device, meaning the child only has one 'needle' every 3–4 days.
Aim: Investigate the use of insuflon in children with Type 1 diabetes.
Methodology: Insuflon was offered if children had needle phobia, difficulty with injections, lipohypertrophy, wanted greater lifestyle flexibility or a break from normal routine/injections. A trial of three days was offered and a pre trail questionnaire was completed. On completion of the trail, if patients decided to continue using the product, they received further education and purchased supplies. One month later another questionnaire was completed assessing the overall satisfaction of Insuflon. Clinic HbA1c was also noted at this time, if available.
Results: Final results of this study are yet to be completed; initial evaluation shows the primary reason for commencing Insuflon include fear of injections and that injections are 'difficult'. Thus far

twelve children are using Insuflon; of these two have increased injections to MDI. All who have used it gave positive feedback, as diabetes has become more manageable and better control has been achievable.
Conclusion: Surveys indicate Insuflon has decreased anxiety and time taken to do injections; it has also allowed children to become more involved in their diabetes management. Insuflon has changed the lives of many families and has undoubtedly made 'injection time' a lot happier and with much less hassle.

P-97

How to optimise therapy of diabetes in children from Sarajevo?

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Introduction: Good metabolic control of diabetes is the crucial factor in prevention of diabetic complications. Therapy that results in excellent metabolic control of diabetes (HbA1c < 7%) is optimal.
Aim: to determine the most important therapeutic elements for optimising therapy of diabetes in pediatric patients from Sarajevo.
Methodology: We analyzed quality and quantity of all elements of therapy in 87 patients (F 38, M 49) age below 18 (range 3–18 y), average duration of diabetes 4.68 years (range 1–15 y) during the period of one year. According the average yearly HbA1c we classify all patients in 5 groups (range of HbA1c 1% between groups).
Results: Average HbA1c for all patients in study was 8.94 ± 1.64. Only 11 patients (12.64%) had optimal regulation of diabetes (HbA1c < 7%). They had 2.72 ± 0.79 ($p = 0.01$) yearly HbA1c controls; 3.55 ± 0.93 ($p = 0.05$) daily insulin injections; 2.5 ± 1.0 ($p = 0.05$) daily blood glucose controls. All 11 patients (100%) changed their insulin doses every day ($p = 0.05$), 10 patients (91%) had proper timing of insulin and meals ($p < 0.05$), and all had best results in knowledge about diabetes ($p = 0.05$). There was no significant difference between groups of various metabolic control in total daily insulin dose ($p > 0.05$), in application of various dietary recommendations ($p < 0.1$), in technique of insulin application ($p < 0.95$) and in frequency of physical activity ($p < 0.70$).
Conclusion: Our results support the previous studies which stressed importance of: intensified therapy (at least 3 insulin doses daily), frequent blood glucose controls, proper timing of meals and insulin injections, good education and frequent visits to doctor for achieving better metabolic control of pediatric patients with diabetes mellitus.

P-98

Patients perception of 'sweet talk' text messaging support for diabetes care

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Introduction: Recent guidelines on type 1 diabetes management in young people advocate that intensive insulin regimens should be offered as a package of care, including emotional and behavioral support. A meta-analysis of behavioral interventions showed that whilst many moderately improve glycaemic control, they are rarely incorporated into routine clinical practice.
Aim: The challenge is to develop innovative methods of support, which are feasible within existing health resources and engage young people.
Methodology: 'Sweet Talk' (ST) delivers a recognised behavioral intervention by text-messaging. Patients set self-management goals in clinic. These are reinforced by daily, personalised text messages from the automated software system and patients are encouraged to send text-messages to the 'ST' system. A user satisfaction survey was administered to 61 of the 63 patients receiving the 'ST' intervention in a RCT.
Results: Patients usually received 1–3 text-messages daily, and 90% felt this frequency was optimal. 82% of patients felt 'ST' helped their diabetes care during the study, with replies indicating that 'ST' influenced behavior related to the main diabetes self-management tasks. 76% of patients said the weekly goal reminder was helpful, and 77% of patients found the clinic appointment reminders useful. Messages related to diabetes self-management information, research and facts were reported to be most helpful. Patients also appreciated the social aspects of the text-messages, particularly hearing other peoples' experiences of diabetes. Repeated messages were the most frequently cited annoyance with the intervention. 90% of patients wanted the text-messages to continue at the end of the study period.
Conclusion: 'Sweet Talk' seems to have successfully engaged a difficult to reach population, by using a medium integral to teenage culture. Results of the 'ST' user satisfaction survey have highlighted patients' perceptions of its strengths and weaknesses. The challenge is to adapt the text-message database accordingly, to ensure delivery of a patient-centered intervention.

P-99

The north-west England Youth Diabetes Weekend Project – what's the word on the street?

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Introduction: For the past 7 years, we have organised an annual outdoor activity weekend for 24 young people with diabetes aged 14–18 from the North West of England. The activities include ghyll scrambling, kayaking, mountain biking, climbing, assault courses and a group-based educational session on diabetes. Over 120 young people and 21 healthcare professionals have experienced the weekend. We used a structured feedback form find out whether young people attending the weekend found it worthwhile and to suggest any improvements.
Methodology: Feedback questionnaire sent (2 weeks after the event) to all those attending the weekend over the past 2 years. Scoring system from 1 to 6 (with 6 representing the most positive response) for all aspects of the weekend plus free text comments invited. Scores are presented as mean averages.
Results: We received 12 (50%) responses in 2003 and 9 (39%) in 2004. All activities received high scores, the highest score was for ghyll scrambling (mean 5.9 n = 21). The lowest score was for information provided before-hand in 2003 (mean 3.7) which improved after changing to 5.0 in 2004. Food scores were similar for breakfast, supper and snacks (4.8, 4.8, 4.8, n = 21) and lower for packed lunch and evening meals (4.2, 4.2, n = 21). The educational session scored 4.6 (n = 21). Individual free texts comments were generally positive and used to improve the weekend.
Conclusion: Getting feedback from teenagers on diabetes activity weekends is helpful in improving the weekend and suggests that the weekends are enjoyed and worthwhile.

P-100

Concerns of parents of preschool-age children with type 1 diabetes

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Introduction: The incidence of type 1 diabetes in very young children has increased in recent years, yet few studies have examined the concerns of parents of this patient population.
Aim: The objective of this study was to survey parents of preschool-aged children with diabetes about their worries and concerns, and the impact on their work outside the home.
Methodology: Sixty-nine parents (mostly mothers, mean age = 32.5 years) were recruited at their child's clinic visit to complete a survey. The mean age of children was 4.3 years and their mean age at diagnosis was 2.6 years.
Results: Ninety-one percent of parents reported they were worried (pretty much or very much) about low BG; they reported conducting a mean of 4.3 BG checks per week due to fear of hypoglycemia, and woke up at night a mean of 5 times per month to check for low BG. Eighty-two percent of parents were worried that increases in their child's activity levels would result in hypoglycemia. While 17% felt that injections were difficult to administer, 18% admitted sometimes omitting a dose because they forgot, and 23% reported sometimes omitting a dose while away from home. Forty percent of parents were worried about getting their child to eat after taking insulin. Eighty-five percent of parents were worried about their child's future health, 33% about socialization, 36% about academic success, 32% about career success, and 49% were worried about their child's future marriage and family life. Seventy percent of parents felt that what they are doing now will affect their child's future. Fifty-four percent of mothers reported they stopped working or decreased their hours to care for their child, 86% said they would not have stopped working if their child did not have diabetes, and 66% reported they would go back to work if they had confidence in caretaker's ability to care for their child's diabetes.
Conclusion: Parents of preschool-age children are very worried about hypoglycemia, have significant concerns about their children's future health and social adjustment, and have stopped working or decreased their work hours due to their child's diabetes. Interventions are needed to address these issues for parents.

P-101

Benefits of an educational game to train hypoglycemia-awareness in preschool children with diabetes mellitus type-1 and their parents

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Introduction: Several studies attained a high incidence of severe hypoglycemia especially in young children (e.g. Wagner et al. 2005). Since preschooler cannot identify and verbalize their symptoms of hypoglycemia adequately, it is important to teach parents how to observe and communicate with their children about hypoglycemia without arousing fear or defense.
Aim: To compare the variation in blood glucose levels before and after a 1-week parent–child training course focusing on hypoglycemia awareness.
Methodology: An educational card game with illustrated signs of hypoglycemia was introduced during a 1-week outpatient training with 12 children [mean age: 5.3 (SD: 0.9) years, mean diabetes duration: 2.5 (SD: 1.0) years] and their parents. To evaluate the effects on glycemic control, levels of BG (BG = blood glucose) were measured 4-weeks before and 4 weeks after the training with standardized BG-meters with a memory function. Pre- and post-training BG-values were statistically analyzed and compared. Psychological effects have been measured with a parental questionnaire.
Results: A total of 4246 BG-measurements were recorded within the pre- and post-training period. The frequency of low BG-levels (<50 mg/dl) decreased after the parent–child training from 4.9% to 2% ($p < 0.001$). Contrary, the number of high blood glucose values did not change significantly ($p = 0.34$). Parents rated the training as helpful to learn and to talk about sign of hypoglycemia with their children.
Conclusion: The child-parent training may significantly contribute to the reduction of dangerously low BG-levels without increasing the number of elevated BG-values. Specific training methods are necessary to motivate preschooler to learn about hypoglycemia awareness.

P-102

Satisfaction of care in a tertiary level diabetes clinic: correlations with diabetes knowledge, clinical outcome and health-related quality of life

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Introduction: Satisfaction of care (SOC) is now accepted as a valid outcome measure in chronic disease. Other outcome measures include clinical outcomes and health-related quality of life. The primary aim of this study was to assess SOC amongst children and their care-givers in a tertiary level pediatric diabetes clinic. Secondary aims were to assess whether SOC was correlated with contemporaneous diabetes metabolic, diabetes knowledge and health-related quality of life.
Methodology: Sequential families attending the RCH diabetes clinic were approached over a 1-month period. English-speaking patients aged 6–18 years and their care-givers were asked to fill out the patients' Evaluation of Quality of Diabetes Care (PEQD), Child Health Questionnaire (CHQ PF-50 for parents, CHQ CF-80 for adolescents) and a diabetes knowledge questionnaire. Contemporaneous HbA1C (Bayer 2000, Calabria) was also recorded. When the child was aged 6–11 years the care-giver filled out all questionnaires. When the patient was aged 12–18 years both the patient and the care-giver were invited to complete the questionnaires.
Results: One hundred and forty-three patient/care-giver groups participated. Over 70% of patients and their care-givers were either highly satisfied or satisfied with their diabetes care. The were no significant differences between SOC levels between patients and their care-givers in the adolescent group ($p = 0.48$). There was no significant correlation between SOC levels in either patients and care-givers and HbA1C ($p = 0.3$ and $p = 0.8$ respectively). There was no significant correlation between SOC levels in either patients and care-givers and level of diabetes knowledge ($p = 0.1$ and $p = 0.4$ respectively). Analyses regarding SOC and HRQOL are ongoing.
Conclusions: In our clinic levels of SOC are generally acceptable, however a significant minority are dissatisfied with their diabetes care. The lack of correlation between clinical outcomes and diabetes knowledge mean that levels of SOC cannot be presumed according to these variables.

P-103

The KICK-OFF (Kids In Control OF Food) course: families and teachers participation in the development of an educational curriculum for 11–16 year olds with type 1 diabetes

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Introduction: Few doubt the importance of patient education in diabetes. Intensive insulin regimes with carbohydrate estimation are increasing yet few structured education courses for children exist in the UK. The DAFNE (Dose Adjustment For Normal Eating)

course has been shown to improve glycaemic control and quality of life in adults but its format is unsuitable for children.
Aim: To design an education course for 11–16 year olds, to teach the principles of insulin dose adjustment within an intensive insulin regimen.
Methodology: 29 Children and 34 parents attended focus groups which explored their views on current education and how the adult DAFNE course could be adapted. Secondary school teachers worked with diabetes staff to ensure curriculum lesson plans were compatible with current educational practice and teaching material age appropriate. They advised on teaching of biology, food technology, mathematics and personal and social aspects of diabetes.
Results: Families made several novel suggestions that influenced curriculum design. They highlighted problems managing diabetes in school, to be addressed with a school resource pack. A friend is included in one session. The main focus is on carbohydrate estimation and insulin adjustment within medical and social situations. The format is very interactive including practical cookery and sport sessions. Parents attend certain relevant sessions. The course will be delivered over 5 days to groups of eight, aged 11 to 13 or 14 to 16 years.
Conclusion: By involving young people and teachers we have produced an education course that we hope will meet their needs and empower them to manage their diabetes more skillfully. Six pilot courses have been held to refine the curriculum, prior to a multicenter randomised controlled trial.

P-104
Initial evaluation of a structured education course for 11–16 year olds with type 1 diabetes: the KICK-OFF course

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Introduction: Structured education is relatively uncommon in the UK. The KICk-OFF (Kids In Control OF Food) course aims to teach insulin dose adjustment within an intensive insulin regime. This novel curriculum has been developed with input from families and secondary school teachers and includes many practical, group sessions.
Aim: 1. Assess initial response to the course. 2. Refine the curriculum and course format. 3. Inform planning of a randomised controlled trial.
Methodology: Six 5-day courses were run in three centers in the UK to groups of 8 individuals aged 11–13 or 14–16 years. All patients within these age groups were invited and participants randomly selected. Two trained research educators and a diabetes nurse from each center delivered the education. Evaluation: Course content and format: Independent observation by educationalist, daily feedback forms, pre and post course interview with child and parent Psychological: questionnaire at baseline, 2 weeks, 3 and 6 months Biomedical: HbA1c, Weight, BMI, hypoglycemia at baseline, 3 and 6 months.
Results: All participants completed the course. Patient and professional feedback was positive, but informed changes to course format. Preliminary analyses have found significant improvements in mean responses to psychological measures, including quality of life (Physical functioning: Child [$t(36) = 2.13$, $p < 0.05$]; Parent [$t(36) = 2.93$, $p < 0.01$], Psychosocial functioning: Child [$t(38) = 3.78$, $p < 0.01$]; Parent [$t(37) = 4.82$, $p < 0.001$]), satisfaction with treatment [Child ($t(38) = 4.57$, $p < 0.001$]; Parent [$t(37) = 6.10$, $p < 0.001$)] and self-management [Child ($t(37) = -4.09$, $p < 0.001$]; parent [$t(37) = 5.78$, $P < 0.001$)]. Biomedical and 3-month follow-up data will be available shortly.
Conclusion: The Kick-off course has proved popular and preliminary results suggest it may have a beneficial effect. Detailed feedback resulted in changes to the course format and will give an indication of sample size for a randomised controlled trial.

P-105
How diabetes education is reflected by young people with type 1 DM

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Introduction: Education is a key factor in successful management of diabetes. In spite of development different approaches to teaching problem of optimizing diabetes education still exists especially in adolescent group.
Aim: To analyze influence of diabetes re-education on adherence to self-monitoring, its impact on glycemic control and quality of life in young people with type 1 DM.
Methodology: The study involved 72 children and adolescents with type 1 DM: M/F 29/43, mean age 16.5 ± 0.3 yrs (range 11–21), mean diabetes duration (MDD) 6.5 ± 0.36 yrs, BMI 20.9 ± 0.27 kg/m^2, insulin dose 0.98 ± 0.2 U/kg/day (there was no statistical difference between males and females). Young patients filled up the questionnaire which evaluated number of diabetes school (DS) attended during previous years of diabetes (including DS at hospitals, outpatient, camps), blood glucose (BG) and urine glucose (UG) tests per day, diabetes-related hospitalizations during last year, attitude to carbohydrates etc. QoL was assessed by a modified Diabetes QoL questionnaire (51 questions). Metabolic control was estimated by fructosamine (FA).
Results: Accordingly to number of different DS attended the participants were divided into 3 group: Group 1 (G1) where young people with diabetes claimed 3 DS attended, Group 2 where 2 DS and Group 3 where 1 DS. The patients in G 1 were younger and performed significantly more BG tests per day. There was no statistical difference in metabolic control and diabetes QoL score between three groups.

	Number: M/F	Mean age, yrs	MDD, yrs	FA, mmol/l	BG tests/day	QoL score
Group 1	18 (8/10)	14.42 ± 0.63	5.8 ± 0.49	387.2 ± 7.38	2.39 ± 0.18	109.6 ± 4.47
Group 2	20 (9/11)	16.45 ± 0.49*	6.7 ± 0.64	406.8 ± 10.3	1.22 ± 0.6*	112.1 ± 4.15
Group 3	34 (12/22)	17.9 ± 0.29*	6.61 ± 0.67	388.8 ± 7.72	1.19 ± 0.11*	114.9 ± 3.6

*$p < 0.05$

11.1% of participants used UG testing. 40% reported that they counted carbohydrates regularly, 43% sometimes and 17% never. 86% showed that they took all insulin injections and 14% that most of injections. 38% of participants reported that they needed more knowledge on diabetes management (with bigger rate in G 3–47%).

Conclusion: Re-educaton is important tool in maintenance of diabetes control and self-monitoring but there is necessity of optimizing the process of teaching with more attention to practical skills.

P-106

Locus of control related to metabolic control in adolescent boys

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Introduction: The psychological measure internal Locus of Control (LoC) sometimes have been related to treatment outcome in chronic disease, probably through self-care behavior. Little is known about the role of LoC in intensively treated type 1 diabetes adolescents.
Aim: To study Locus of Control in relation to metabolic control, in adolescents with type 1 diabetes.
Methodology: We have studied Locus of Control in a geographic population of 13–19 years type 1 diabetes adolescents (LoCA) and their parents (LoCP, mainly mothers responded). Two large clinics n = 113 and n = 124 participated, response rate 60% adolescents, 63% parents. We used a previously validated 8-items 4-point scale and analyzed it in relation to sex, age, diabetes duration, insulin regimen, BMI, severe hypoglycemia and HbA1c.
Results: Mean LoCA was higher in boys than in girls (2.74 SD 0.36 vs. 2.60 SD 0.35, p = 0.016). LoCA was correlated to LoCP (r = 0.24, p = 0.003) in girls (r = 0.42, p < 0.001) but not in boys (r = 0.06, ns). LoCA was correlated to lower HbA1c in boys (r = –0.24, p = 0.038) but not in girls (r = 0.01, ns). Differences between clinics were seen in LoCA (2.74 SD 0.34 vs 2.62 SD 0.37, p = 0.038).
Conclusion: LoC seems associated to metabolic control in boys. The difference between genders needs further investigation. Quality of care may be important for LoC, as mean LoC differs between clinics. Interventions to enhance internal LoC may be of clinical value.

P-107

Quality of life in intensively treated adolescents

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Introduction: Quality of Life (QoL) may be influenced both by treatment procedures necessary to control blood glucose levels, and by fear of high or low blood glucose levels, by acute or long-term complications.
Aim: To study QoL in intensively treated type 1 diabetes adolescents.
Methodology: We have studied a geographic population of adolescents from two clinics (n = 113, n = 124; 112 girls, 125 boys) using a 5-point scale pilot version of the DISABKIDS QoL questionnaire, adolescent and parent proxy versions. We analyzed it in relation to sex, age, diabetes duration, insulin regimen, BMI, severe hypoglycemia and HbA1c. Response rate in adolescents 60%, parents 63%.
Results: Adolescents reported lowest QoL for the factors physical limitation, medication and mental independence, and parents as proxy for medication, social exclusion and emotions respectively. Girls responded lower than boys for mental independence (3.9 SD 0.76 vs. 4.2 SD 0.74, p = 0.033) and emotions (4.1 SD 0.69 vs. 4.4 SD 0.67, p = 0.032). Diabetes specific QoL (QoLD) was lower in girls than in boys (3.2 SD 0.76, vs. 3.6 SD 0.71, p = 0.001), also when reported by parents (3.4 SD 0.65, vs. 3.6 SD 0.58, p = 0.014). QoLD in adolescents was correlated to lower HbA1c in boys (r = –0.230, p = 0.044) but not in girls (r = –0.071, ns). QoLD was correlated to lower BMI in adolescents (r = –0.195, p = 0.017). QoLD in girls was correlated to lower insulin dose (r = –0.238, p = 0.043) and age (r = 0.322, p = 0.006).
Conclusion: Diabetes, especially limited independence, decreases QoL of diabetic adolescents, especially girls. Higher diabetes specific QoL was related to better metabolic control in boys.

P-108

Parents' experience of having a child diagnosed with type 1 diabetes

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Introduction: Having a child diagnosed with type 1 diabetes is believed to be an anxious and distressing time but little is known about the peri-diagnostic period from the parents' perspective. This paper comprises the first stage of a longitudinal qualitative study exploring the experience of parents of newly diagnosed children.
Aim: To increase understanding about parents' response, coping and adaptation to a diagnosis of childhood diabetes from their perspective.
Methodology: Nineteen parents of ten children, who were clinically well (blood pH > 7.30) at presentation and managed at home, participated in in-depth interviews within ten days of their child's diagnosis at a hospital in Wales. Interviews were transcribed verbatim, and data systematically coded into categories that emerged from parents' accounts.
Results: Following a gradual realisation that something was wrong with their child, parents were devastated by the diagnosis. Their anxiety was exacerbated by the speed of diagnosis and commencement of treatment. Parents experienced an intense sadness about the diagnosis, which represented a number of losses. They coped initially by focusing on the practical skills and gaining knowledge about diabetes. A fear of hypoglycemia dominated their thoughts and affected many aspects of their life. They experienced a loss of spontaneity but established new routines to accommodate their child's needs. Professional support was important to parental coping, particularly accessibility to advice via an on-call phone.
Conclusion: Parents' response to a diagnosis of childhood diabetes corresponds to the grief reaction normally associated with bereavement. Parents need reassurance about the speed of diagnosis, to be kept informed throughout the diagnostic process and have access to advice and support out of office hours. Findings from this study can help health professionals to better support parents of newly diagnosed children.

P-109

Quality of life (QOL) study on type 1 diabetes patients

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Introduction: Type 1 diabetes is a chronic disease where good metabolic control is essential to prevent complications. Practitioners have a tendency to equate good metabolic control with quality of life.
Aim: To assess the quality of life (life satisfaction, disease-related worries and impact of disease) and to determine the correlation between metabolic control (HbA1c) and specific aspects of DQOL questionnaires.
Methodology: Cross-sectional questionnaire survey of type 1 diabetes adolescents and young adults aged 10 to 20 years managed at Pediatric Endocrine Clinic, University Malaya Medical Centre, Kuala Lumpur. Those with psychopathology or intellectual retardation were excluded. Questionnaires on quality of life derived from Diabetes Quality of Life Questionnaire (DQOL) prepared by the Diabetes Control and Complication Trial Research Group (DCCT 1988) were given during their clinic visits. These question-

naires were then analyzed. At the same clinic visit, blood for HbA1c were taken.
Results: 19/20 (95%) patients were involved. Male to female ratio 1.1 : 1.0. Mean age 14.3 ± 2.7 (range 10.2 to 18.8) years. Mean duration of diabetes 6.9 ± 4.7 (range 0.6 to 15.5) years. Mean HbA1c 9.9 ± 2.4 (range 6.5 to 15.4%). No significant difference in age, duration of diabetes and HbA1c with gender. Patients were satisfied with the management of their disease and very seldom felt worry about it. This study failed to correlate between good HbA1c and quality of life but correlated significantly with self-perceived disease.
Conclusion: While the value of good metabolic control should not be underestimated, this study suggested that self-perceived quality of life holds a very different meaning to adolescents with type 1 diabetes.

P-110

Cognitive and psychosocial functioning in preschool-aged children with type 1 diabetes

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Introduction: Research indicates the incidence of type 1 diabetes has been increasing in preschool-aged children, yet little is known about how diabetes may impact their cognitive development and psychosocial functioning.
Aim: This study examined cognitive and psychosocial functioning in preschool aged children as a function of their history of glycemic control.
Methodology: The study sample consisted of 36 children with diabetes (21 girls and 15 boys) with mean age of 4.7 years, age at diagnosis of 2.8 years, and HbA1c of 8.3%. Diabetic children were compared to a healthy control group of 32 children (14 girls and 18 boys) with mean age of 4.1 years on measures of cognitive (Differential Abilities Scale), language (Peabody Receptive Vocabulary and One-Word Expressive Vocabulary Test), motor (Purdue Pegboard, Finger Tapping), behavioral (Child Behavior Checklist) and family (Parenting Stress Index and Family Assessment Measure) functioning.
Results: Results indicated no significant differences between diabetic and healthy children on any measure of cognitive or psychosocial functioning. However, analyses within the diabetic sample revealed that those children with a history of hypoglycemia requiring medical intervention (40% of the sample) had more internalizing behavior problems ($p < 0.07$) and family problems ($p < 0.04$). Correlational analyses showed that higher HbA1c was associated with greater parenting stress and family problems, lower cognitive abilities, lower receptive vocabulary, and decreased right-handed finger tapping (ps < 0.04).
Conclusion: These findings indicate that young children with diabetes are generally not different from normal healthy children on measures of cognitive and psychosocial functioning. However, poor glycemic control may be associated with some adverse effects on cognitive development and psychosocial functioning. Interventions to promote optimal glycemic control are needed for this patient population.

P-111

The efficacy of complex treatment including participation in psychological support group (PSG) in adolescents with diabetes mellitus type 1

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Introduction: The maturation process in diabetic adolescent is characterized by insufficient metabolic level. The diabetes requires from young people during development changes maintaining the normoglycemia. The appearance of emotional disorders as a result of this burden inhibits their therapeutic activity.
Aim: Estimation of treatment efficacy of adolescents with DM type 1 who actively participate in program.
Methodology: 30 adolescents in mean age 14.8 ± 1.0 suffering from DM type 1 for 1.1–12 years (mean 4.3 ± 2.9), treated with functional intensive insulinotherapy were subjects of study. The study group participated (1/week) in program homogeneous Psychological Support Group for Adolescents with DM type 1 (7.7 ± 4.8 month). The aim of this program was to help young people recognize and effectively copy with situations provoking unwillingness to realize the therapeutic indications. The estimation of complex treatment efficacy included comparison of initial HbA1c and BMI with the values at the of the study. Statistical analysis was performed using Student-t test ($p < 0.05$).
Results: HbA1c levels decreased significantly in study group (8.7 ± 1.4 vs 7.8 ± 1.3, $p = 0.00048$; girls: HbA1c 8.9 ± 1.5 vs 7.8 ± 1.2, $p = 0.0018$; boys: 8.4 ± 1.4 vs 7.8 ± 1.5, $p = 0.11$). In boys statistically significant difference wasn't confirmed. Initial BMI values were normal and didn't change during the study. The differences in mean BMI values (study group: 20.2 ± 2.1 vs 20.5 ± 2.0; girls: 20.1 ± 2.4 vs 20.4 ± 2.2; boys: 20.4 ± 1.8 vs 20.7 ± 1.8) weren't statistically confirmed ($p > 0.05$).
Conclusion: Connection medical treatment and psychotherapy increases efficacy, efficiency of DM type 1 treatment. The therapy method applying PSG is effective element of general therapy in adolescents with DM type 1.

P-112

Psychosocial adjustment in young people with type 1 diabetes 13 years after diagnosis

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Introduction: Adjustment difficulties in adolescents with type 1 diabetes are thought to be two to three times higher than in the general community. Relationships between adjustment and metabolic control have been reported, although findings are inconsistent. This study aimed to examine the prevalence of adjustment difficulties and the relationship to metabolic control in a subset (n = 70) of a larger cohort of young people with type 1 diabetes who were diagnosed 13 years ago.
Methodology: Participants completed the Young Adult Self-Report Questionnaire or the Youth Self Report Questionnaire as part of a larger battery of neuropsychological tests. HbA1C's since diagnosis were collected and used to categorise participants with either (1) good control, (2) a history of hypoglycemic seizure with no chronic hyperglycemia, (3) chronic hyperglycemic with no history of hypoglycemic seizure or (4) a history of both hypoglycemic seizure and chronic hyperglycemia (Mixed).
Results: Overall, internalising behaviors at diagnosis significantly predicted internalising behaviors 13 years post-diagnosis. Similarly, externalising behaviors at diagnosis predicted externalising behaviors 13 years later. Mean HbA1C since diagnosis positively correlated with attention, delinquent and somatic problems at the 13 year follow-up. There were no differences in the frequency of clinically significant internalising or externalising behaviors between metabolic groups. However, the Mixed group scored significantly higher on the anxious scale ($p < 0.05$) and lower on the

thought problems scale ($p < 0.05$), compared to the Good-control and Hyperglycemia-only groups. Furthermore, the Mixed group scored significantly higher on the attention scale compared to the Hypoglycemia-only group ($p < 0.05$). There was a trend for the Mixed group to score higher than all other groups on the Total Problems scale ($p = 0.07$).
Conclusions: Adjustment difficulties at diagnosis continue over time in young people with type 1 diabetes. Participants with a history of both chronic hyperglycemia and hypoglycemic seizure report higher levels of adjustment difficulties, compared to participants with good control or those with a history of hypoglycemia-only and hyperglycemia only.

P-113
Impact of adiponectin and leptin levels in differential diagnosis of younger-onset non-obese patients with diabetes in Japan

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Introduction: Recently remarkable increase of younger-onset type 2 diabetes has been noticed as diabetic population has become endemic in Japan. Sometimes it is very hard to distinguish younger-onset non-obese type 2 diabetes from type 1 diabetes on initial stage. It has been reported that leptin and adiponectin, adipokines secreted from adipose tissue, are related to patients with type 2 diabetes, however, there are no reports of these adipokines in non-obese type 2 diabetes.
Aim: In the present study we investigate these adipokine levels in younger-onset type 1 diabetes (T1), non-obese (N2) and obese type 2 diabetes (O2), and study whether these are useful for differential diagnosis of diabetes classification.
Methodology: The study involved 91 diabetic patients (M/F: 41/50; age 20 ± 6 years) who registered in our institute within 2 years from the onset. Thirty-seven patients with T1, 35 with N2 and 19 with O2 were enrolled. 'Non-obese' was defined as having no history of obesity and current BMI < 22, and 'obese' was defined with BMI > 25. Serum leptin and adiponectin levels were measured by ELISA with serum taken on the date near registration.
Results: Islet autoantibody positivity was 62% for type 1 diabetes, 0% for type 2 diabetes. There were no difference in blood glucose and HbA1c among these 3 groups. Average fasting CPR levels were 0.6 ng/ml for T1, 1.3 ng/ml for N2 and 2.3 ng/ml for O2, and average BMI were 18.7, 19.0 and 31.2, respectively. There was no difference in CPR between T1 and N2, however, significant difference in BMI between O2 and T1 or N2. Serum leptin in O2 were higher than those in other 2 groups. On the other hand, serum adiponectin levels were 13.7 ± 4.8, 8.7 ± 4.6 and 5.2 ± 5.9 μg/ml, respectively, and there were significant differences among these 3 groups ($p < 0.0001$). Furthermore, significant differences were found in adiponectin/leptin ratio ($p < 0.05$).
Conclusion: It indicates that the measurements of serum adiponectin or adiponectin/leptin ratio are clinically useful for differential diagnosis of diabetes classification in younger-onset patients.

P-114
Serum adiponectin level in obese children and its clinical significance

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Introduction: Adiponectin, a novel adipokine with anti-inflammatory and insulin-sensitizing properties, has been found to have independent negative associations with obesity and hyperinsulinemia/insulin resistance in adults.
Aim: To investigate the levels of plasma adiponectin in obese children and to explore its clinical significance.
Methodology: 52 obese children (16 with IGT and 36 with NGT according to the oral glucose tolerance test) and 41 normal controls were enrolled in the study. Their ages ranged from 7 to 15 years. Serum glucose and lipid profiles were measured by automatic biochemistry analyzer and serum insulin was determined by electrochemiluminescence immunoassay. Serum adiponectin were detected by ELISA technique. Insulin resistance index (HOMA-IR) and body mass index (BMI) were calculated.
Results: Serum level of adiponectin was significantly lower in obese group than that in control group and the lowest in obese group with IGT ($P < 0.01$), while HOMA-IR was significantly higher in obese group than that in control group and the highest in obese group with IGT ($P < 0.01$). Serum adiponectin level in obese group was inversely correlated with TG, LDL-C and FINS ($P < 0.05$).
Conclusion: Serum level of adiponectin in obese children was significantly decreased and was related to lipid metabolic disturbance and insulin resistance. Serum level of adiponectin in obese children with IGT was significantly lower than that in obese children with NGT. It was suggested that oral glucose tolerance test should be taken in obese children with decreased serum levels of adiponectin to screen out obese children with IGT and prevent them to develop to type 2 diabetes.

P-115
Ghrelin, growth hormone and IGF-1 in children with IDDM

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Introduction: Abnormalities of growth hormone axis play a great role in patients with IDDM in: diabetes complications, insulin resistance, fat disorders and dawn phenomenon.
Aim: evaluation of ghrelin and IGF-1 in blood and growth hormone in urine of pre-pubertal children with IDDM and estimate of the influence of different therapeutic modalities.
Methodology: Sixty seven children and 15 age-matched, healthy children were included into the study. All children were pre-pubertal, diagnosed with IDDM for more than two years and without any coexisting diseases. All children were divided into groups according to the type of therapy: 22 were treated with conventional insulin therapy (CIT), 21 received multiple insulin injections (MII) and 24 were treated with continuous subcutaneus insulin infusion (CSII). Blood and urine samples were obtained between 7:30 and 8:30 a.m. from children with normoglycemia (after a night without episodes of hyperglycemia or hypoglycemia). All analyses were made by ELISA commercial kits.
Results: Ghrelin levels were lower in children with IDDM. The lowest levels were in CSII group, higher in MII and the highest in CIT group (higher even than in control). Growth hormone levels in urine were lower in children with IDDM regardless of the kind of therapy. IGF-1 levels were higher in children with IDDM (the highest in MII).
Conclusion: Ghrelin levels in blood and growth hormone levels in urine were lower and IGF-1 higher in IDDM patients. The kind of therapy appears to have an influence on ghrelin and IGF-1 levels but not on growth hormone levels.
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P-116

Relationship between insulin resistance and adiposity markers in children and adolescents with type 1 diabetes mellitus

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Introduction: Changes in life style (more frequent obesity, decreasing physical activity) and increasing incidence of type 1 and type 2 diabetes mellitus cause new interest in insulin resistance in children with diabetes.
Aim: was to estimate the relationship between insulin resistance and adiposity markers in children and adolescents with type 1 diabetes mellitus (T1DM).
Methodology: 132 patients with T1DM (77 male) aged 8.2–20 years (median – 15.4 years) with diabetes duration of 1.6–10.5 years (median – 3.0) and adequate metabolic control (HbA1c < 8.0%) were included into the study. Euglycemic-hyperinsulinemic clamp by DeFronzo was performed to estimate insulin resistance. The height, weight, skinfolds thickness, waist and hip circumferences were measured. The BMI, waist circumference and waist/hip ratio (WHR) were calculated as standard deviation scores (SDS). The multivariable linear regression analysis was conducted for M index as dependent variable and for adiposity markers, body surface, gender and age as independent variables.
Results: In T1DM children and adolescent M index ranged from 2.50 to 14.0 mg/kg/min, median 6.74 ± 0.21 mg/kg/min. In 9 patients obesity (BMI-SDS > 1.9) was observed. The negative correlation was found between M-index and BMI-SDS ($r = –0.29$; $p < 0.001$), waist circumference ($r = –0.39$; $p < 0.001$) and WHR – SDS ($r = –0.33$; $p < 0.001$). In multivariable linear regression analysis the insulin resistance was associated with BMI ($R^2 = 0.24$; $p < 0.001$), waist ($R^2 = 0.30$; $p < 0.001$), WHR ($R^2 = 0.23$; $p < 0.001$), body surface ($R^2 = 0.25$; $p < 0.001$) and skinfolds: triceps ($R^2 = 0.22$; $p < 0.001$), subscapular ($R^2 = 0.26$; $p < 0.001$), abdominal ($R^2 = 0.27$; $p < 0.001$).
Conclusion: In T1DM patients insulin resistance is related to overweight. The waist circumference seems to reveal the strongest correlation with insulin resistance in diabetic children.
Acknowledgement: Supported by Medical University of Lodz – 503-127-3.

P-117

Daily insulin dose adjusted for fat free mass and HbA1c is directly correlated to fat mass

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Introduction: Insulin resistance is more frequent among overweight subjects, however it is not yet shown a relation between insulin resistance and overweight in Type 1 diabetes. A recent paper on this topic (T. Reinehr et al., Pediatric Diabetes, 2005), performed in a very large population, failed to show such a relation.
Aim: To show a relation between insulin dose and fat mass in Type 1 diabetes.
Methodology: 64 Type 1 diabetes children and adolescents (age 15 ± 4 years; 39 males and 25 females) with a disease duration ranging from 0.5 and 15 years, in treatment with a mean insulin dose of 0.93 ± 0.20 U/kg/day and with an HbA1c ranging from 6 to 11.6% (mean ± 1SD 8.3 ± 1.1%) were cross-sectional studied. The Fat Free Mass (FFM) was evaluated by bio-impedance-analysis (BIA) and the fat mass (FM) by skin-folds. For each patient we measured also height, weight, waist and hip circumferences and we calculated BMI, BMI z-score and waist-to-hip ratio.
Results: A significant correlation was present between Insulin doses per Kg of FFM adjusted for HBA1c (I/FFM) and percent of FM (FM percent) ($p < 0.05$; $r = 0.25$). On the contrary we didn't find any correlation between BMI z-score and insulin dose per kg, square meter or adjusted for FFM.
Conclusion: Insulin dosage per Kg of body weight is a poor insulin resistance index unless adjusted for HbA1c. Excess of fat mass in type 1 diabetes mellitus is responsible of insulin resistance.

P-118

What children do all day: the physical activity of 7-year-olds and its impact on adiposity (the EarlyBird diabetes study)

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Introduction: Physical under-activity is perceived to be an important cause of obesity and future diabetes, although such data are mostly derived from self-report.
Aim: We sought to characterize children's habitual daily physical activity (PA) using objective measures, and relate it to adiposity and UK recommendations.
Methodology: MTI accelerometers worn by 217 healthy children, mean age 6.9 ± 0.3 y for seven days. Main outcome measures: three intensities of PA: low (equivalent to walking <1 km/h), medium (1–4 km/h) and high (>4 km/h), BMI and adiposity (percent fat by DEXA).
Results: Three-quarters (B: 8.9 h, G: 9.2 h, $p = 0.04$) of waking time was spent in low intensity PA, but this may be normal and may always have been the case. High intensity PA, despite occupying only 6% of waking time in girls and 8% in boys, contributed to 34% and 39% of total PA respectively. Time spent in low intensity PA correlated inversely with high intensity counts (B: $r = –0.63$, G: $r = –0.49$, both $p < 0.001$) and total PA counts (B: $r = –0.66$, G: $r = –0.52$, both $p < 0.001$). Only 43% boys, and 17% girls, met UK recommendations – 1 h/day of at least 'moderate' intensity PA. This does not necessarily imply under-activity, nor that more opportunity would increase it. Importantly, there were no differences in BMI between those who did and did not meet the guidelines (B: 15.9 v 16.2 kg/m^2, $p = 0.42$ G: 17.1 v 17.1 kg/m^2, $p = 0.99$) and only a small difference in body fat in boys only (B: 13.0 v 15.7%, $p = 0.03$, G: 21.5 v 22.4%, $p = 0.72$).
Conclusion: Time spent in low intensity PA appears to displace time available for higher intensity PA, thereby reducing the total. Nevertheless, while PA is associated with a reduction in adiposity, at least in boys, it is modest. There is an urgent need to base guidelines on evidence.

P-119

Effects of rosiglitazone and metformin on the insulin resistance parameters in patients with pubertal hypothalamic syndrome

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Introduction: The aim of study was to evaluate the effects of rosiglitazone (RGZ) and metformin (MET) plus Hypocaloric Diet (HD) in obese patients (pts) with pubertal hypothalamic syndrome (PHS) and impaired OGTT.
Aim: 49 pts (17.1 ± 1.2 yrs) were allocated in four groups: A received RZG 4 mg tid plus HD (n = 14); B – MET 1000 mg tid plus HD (n = 12); C – RGZ + MET + HD (n = 11); D – only HD (n = 12). The duration of the study was 3 months.
Methodology: We investigated Body Mass Index (BMI), Waist/Hip ratio (W/H), triglyceridaemia (TG), Systolic (SBP), Diastolic Blood

Pressure (DBP). Insulin resistance (IR) state: HOMA. Statitics: ANOVA.
Results: Patients with PHS and impaired OGTT showed the signs of metabolic syndrome X, the amplication of IR were releaves (the increase of BMI, W/H, TG, hyperinsulinemia, HOMA IR index, SBP, DPB, the decrease of β-cell function HOMA (HOMA βCF). Results after treatment: no positive dynamics of OGTT, W/H ratio were observed. RZG lead to the decrease of postprandial TG (2.5 ± 0.03, $p < 0.05$), HOMA-IR ($p < 0.05$), some increase of BMI ($p > 0.05$), improvement of HOMA-βCF (0.24 ± 0.003, $p < 0.05$) and did not influence SBP and DBP. MET lead to the decrease of BMI (27.1 ± 2.6, $p < 0.05$), TG, SBP, DBP ($p < 0.05$), but in a smaller degree, than RZG. RZG plus MET lead to more expressed positive dynamics: BMI made 26.4 ± 3.6 ($p < 0.05$), HOMA IR index ($p < 0.01$), HOMA βCF 0.28 ± 0.004 ($p < 0.01$), postprandial TG – 1.77 ± 0.03 ($p < 0.01$), SBP, DBP ($p < 0.05$). The use of HD only lead to some decrease of BMI ($p < 0.05$).
Conclusion: The combined administration of RZG and MET in patients with PHS is accompanied with more expressed positive dynamics of parameters, which characterize IR.

P-120
The correlations between white blood cell count and metabolic syndrome in adolescents

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Introduction: MS is with high prevalence in well-developed countries. So monitoring of those risk factors known to be part of MS should become part of routine medical care for overweight or obese adolescents. Recent studies showed that the elevated C-reactive protein level and low-grade inflammation were associated with MS. In this study, we measured of WBC count and components of MS in Chinese, both males and females between 14 to 19 years old.
Aim: The correlations between white blood cell count and metabolic syndrome in adolescents.
Methodology: We enrolled 1657 subjects with age 14 to 19 years in 1997. The qualified subjects were separated into young male group (YM) and young female group (YF). To evaluating each of the components of MS, we again divided the subjects in both groups (YM and YF) into 4 quartiles according to WBCC (WBCC1 to WBCC4, from the lowest to highest WBCC). We also checked each variable of MS (BMI, SBP, DBP, FPG, HDLC and TG). Statistic analysis was performed using SPSS version 13.0 statistical package for Windows (SPSS, Chicago, IL).
Results: That subjects with higher BMI will have higher WBCC in YM and YF. Correlations after the adjustment of the BMI and age still showed the same finding. We also found in YM, the BMI and TG were significantly higher and HDLC lower in the WBCC4 group. In the meanwhile, only BMI were significantly higher in the WBCC4 in YF.
Conclusion: In conclusion, in subjects with normal WBCC and no history of significant medical diseases, BMI is significantly related to the levels of WBCC and are the earliest components of MS to be noted in adolescents. And the overweight may be associated with a state of chronic low-grade inflammation in children.

P-121
Fasting intact proinsulin (HPI) and IGFBP-1 as indices for development to type 2 diabetes mellitus in children and adolescents

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Introduction: There have been several parameters or indices such as HOMA-R, HOMA-B etc regarding insulin secretion and insulin resistance to evaluate the progress to type 2 diabetes mellitus. T2DM.
Aim: We aim to examine fasting intact proinsulin (HPI) and IGFBP-1 whether these are able to distinguish T2DM from non-obese control and simple obesity, in comparison with other indices.
Methodology: Four groups of subjects were tested for fasting blood glucose, insulin (IRI), HPI and IGFBP-1: twenty-six with non-obese non-diabetes (13.3 + 1.9 years old), 43 with simple obesity (13.3 + 1.8 years old), 29 with T2DM of HbA1c < 8% (15.2 + 3.0 years old) and 25 with T2DM of HbA1c ≤ 8% (15.2 + 1.8 years old). We compared these parameters and the relevant indices regarding insulin secretion and insulin resistance between four groups.
Results: HOMA-R was significantly higher in obesity than in non-obesity, while there was not a significant difference between two diabetes groups. Regarding HOMA-B, obesity was significantly higher than other three groups. Fating glucose to insulin ratio, FGIR, was significantly higher in T2DM of HbA1c ≤ 8% than T2DM of HbA1c < 8% and obesity, but not higher than non-obese group. As to QUICKI, non-obese group was significantly higher than other three groups. While HPI itself was not significantly different between obesity and two groups of T2DM, HPI/IRI differentiated these three groups more significantly. However a problem was left in distinction between non-obesity and T2DM of HbA1c < 8%. IGFBP-1 in non-obese group was significantly higher than those in T2DM of HbA1c > 8%, T2DM of HbA1c < 8% and obesity. However IGFBP-1 in T2DM of HbA1c ≤ 8% was, to a lesser degree, higher than obesity.
Conclusion: We suggest that HPI, especially expressed by HPI/IRI, may become a promising index to tell the progress to T2DM. But there was difficulty in setting reference value between non-obese controls and other morbid states. Again IGFBP-1 increase may be so far useful to evaluate only longitudinal diabetic deterioration.

P-122
Type 2 diabetes mellitus in obese children

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Introduction: Obesity in childhood is increasing in prevalence and is of public health concern. It causes serious metabolic consequences, of which type 2 diabetes is significant.
Aim: To determine the prevalence of type 2 diabetes in obese children in an urban center in Malaysia.
Methodology: Obese children younger than 18 years attending the growth clinic from 2000–2004 had their demographic profile, anthropometric measurements taken and were physically examined. All had fasting blood taken for glucose (FBG) and lipids. OGTT was performed if FBG was normal. Obesity was defined as BMI >95th centile for age and sex, diabetes as RBG > 11.1 mmol/L or FBG >7.0 mmol/L on 2 occasions or 2 hour OGGT glucose >11.1 mmol/L. Impaired fasting glucose was defined as FBG 5.6–7.0 mmol/L, impaired OGTT as 2 hr BG of 7.0–11.1 mmol/L, hypertriglyceridaemia as fasting triglyceride >2.0 mmol/L and hypercholesterolaemia as fasting cholesterol >5.5 mmol/L.
Results: Out of 75 obese children, only 55 (73%) were evaluated, rest had missing records. Diabetes was present in 21.8% (n = 12) patients, 50% diagnosed by OGGT. 7.2% (n = 4) had impaired glucose tolerance. Their mean age was 10.4 years (range 7.9–13.0),

mean BMI 28.0 ± 4.8 kg/m^2 (range 21.0–40.8), males to female ratio 1.3 : 1.0. Malays were more affected followed by Indians and Chinese. Acanthosis nigricans was present in 25 (45%) obese patients, 12 were already diabetic, 4 with impaired OGTT. A third of obese patients had family history of diabetes, another third had hyperlipidaemia: hypertriglyceridaemia in 18.7%, hypercholesterolaemia in 31%.

Conclusion: Acanthosis nigricans were positive in 45% obese children, twenty one percent of whom were already diabetic while another 7.2% had impaired OGTT. Half of the diabetic patients were asymptomatic. Hyperlipaedaemia is present in a third of obese children. Routine screening for diabetes and hyperlipidaemia is indicated in obese children so that specific treatment can be given to prevent or delay diabetes complications.

P-123

Type 2 diabetes management program for youth: assessment of diabetes knowledge and quality of life

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Introduction: Type 2 diabetes (T2DM) has historically been considered a disease of adults, but is now increasingly common in childhood. Despite this increase, programs that specifically address the unique needs of this group are lacking.

Methodology: This was a prospective study to evaluate (i) diabetes knowledge (DK), (ii) QOL and (iii) active and sedentary behaviors in youth with T2DM, to facilitate design of a T2DM-specific pediatric diabetes education program. Youth with T2DM (n = 26) were compared to youth with Type 1 diabetes (T1DM; n = 64) and their parents, attending the same diabetes outpatient clinic. Comparison between T1DM and T2DM were performed using t-tests, and repeated measures ANOVA to model correlation of parent and child scores with T1DM and T2DM.

Results: There was no difference in SES status (Hollingshead Index) Youth with T2DM exercised less frequently (mean 3.3 ± 3 vs. 5.6 ± 5 hrs/wk, p = 0.04) and were more sedentary (39.0 ± 18 vs. 29.3 ± 17 hrs/week; p = 0.02) than those with T1DM. DK was significantly lower in both parents and youth with T2DM (p = 0.04). QOL was not different between youth with T1DM and T2DM. There was no effect of A1c on DK or QOL.

Conclusion: Youth with T2DM are heavier, more sedentary, and less knowledgeable about diabetes, but did not demonstrate lower perceived QOL.

Variable (mean ± SD)	T2DM (n = 26)	T1DM (n = 64)
Age (years)	15.1 ± 2.2*	14.0 ± 2.0
Duration DM (years)	2.6 ± 1.9*	5.4 ± 3.9
A1c (percent)	7.7 ± 2.4	8.2 ± 1.2
BMI (kg/m^2)	32.3 ± 8.1 *	23.1 ± 4.9

*p < 0.05 compared to T1DM

P-124

Low glycaemic index (GI) foods improve glucose control in children with type 1 diabetes

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Introduction: Glycaemic index (GI) is a way of ranking carbohydrate foods on the basis of their postprandial glycaemic response, low-GI foods are characterized by a slow response. Low-GI foods could be important for diabetic patients, since low-GI meals produce less fluctuations in blood sugar.

Aim: To evaluate if it is possible to improve metabolic control in children with IDDM, when the quality of carbohydrates is modified by introducing low-GI foods.

Methodology: We studied 17 prepubertal children with IDDM. They had a moderate metabolic control reflected by glycosylated hemoglobulin (HbA1c) levels between 6.5–9.0%. It was a blind crossover study, each study period was 6 weeks long and in between a three-week washout period. We modified the test diet from normal diabetes diet (reference diet) by changing type of bread, cereals, rice and excluded potatoes. Both diets had guidance for the main carbohydrate source, the lunch meal was not regulated at all. A diet record was made prior to study start, and once during each study period. Blood sugar was checked by regular self-testing. We checked HbA1c, triglycerides and total cholesterol at the beginning and the end of each study period.

Results: For the whole population, the change in HbA1c during the reference diet period was –0.06 ± 0.4% (mean ± SD). During test diet period, the change in HbA1c was –0.34 ± 0.4% (mean ± SD), (p = 0.039). There were no change in total energy intake, but a significant larger intake of fibers during test period. Regarding serum lipids, there were no significant changes.

Conclusion: The concept of low-GI foods is relevant for children with IDDM. It could be a useful tool to optimize slightly elevated HbA1c and it should be considered when giving diet counsel.

P-125

Dietary habits, insulin adjustments and glycaemic control

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Introduction: The DCCT found that those who adhered to a prescribed meal plan, adjusted insulin/food in response to hyperglycemia and intensively monitored blood glucose (BG) achieved significantly lower HbA1c levels. Over-treating hypoglycemia and consuming extra snacks were associated with higher HbA1c levels. These effects were observed in a pediatric diabetic population.

Methodology: Children and parents completed an observational anonymous questionnaire in the out-patient clinic. Children of diabetes duration less than 2 yrs were excluded.

Results: 72 questionnaires were analyzed. Mean HbA1c 8.7%. We compared 29 children (mean age 13 years) mean HbA1c < 8% with 17 children (mean age 13 years) mean HbA1c > 10%.

	HbA1c < 8%	HbA1c > 10%
Eat Breakfast	87% often or always	71% often or always
Eat Evening Meal	86% always	65% always
Eat During Night	70% never or rarely	53% never or rarely
Portions of Vegetables	79% 2 or more a day	35% 2 or more a day
Portions of Fruit	72% 2 or more a day	53% 2 or more a day
Packets of Crisps	33% 2 or more a day	41% 2 or more a day
Take rapid acting insulin for hyperglycemia	56% often or always	65% often or always
Number daily BG tests	34% 4 or more times	0% test 4 or more times

Conclusions: Children and adolescents with HbA1c < 8 appear to follow a more desirable healthier meal plan and do more BG tests each day. They are also more likely to eat 2 or more portions of fruit and 2 or more portions of vegetables a day. The consumption of high fat potato crisps is worryingly high. Rapid acting insulin was used by 60% of the study group for hyperglycemia.

P-126

Food habits, energy and nutrient intake in adolescents with type 1 diabetes

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Introduction: Food recommendations for children and adolescents with type 1 diabetes have changed over the past decades. The impor-

tance of adequate food intake in the treatment of type 1 diabetes is well established, but the knowledge of food habits among adolescents with diabetes is poor.
Aim: To describe the food habits and dietary intake of adolescents with type 1 diabetes in comparison with healthy control subjects and current recommendations. Associations between dietary intake, metabolic control, body weight, and socio-economic conditions are also investigated.
Methodology: A validated food frequency questionnaire was filled in by 174 adolescents with type 1 diabetes and 160 control subjects. Thirty eight randomly chosen patients also filled in a 4-day food record.
Results: Adolescents with type 1 diabetes eat more regularly and eat more often sour milk/yoghurt, fruit, potatoes and roots, meat, sausage, vegetables, and porridge than healthy controls. Patients choose sugar free sweets, course rye bread, and diary products with less fat to a higher extent than control subjects. The intake of protein is slightly above and the intake of carbohydrates is slightly below current recommendations, in both girls and boys with diabetes. Adolescents with poor metabolic control have a higher intake of fat and lower intake of carbohydrates, and eat less often vegetables, fruit, and fish, than adolescents with better metabolic control. Patients whose mother only has a nine-year school degree consume more fat and less carbohydrates than patients whose mother has a university degree. Adolescents with type 1 diabetes are heavier than control subjects.
Conclusion: The dietary intake of adolescents with type 1 diabetes is in fairly good accordance with current recommendations and is more wholesome than that of control subjects. The possible causative relationship between dietary intake and metabolic control needs to be investigated in studies with a prospective design.

P-127
Illustration of the effect of physical exercise – a possible way to improve HbA1c

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Introduction: In controlled studies of the effects of physical exercise on diabetes, HbA1c is not shown to improve while the physical exercise is healthy in other perspectives.
Aim: To evaluate if systematized registration of SMBG, CGMS and food intake, performed without clinical feedback, could result in an improved HbA1c.
Methodology: One adolescent (18 years), with 4 years duration of type 1 diabetes, volunteered to participate in this case study. SMBG and food intake were registered in three exercise conditions of each one week duration. Each condition represented inactivity (i), moderate (m.a) and intensive activity (i.a). CGMS were used during three days in each condition. The adolescent looked at the results but received no feedback from the diabetes clinic. HbA1c was controlled before and after the case study. The amount of insulin and carbohydrates was recorded during the study.
Results: During three years prior to this case study the patient had an HbA1c between 7.0 and 8.2. Prior to this study the HbA1c was 7.0, immediately following the study it was 6.7 and one month later 6.2. The number of hypoglycemic episodes with awareness rose as the activity was increased – on average 0.33/day (i), 1.5 (m.a) and 1.8 (i.a). Duration of values between 4 and 10 mmol/L was 78.8% (i), 59.7% (m.a) and 48.7% (i.a). The duration of hypoglycemia with values below 4 mmol/L increased with raised intensity of exercise; 14.7% (i), 15.7% (m.a) and 30.7% (i.a). The duration of hyperglycemia with values above 10 mmol/L also increased during exercise; 6.7% (i), 24.7% (m.a) and 20.7% (i.a).
Conclusion: In this case study, with a highly motivated volunteer, non-clinical feedback for glucose values, as demonstrated by CGMS, can be shown to have a positive effect on glycaemic control. It is hypothesised that this effect can be replicated in larger groups and increased with clinical support.

P-128
Impaired insulin resistance indexes in children and adolescents after bone marrow transplantation

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Introduction: Few data are reported about the late effects of bone marrow transplantation in childhood on glucose metabolism.
Aim: To assess the prevalence of both type 1 and type 2 diabetes markers in children and adolescents with acute or chronic leukemia or non-malignant diseases who underwent total body irradiation or thoraco-abdominal irradiation before autologous or allogenic BMT.
Methodology: In 21 patients (14 males and 7 females, aged 6–17.5 years) we detected autoantibodies against beta-cells (ICA, IAA) and assessed the insulin resistance and secretion indexes like homeostasis model assessment of insulin resistance index (HOMA-IR) and HOMA of percent beta-cell function (HOMA-beta percent). HOMA-IR was measured as fasting plasma insulin in mU/l × fasting plasma glucose (FPG) in mmol/l divided for 22.5; HOMA-beta percent was measured as (20 × fasting insulin in mU/l)/(fasting glucose in mmol/l – 3.5). As controls, 98 healthy age-and sex matched subjects were considered.
Results: All patients showed normal levels of FPG and HbA1c. Autoantibodies against beta-cells were absent in all cases. HOMA-IR was significantly higher in patients than in controls [2.07 (1.5–3.33) vs 1.41 (0.89–2.24), p = 0.0068; (median (1st–3rd quartile)]. HOMA-beta cell values were higher in patients than in controls {206.64 (133.69–556.51) vs 123.05 (72.17–197.89), p = 0.0008 [median (1st–3rd quartile)]}.
Conclusion: Elevated insulin resistance and secretion indexes have been found in our patients who underwent BMT in childhood, and could be due to direct or indirect action of irradiation. All subjects, in particular children, exposed to irradiation should be regularly investigated for diabetes mellitus, through detection not only of autoantibodies against beta-cells but also of insulin resistance indexes, in order to assess primary prevention strategies. Recently the incidence of type 2 diabetes, whose clinical onset is preceded by insulin resistance, is growing up worldwide also in adolescence.

P-129
Volumetric spine BMD impairment in diabetic children and adolescents is not related to change in calcium homeostasis

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Background: We recently demonstrated that children with type 1 diabetes show a slight negative pattern of spine mineralization, independent on metabolic control and microvascular complications. In the present study we look for relations between bone accretion and biochemical factors involved in calcium homeostasis.
Objective: 1. to confirm the decrease in L2L4BMDvol in type 1 diabetic patients; 2. to establish correlations, if any, with duration of disease, metabolic control, age, gender 3. to evaluate whether the decrease in spine BMD in diabetic is due to impairment in calcium homeostasis.

Research design and methods: We performed a longitudinal study on 38 diabetic children and adolescents. L2-L4 lumbar BMD was assessed three times at one year interval by DXA (lunar DPX) and volumetric bone density (VBD) was calculated using the Kroger formula. L2-L4VBD was adjusted for confounding factors such as age, gender, BMI, height, weight, and pubertal stage. At the third evaluation ALP, 25(OH) vitamin D, PTH, calcium, magnesium and phosphorus were measured in the blood.
Results: The patients were studied respectively at the first, second and third times at a duration of the disease of 62 ± 45, 74 ± 44 and 91 ± 45 months. We confirmed a statistically significant reduction of L2-L4VBD at the third evaluation compared to the first and the second ($t = 3.4$, $p < 0.002$; $t = 3.2$; $p < 0.01$). We found a significant inverse correlation between L2-L4VBD and insulin need only at the third evaluation ($R = 0.45$; $p < 0.01$). We didn't find any correlation between L2-L4VBD variation and the factors involved on calcium and phosphorus homeostasis.
Conclusions: Our study confirms a negative pattern on spine mineralization in young patients with T1DM which is not affected by the metabolic control and/or impairment of calcium homeostasis. The inverse correlation with insulin need suggest a possible direct role of insulin deficiency on bone accretion.

P-130

Idiopathic hypoglycemia in infancy: insulin secretion after long-term treatment with diazoxide

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Introduction: Idiopathic hypoglycemia of infancy (IHI) is required immediate treatment to avoid the devastating sequelae of brain damage. The diazoxide is a first choice of treatment. Infants properly control with diazoxide (diazoxide sensitive) require for long-term treatment.
Aim: We evaluated insulin secretion before, during and after discontinuation of treatment.
Methodology: Two patients with IHI are subjects of our study. Case 1, N.M. was diagnosed as IRI at three months. Diazoxide was started at seven months. Case 2 (K.J.) was diagnosed as IHI at 5 months and was started immediately. Diazoxide was discontinued at the age of 18 and 12 years in case 1 and 2 respectively. OGTT were performed to determine blood glucose, insulin (IRI) before, during and after treatment.
Results: Blood glucose and IRI level at diagnosis were 25, 32 mg/dl and 15.3, 11 µU/ml respectively. IRI/BG was 0.34 0.61 respectively and was elevated than those of normal control (0.19 ± 0.04). Blood glucose was elevated in both cases and IRI/BG ratio was decreased. Blood glucose, IRI and IRI/BG level remained within normal range after discontinued of diazoxide treatment in both cases.
Conclusion: We tried to discontinue at the age of 6 years in both cases, however, hypoglycemia reoccurred and have to continue diazoxide. We could finally discontinued at the age of 18 and 12 years respectively. dazoxide is effective in case of diazoxide sensitive hypoglycemia in infancy and have to continue until development of puberty.

P-131

New technology advances and its impact on quality of diabetes treatment in children

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Objective: To evaluate the hypothesis whether alternative methods of treatment of type 1 diabetes with new technology advances like insulin pumps have an influence on metabolic control in children with type 1 diabetes.
Materials and methods: We have retrospectively analyzed registered at our outpatient clinic during years 1999–2004 data of our patients aged 0–18 years with type 1 diabetes. All patients were treated with human and/or analogue insulin: Lispro, Aspart or Lantus. Mann-Whitney test and ANOVA test were used for statistical analyses.
Results: We observed statistically significant decrease in the mean value of all registered HbA1c results during consecutive years from 8.83%, SD 1.24 (year 1999; n = 314; CSII–0%) to 8.08%, SD 1.4 (year 2004, n = 737; CSII 53%). We have analyzed two groups of patients: the first group was treated continuously from 2000 with insulin pumps and the second group was treated with MDI method. Among patients treated with CSII method the baseline HbA1c in 2000 was comparable to the value in patients treated with MDI method: 8.72%, SD 1.7, n = 30 vs 8.76%, SD 1.37, n = 284 respectively. In 2004 there was a significant decrease in HbA1c value in pump treated patients: 7.66%, SD 1.15, n = 393 vs 8.59%, SD 1.51%, n = 344 respectively, ($p = 0.0001$). Patients treated with insulin pumps differ in their HbAa1c value from patients treated with other methods ($p = 0.0003$). HbA1c level decreases with time independently from the method of treatment ($p = 0.011$) and we have observed the same tendency in both groups. There were no differences in BMI values between the both groups and the changes observed during years 2000–2004 in BMI values were comparable between both groups ($p = 0.69$). Insulin requirement during years 2000–2003 was comparable in both groups with the exception of 2004 where we observed a significant decrease in insulin requirement in CSII group: 0.91 U/kg/d, SD 0.15 vs 0.97 U/kg/d SD 0.16.
Conclusions: During last five years introduction of alternative method of treatment with CSII significantly improved metabolic in children with type 1 diabetes.